UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-39247

IMARA INC.

(Exact name of Registrant as specified in its charter)

Delaware	**81-1523849**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
116 Huntington Avenue, 6th Floor	
Boston, Massachusetts	**02116**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 206-2020

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	IMRA	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market on June 30, 2020 was $190,476,799.

The number of shares of Registrant's Common Stock outstanding as of March 1, 2021 was 17,575,248.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the impact of the ongoing COVID-19 pandemic and our response to it;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including our ongoing open label extension clinical trial of IMR-687 in sickle cell disease, or SCD, and our ongoing Phase 2b clinical trials of IMR-687 in SCD and ß-thalassemia and our potential clinical development of IMR-687 in heart failure with preserved ejection fraction;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and need for additional financing;
- our plans to develop and, if approved, subsequently commercialize IMR-687 and any other product candidates, including in combination with other drugs and therapies;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for IMR-687 and any other product candidates we may identify and pursue;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents and investments;
- the potential advantages or differentiating features of IMR-687 and any other product candidates we may identify and pursue;
- the rate and degree of market acceptance and clinical utility of IMR-687 and any other product candidates we may identify and pursue;
- our estimates regarding the potential market opportunity for IMR-687 and any other product candidates we may identify and pursue;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for IMR-687 and any other product candidates we may identify and pursue;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position and expectations regarding developments and projections relating to our competitors and any competing therapies that are or become available;
- our ability to maintain and establish collaborations or obtain additional funding; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this Annual Report on Form 10-K involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

RISK FACTOR SUMMARY

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in Part I, Item 1A. “Risk Factors” of this Annual Report on Form 10-K. Our principal risks include the following:

- We have incurred significant losses since our inception, and we expect to incur losses over the next several years.
- We are early in our development efforts and heavily dependent on the success of our sole product candidate, IMR-687. If we are unable to successfully complete clinical development, obtain regulatory approval for, and commercialize IMR-687, or experience delays in doing so, our business will be materially harmed.
- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic as may the operations of our suppliers and manufacturers and other third-party service providers.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.
- Because we are developing IMR-687 using new endpoints and methodologies, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- If we fail to comply with our obligations under our existing license agreement with H. Lundbeck A/S, or under any future intellectual property licenses, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.
- If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.
- Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

PART I

Item 1. Business.

We are a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin, known as hemoglobinopathies. Our pipeline is built on the differentiated therapeutic potential of our initial product candidate, IMR-687, which is an oral, once-a-day, potentially disease-modifying treatment for sickle cell disease, or SCD, and β-thalassemia. IMR-687 is a highly selective, potent small molecule inhibitor of phosphodiesterase-9, or PDE9, that has a multimodal mechanism of action that acts primarily on red blood cells, or RBCs, and has the potential to act on white blood cells, or WBCs, adhesion mediators and other cell types that are implicated in these disorders. We recently completed a Phase 2a clinical trial of IMR-687 in adult patients with SCD and are currently conducting an open label extension, or OLE, clinical trial, which allows patients from the Phase 2a clinical trial to continue into a long-term four-year trial to test safety and measure tolerability of IMR-687. In the second quarter of 2020, we initiated a Phase 2b clinical trial for the treatment of patients with SCD and a Phase 2b clinical trial for the treatment of patients with β-thalassemia. We are currently enrolling patients in each Phase 2b clinical trial and expect to report interim data from each of these trials in the second half of 2021. We continue to evaluate the impact of the COVID-19 pandemic on these Phase 2b clinical trials, and therefore, our estimated timelines for these clinical trials could be delayed. Our goal is to leverage IMR-687's differentiated mechanism of action, its ease of administration and stable drug properties to potentially serve a broad range of patients suffering from hemoglobinopathies around the world, including those in underserved regions. In addition, we recently completed preclinical research of IMR-687 in heart failure with preserved ejection fraction, or HFpEF, and are developing a Phase 2 protocol to support potential future clinical development of IMR-687 in this indication.

Hemoglobinopathies are a diverse range of rare inherited genetic disorders in which there is abnormal production or absence of hemoglobin, the iron-containing protein in RBCs responsible for transporting oxygen in the blood. Hemoglobinopathies can be broadly categorized into two groups. The first group of hemoglobinopathies, which includes SCD, results from structural abnormalities in hemoglobin that cause RBCs to become inflexible and elongated, ultimately blocking blood flow to organs, which can lead to vaso-occlusive crises, or VOCs. SCD is characterized by debilitating pain, progressive multi-organ damage and early death. The second group of hemoglobinopathies, which includes β-thalassemia, results from decreased or absent production of hemoglobin, thereby producing smaller, paler RBCs that do not deliver adequate oxygen to vital tissues. β-thalassemia is often grouped into two subsets: patients who are non-transfusion dependent, or NTDT, or patients who are transfusion dependent, or TDT. If left untreated, β-thalassemia causes severe anemia, splenomegaly, skeletal abnormalities, organ failure and early death. Both groups of hemoglobinopathies share similar pathophysiology and have limited treatment options, which results in a significant unmet medical need for patients. The global prevalence of SCD and β-thalassemia are estimated to be approximately 4.4 million and 288,000 patients, respectively. SCD and β-thalassemia are both designated as rare diseases in the United States and the European Union. For SCD, prevalence is estimated to be approximately 100,000 patients in the United States and 134,000 patients in the European Union. For β-thalassemia, total combined prevalence in the United States and the European Union is estimated to be approximately 19,000 patients.

Our product candidate, IMR-687, is a highly selective and potent small molecule inhibitor of PDE9. PDE9 selectively degrades cyclic guanosine monophosphate, or cyclic GMP, an active signaling molecule that plays an important role in vascular biology. Lower levels of cyclic GMP are found in patients with SCD and β-thalassemia and are associated with reduced blood flow, increased inflammation, greater cell adhesion and reduced nitric oxide mediated vasodilation. Blocking PDE9 acts to increase cyclic GMP levels, which is associated with reactivation of fetal hemoglobin, or HbF, a natural hemoglobin produced during fetal development. Increased levels of HbF in RBCs have been demonstrated to improve symptomology and substantially lower disease burden in both patients with SCD and patients with β-thalassemia. Increasing cyclic GMP is associated with lower WBC activation and reduced adhesion across various cell types, both of which also contribute to SCD. Finally, activation of the nitric oxide-cyclic GMP pathway has been shown to induce red cell maturation and production, which are particularly relevant in treating β-thalassemia. We believe IMR-687 has several differentiating features that make it an optimal therapeutic for SCD and β-thalassemia, as supported by our preclinical data:

- **Highly Potent PDE9 Inhibitor**: IMR-687 is a highly potent PDE9 inhibitor, as measured by induction of cyclic GMP across escalating doses. IMR-687 has been designed to rapidly increase cyclic GMP, which translates to HbF induction and potentially reduced WBC adhesion.
- **Differentiated Selectivity and Tolerability Profile**: IMR-687 is highly specific to PDE9 and not selective for other phosphodiesterase family members. Toxicology studies of IMR-687, including fertility and juvenile studies, support its potential benefit as a long-term therapy in adults and children. We believe this selectivity will allow us to optimize dose while minimizing off-target effects.

- **Minimal Brain Penetration**: IMR-687 was observed to have minimal brain penetration in preclinical *in vivo* models relative to other PDE9 inhibitors that have been studied. We believe this will reduce the potential impact of PDE9 inhibition on central nervous system development and function.
- **Drug Product Stability**: IMR-687 has been shown to be stable at high temperatures and in humid conditions, potentially enabling worldwide access, including in underserved regions where SCD and β-thalassemia are endemic.

Managing hemoglobinopathies and their various clinical manifestations is complex and patients have had limited treatment options. In November 2019, the U.S. Food and Drug Administration, or FDA, approved Oxbryta™ (voxelotor) and Adakveo® (crizanlizumab) for the treatment of SCD, which are important milestones for patients with SCD as previously approved therapies for SCD all have significant limitations, including safety concerns, complex dosing regimens, variable response rates and potential adverse effects from long term use. We believe that IMR-687's differentiated mechanism of action that seeks to increase HbF in patients with SCD, and the association between increases in HbF and reductions in disease risk, have the potential to provide IMR-687, if approved, with competitive advantages over Oxbryta, where the correlation between increases in hemoglobin and disease risk is being tested in a post-approval confirmatory trial, and Adakveo, which is administered intravenously and does not target RBC sickling.

There are no currently approved oral therapies for β-thalassemia; however, in November 2019, the FDA approved REBLOZYL™ (luspatercept-aamt), which is dosed subcutaneously, for the treatment of anemia in adult patients with β-thalassemia who require regular RBC transfusions. Blood transfusions are used to treat both SCD and β-thalassemia, but are suboptimal due to limited patient access and potential serious complications that include iron overload, adverse immune response and transmission of transfusion-associated infections. Allogeneic hematopoietic stem cell transplant, or HSCT, is a potentially curative treatment for both disorders, but is rarely used due to the difficulty in finding a matched donor and an approximately 5% mortality rate. More recent approaches to treating both disorders are emerging, such as gene therapy and gene editing, with promising early clinical data being observed in each. These approaches, however, are complex, costly, difficult to administer and potentially only suitable for a limited subset of patients.

Based on promising preclinical data and data from a Phase 1 clinical trial of IMR-687 in healthy volunteers, in 2018 we initiated our Phase 2a randomized, double-blinded, placebo-controlled clinical trial of IMR-687 in adult patients with SCD. The goals of this trial were to evaluate the safety, tolerability, pharmacokinetics, or PK, exploratory pharmacodynamics, or PD, and clinical outcomes of IMR-687 administered once daily for 16 or 24 weeks in two populations of patients with SCD: one on monotherapy IMR-687 and one on background hydroxyurea, or HU, in combination with IMR-687 to test drug-drug interaction.

In January 2021, we reported final results from the Phase 2a clinical trial. The results showed a lower rate of vaso-occlusive crises/sickle cell-related pain crises, or VOCs/SCPCs, as part of the safety analysis, and VOC-related hospitalizations in specified monotherapy IMR-687 treated patients, as compared to placebo. Changes in HbF and F-cells varied across patient populations in the clinical trial. The results further showed IMR-687 was well tolerated as a monotherapy and in combination with HU.

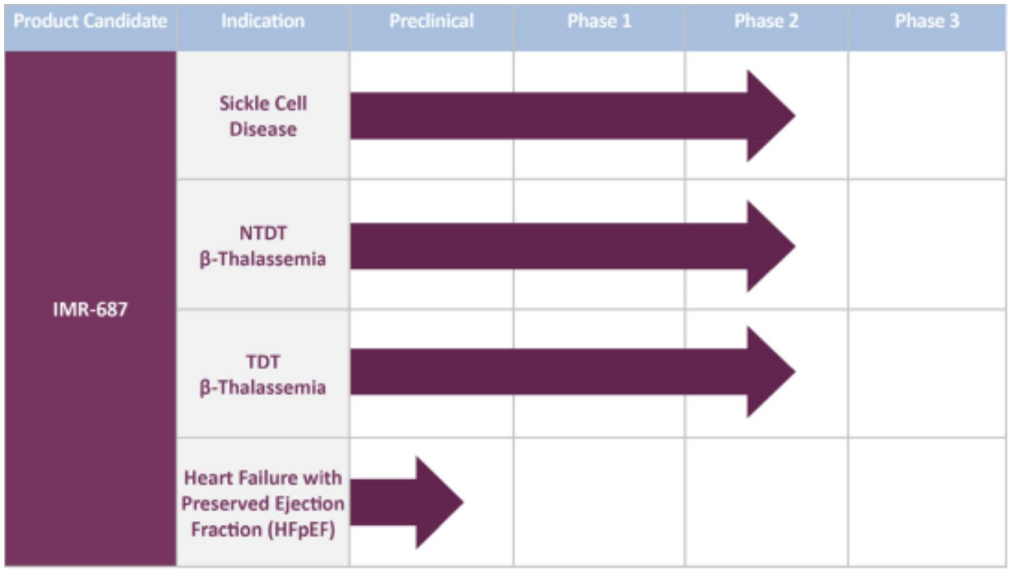
We are also conducting an OLE clinical trial, which allows patients from the Phase 2a trial to continue into a long-term, four-year trial to evaluate safety and tolerability of IMR-687. A review of approximately 12 patients with evaluable PD biomarker data for at least four months of treatment on the OLE clinical trial as of December 31, 2020, demonstrated increases in both HbF and F-cells and minimal changes in total hemoglobin.

In the second quarter of 2020, we initiated a Phase 2b clinical trial of IMR-687 in adult patients with SCD and a Phase 2b clinical trial of IMR-687 in adult patients with ß-thalassemia. We are currently enrolling patients in each trial and expect to report interim data from each of these trials in the second half of 2021. Based on the supportive safety and PK data from the Phase 2a interim analyses, we designed the Phase 2b clinical trials to evaluate higher doses, longer treatment periods, and additional clinical endpoints as compared to the Phase 2a clinical trial.

In addition to our clinical programs with IMR-687 in patients with SCD and β-thalassemia, in the second quarter of 2020, we commenced preclinical development of IMR-687 in HFpEF. Published literature suggests that the inhibition of PDE9, and resulting increases in cyclic GMP through natriuretic peptide modulation, can serve as an attractive target for the prevention and treatment of vascular disease, including HFpEF. An exploratory analysis co-led by Vanderbilt University Medical Center, or VUMC, on data from the second interim analysis from our Phase 2a clinical trial of IMR-687 demonstrated the potential of IMR-687 to reduce N-terminal pro-B-type natriuretic peptide, or NT-proBNP, a well-established biomarker of cardiovascular risk in patients with SCD. In April 2020, we entered into an agreement with the Necker Institute of Paris, France to conduct preclinical studies with IMR-687 in HFpEF. The preclinical data from three established mouse models for HFpEF suggest potential benefits of IMR-687 across several relevant cardiac biomarkers. We are collaborating with VUMC and have engaged additional key opinion leaders in heart failure, with the aim of developing a Phase 2 protocol to support potential future clinical development of IMR-687 in this indication.

Our Pipeline

We are advancing a pipeline of therapeutic programs to address diseases with significant unmet medical need. The following chart summarizes key information about our programs:



Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the development and commercialization of novel therapies for the treatment of hemoglobinopathies. To achieve this, we are focused on the following key strategies:

- ***Rapidly advance IMR-687 through clinical development for the treatment of SCD.*** There remains a significant need to develop additional differentiated disease-modifying, oral therapies to treat SCD. We recently completed a Phase 2a clinical trial of IMR-687 in adult patients with SCD and are conducting a Phase 2b clinical trial of IMR-687 for SCD. We currently expect to report interim data from the Phase 2b clinical trial in the second half of 2021. In addition, we intend to expand clinical development of IMR-687 by initiating a pediatric program in the first half of 2021.
- ***Expand clinical development of IMR-687 for the treatment of ß-thalassemia.*** Based on the similar pathophysiology and symptomology shared between SCD and β-thalassemia, we believe there is a compelling rationale to expand clinical development of IMR-687 into β-thalassemia. Various preclinical studies, as well as favorable safety data from our Phase 1 and Phase 2a clinical trials, further support the development of IMR-687 in this indication. We are conducting a Phase 2b clinical trial in adult patients with β-thalassemia. We currently expect to report interim data from this trial in the second half of 2021.
- ***Continue efforts to expand our pipeline.*** We believe that our extensive expertise and experience with IMR-687 will allow us to expand development of IMR-687 into additional hemoglobinopathies and diseases where PDE9

is overexpressed, including HFpEF. We recently completed preclinical research of IMR-687 in HFpEF and are developing a Phase 2 protocol to support potential future clinical development of IMR-687 in this indication. We are also exploring business development opportunities to identify novel product candidates.

- ***Maximize the commercial opportunity of our product portfolio.*** We have retained worldwide development and commercial rights to IMR-687 and are pursuing a clinical and regulatory development strategy for IMR-687 in the United States, Europe and certain other international regions. As we advance IMR-687 through clinical development, we intend to establish a focused marketing and sales infrastructure in order to maximize the commercial opportunity in the United States and Europe, and potentially other international regions.
- ***Strategically evaluate licensing and collaboration opportunities to maximize value.*** We may selectively evaluate the merits of entering into licensing and collaboration agreements for regions in which we are unlikely to pursue independent development and commercialization, or where a collaborator could provide specialized expertise and capabilities to create additional value.

Sickle Cell Disease Overview

SCD is the most common type of inherited hemoglobinopathy. SCD is characterized by debilitating pain, progressive multi-organ damage and early death. Beginning early in life, patients suffer from blocked blood flow to tissues, known as vaso-occlusion, destruction of RBCs, known as hemolysis, and inadequate oxygen delivery, or hypoxia. The most common complication of SCD is pain, often a consequence of VOCs. A VOC occurs when circulation is obstructed by sickled RBCs, causing tissue damage to the organ and resultant pain. The outcomes of these events begin presenting early in childhood and quickly lead to heart and lung complications, renal disfunction, prolonged refractory penile erection (known as priapism), spleen enlargement and failure, stroke, retinopathy and mental and physical disabilities. Given the constellation of these comorbidities, patients with SCD have a diminished quality of life and on average have a significantly shorter lifespan than normal healthy adults, sometimes up to 20 to 30 years shorter.

SCD is caused by a single mutation in the gene that expresses the beta globin subunit of hemoglobin. Hemoglobin in RBCs consists of two beta globin and two alpha globin subunits. Hemoglobin's primary function is to transport oxygen from the lungs to tissues throughout the body and return carbon dioxide back to the lungs. In oxygen rich environments, like the lungs, hemoglobin has a high affinity for oxygen and binds to it rapidly. In lower oxygen surroundings, like peripheral tissues, hemoglobin has a low affinity for oxygen and releases it quickly. The beta globin subunit mutation in SCD leads to the production of abnormal hemoglobin known as sickle hemoglobin, or HbS. HbS is comprised of two mutant beta globin and two normal alpha globin subunits. In reduced oxygen settings, HbS permits hydrophobic associations between the mutated beta globin subunits and the normal alpha subunits. This causes the oxygen deficient hemoglobin units to assemble into long chains in an event known as polymerization. These long, fixed chains of hemoglobin distort the flexible disc-like RBC into an inflexible crescent or "sickled" shape. Although the sickled RBC may convert back into a regular RBC in oxygen rich environments, it will return to its sickled form in lower oxygen environments and ultimately may be permanently sickled and/or be destroyed.

There are several genetic variations of SCD, including:

- **HbSS,** also known as sickle cell anemia, is the most common and severe form of SCD where patients inherit one mutated beta-globin gene from each parent. Approximately 60% of patients with SCD have HbSS.
- **HbS/**b-**0 thalassemia** is a form of SCD where patients inherit one mutated beta-globin gene and one mutated ß-thalassemia gene, and is often clinically indistinguishable from patients with HbSS. Approximately 10% of patients with SCD have HbS/ß-0 thalassemia.
- **HbSC** is a form of SCD where patients inherit one mutated beta-globin gene and one mutated hemoglobin C gene. Approximately 30% of patients with SCD have HbSC, which is a milder form of disease.

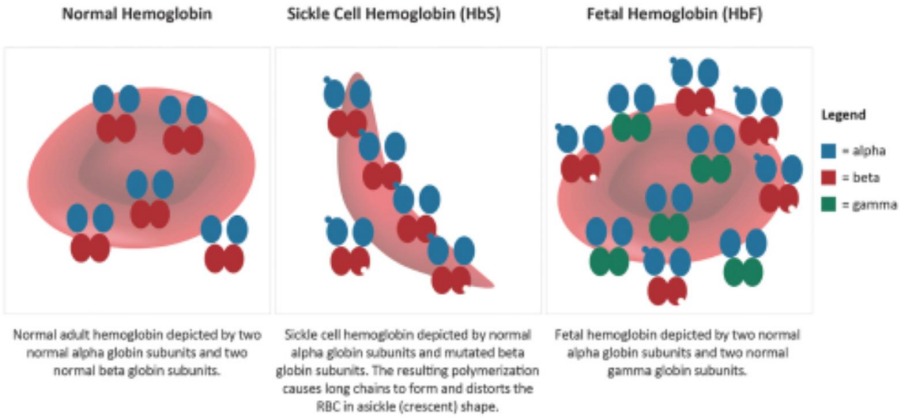
Although patients with SCD often present a spectrum of symptoms that can vary over time, patients are often grouped by their predominant symptomology: those that present with hemolytic anemia, which is largely driven by sickled RBCs, and those that present with painful VOCs, where RBCs, WBCs and other cell types play a role.

The Role of Fetal Hemoglobin on RBC Pathophysiology and SCD

One way to prevent the polymerization of HbS that results in sickled RBCs is to enhance the overall affinity of hemoglobin for oxygen, which reduces sickling in low oxygen environments and ameliorates pathophysiology of the disease. A promising approach to enhance hemoglobin-oxygen affinity is to reactivate production of inactive HbF, which we refer to as HbF induction. HbF is a natural hemoglobin that is activated during fetal development and is designed to give the growing

fetus better access to oxygen from the maternal bloodstream. HbF has higher affinity for oxygen and ceases production approximately six months after birth, at which time it is replaced by adult hemoglobin that has lower oxygen affinity. Accordingly, newborns with SCD do not experience RBC sickling and resulting symptomology in the first four to five months of life. As HbF production declines and mutated HbS is produced in its place, SCD clinical manifestations begin to rapidly emerge. Some children with SCD mature into adulthood with persistence of HbF, otherwise known as hereditary persistence of HbF, and this reduces the long-term clinical manifestations of SCD. In some cases, these patients are essentially asymptomatic. We believe that the protective aspects of naturally occurring HbF supports the development of therapies that induce HbF as a means to treat SCD.

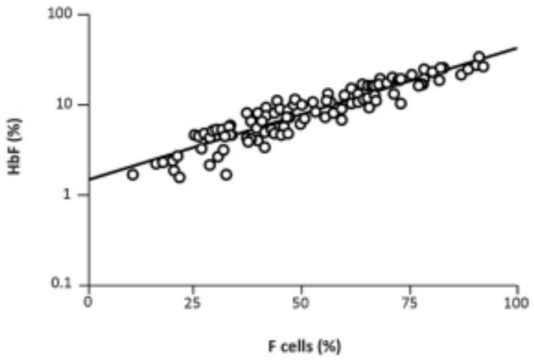
The image below depicts how RBCs can change shape in low oxygen environments. In healthy individuals, there is no change to the hemoglobin organization or RBC structure. In SCD, hydrophobic interactions with the hemoglobin subunits lead to polymerization and cause RBC distortion. In cells with reactivated HbF, polymerization is avoided because HbF reduces the ability of mutated hemoglobin to polymerize.



Reactivation of HbF occurs in immature RBCs, known as erythroblasts and reticulocytes. These cells are found in the bone marrow and have the cellular machinery to produce HbF. Once HbF is induced in nascent RBCs, they eventually grow into mature RBCs that contain HbF. Mature RBCs that are already in circulation are not viable targets for HbF induction because they do not contain DNA. Over time, these mature RBCs without HbF die out and are replaced by newly mature RBCs that contain HbF, further increasing the population of HbF containing RBCs. This time course can be up to 120 days, which is the lifespan of a normal RBC, or substantially shorter, as sickled RBCs live for only eight to 40 days. Therapies that increase HbF must focus on immature RBCs to ensure HbF is increasingly part of the mature and circulating RBC population.

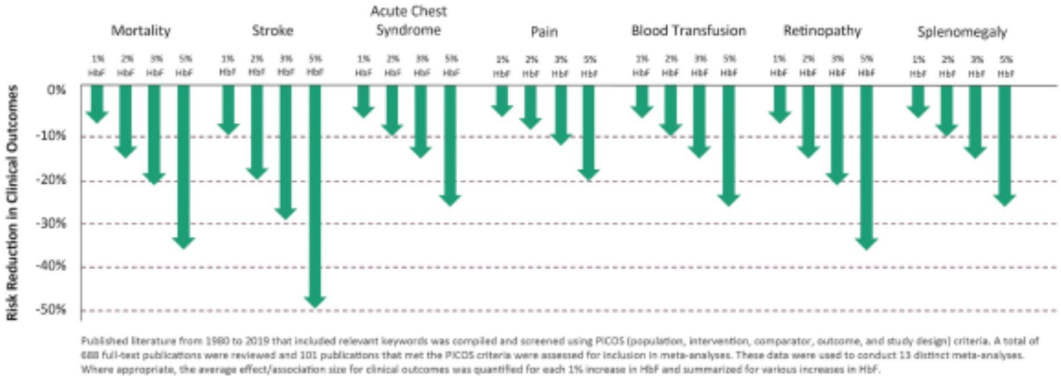
Measuring the reactivation of HbF is accomplished in two interrelated ways. The first assay confirms if an RBC contains HbF, in which case it is known as an F-cell. We believe that measurements of the percentage of F-cells relative to total RBCs, which we refer to as %F-cells, establish whether a therapy is reactivating HbF production. The second assay quantifies the amount of HbF across RBCs, expressed as a percentage of total hemoglobin, or HbF%. Increasing HbF% is key to addressing SCD disease pathology and ultimately drives the improved hemoglobin-oxygen affinity. As illustrated in the graphic below, which is based on data from 242 pediatric patients with SCD across various genotypes, the relationship between %F-cells and HbF% is exponentially correlated in that linear increases in %F-cells yield multi-fold increases in HbF%.

Relationship Between %F-cells and HbF%



While %F-cells increases are important measurements, absolute increases in HbF% ultimately drive reduction in disease risk. We commissioned a third-party to perform a systematic literature review and series of quantitative meta-analyses to identify evidence for clinical outcomes associated with HbF% in patients with SCD. Statistically significant associations between HbF% and clinical outcomes in SCD were found for the following: mortality, stroke, acute chest syndrome, pain, blood transfusion, retinopathy and splenomegaly. The figure below shows how absolute increases in HbF% are associated with reduced disease risk across several of these parameters.

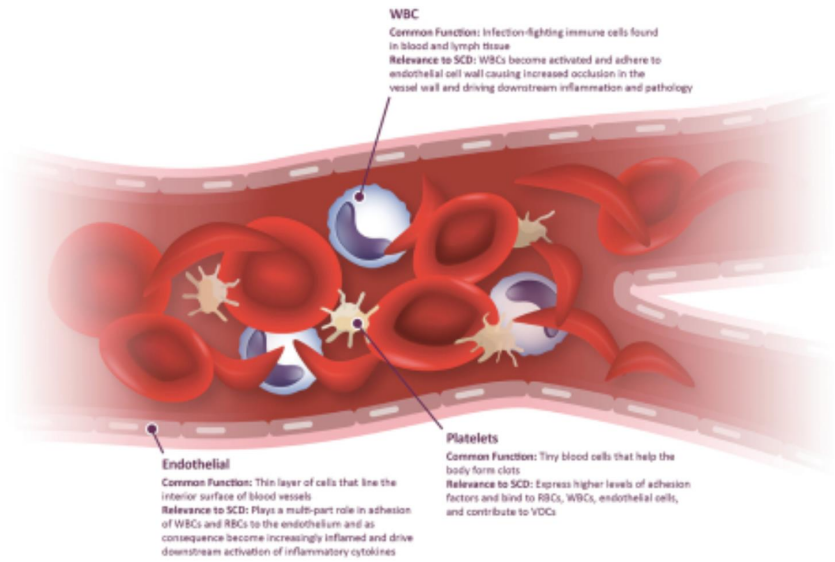
Association Between Increases in HbF% and Disease Risk



The Role of Other Cell Types in SCD

While HbF induction focuses primarily on the RBC aspect of SCD pathophysiology, non-RBC factors also play an important role in SCD. Several other cell types contribute to SCD, including WBCs, endothelial cells and platelets. Dysfunction of these cells, their inter-relationship and resulting downstream inflammatory processes contribute to numerous acute symptoms in SCD patients, such as painful VOCs and multi-organ damage. Third-party clinical data suggest that elevated WBCs are a predictor of increased risk of early death in patients with SCD. Furthermore, in patients with SCD, WBCs are activated and express higher levels of cell surface markers associated with adhesion, such as CD11a, CD11b and CD18. WBCs also interact with sickled RBCs and endothelial cells causing both cell aggregation and adhesion within the blood vessel. As a result, endothelial cells are damaged and secrete inflammatory signals that can ultimately lead to organ damage. Platelets exacerbate this inflammatory cascade by releasing cell signaling molecules known as cytokines and further

contribute to the cellular blockage in blood vessels that causes VOCs and clinical pathology. The following image describes the role of each of these cells and how they may be implicated in SCD.



The Role of Adhesion Mediators in SCD

In addition to specific cell types playing a role in SCD, adhesion mediators cause RBCs, WBCs, endothelial cells and platelets to stick to one another. These adhesion mediators, known as cell adhesion molecules include selectins and vascular factors that form a multi-cellular lattice that contributes to blood vessel blockage. Inhibition of different types of adhesion mediators has recently become an approach to ameliorate SCD pathophysiology, which is distinct from approaches that solely target the underlying sickled RBC. Adhesion mediators can also be easily measured and therefore serve as reproducible biomarkers across RBCs, WBCs, endothelial cells and platelets. These include P-selectin, E-selectin, vascular cell adhesion molecule 1, or VCAM-1, and intercellular adhesion molecule 1, or ICAM-1.

Addressable Patient Population

The global incidence of SCD is estimated to be approximately 300,000 births annually, and by 2050, incidence is expected to rise to approximately 400,000 births annually. In the United States, where newborn screening for SCD is mandatory, the estimated prevalence is approximately 100,000 individuals. In the European Union, the estimated prevalence is approximately 134,000 individuals. The global prevalence of SCD is estimated to be approximately 4.4 million patients. SCD is most common among people of African, Middle Eastern and South Asian descent.

Approved and Emerging Modalities and Their Limitations

Approved Treatments

Managing SCD and its various clinical manifestations is complex, and patients have historically had limited options for treatment. In November 2019, the FDA granted accelerated approval for Oxbryta (voxelotor) for the treatment of SCD in adults and children 12 years of age and older. Oxbryta is an oral therapy taken once daily and is the first approved treatment that directly inhibits sickle hemoglobin polymerization. The accelerated approval of Oxbryta was based on clinically meaningful and statistically significant improvements in hemoglobin levels, accompanied by reductions in red blood cell destruction, known as hemolysis. In November 2019, the FDA also approved Adakveo (crizanlizumab), which has been demonstrated to reduce the frequency of VOCs in adult and pediatric patients aged 16 years and older with SCD. Adakveo is administered intravenously and binds to P-selectin, which is a cell adhesion protein that plays a central role in the multicellular interactions that can lead to vaso-occlusion.

While these two approvals are important milestones for patients with SCD, we believe that there remains a significant unmet need for SCD therapies. Oxbryta was approved on an accelerated basis based on improvements in hemoglobin levels as a surrogate endpoint reasonably likely to predict clinical benefit. Continued approval for this indication may be contingent upon verification and description of the clinical benefit in a confirmatory study which is currently ongoing and is evaluating cerebral blood flow velocity. Adakveo does not treat the underlying cause of SCD and is only available through intravenous administration, not in oral form.

Prior to the approval of Oxbryta and Adakveo for SCD, there were only two FDA-approved drugs in the United States to treat SCD: HU and L-glutamine (marketed as Endari). These therapies have significant limitations in their safety, dosing regimen, efficacy and long-term effects.

HU, an oral chemotherapy that induces HbF and decreases sickling of the RBC, was first approved by the FDA for the treatment of SCD in 1998. In the seminal trial for HU that led to its approval, patients on average saw increased HbF induction of 3.2% over a two-year treatment period, which resulted in improved clinical outcomes, such as reduction of acute chest syndrome. Despite these benefits, HU remains a suboptimal therapy for several reasons:

- **Safety Concerns:** HU has a boxed warning because of its cancer-causing potential.
- **Complex Dosing Regimen:** Due to HU's myelosuppressive effects, which can lead to reduced WBC and platelet counts, patients need to be frequently monitored and HU must be titrated over many months, which prevents many patients from achieving an optimal dose of therapy.
- **Variable Responses:** Patients treated with HU have significant nonresponse rates, and HU may have a delayed onset of activity.
- **Potential Long-Term Effects of Use:** Long-term effects include the potential for infertility in both males and females.

Due to HU's various limitations, only approximately 30% and 22% of patients with SCD in the United States and certain countries in Europe, respectively, are treated with HU. Of those patients treated with HU in the United States, approximately 50% discontinue use within six months.

Endari, an oral powder form of L-glutamine, was approved by the FDA in 2017, becoming the first new FDA-approved treatment for SCD in nearly 20 years. L-glutamine is an amino acid precursor to nicotinamide adenine dinucleotide, or NAD, and is thought to reduce the oxidative stress that is present in patients with SCD. In September 2019, Emmaus Life Sciences, Inc. withdrew its marketing application to the European Medicines Agency, or EMA, for Endari.

Blood transfusions are another suboptimal treatment option for patients with SCD. Transfusions can transiently bolster hemoglobin levels by adding functional RBCs, but can lead to several complications that include iron overload, adverse immune response and transmission of transfusion-associated infections. Due to the lack of uniform accessibility to blood transfusions, they are not widely employed for the treatment of SCD. HSCT is available as a potentially curative treatment for SCD and acts by halting sickled RBC production from the affected marrow and replacing it with healthy hematopoietic stem cells from a matched donor. HSCT is rarely used due to the difficulty in finding a matched donor, the potential for infection and an approximately 5% mortality rate. The possibility of increased mortality risk relegates this to a last option, often utilized only in the most severe cases.

Due to the limitations of existing therapies, we believe there remains a critical need to develop new preventative therapies that are easy to access, safe for long-term use and address the multiple aspects of SCD pathology.

Emerging Modalities

There has recently been an increased focus on the development of new treatments for SCD with a spectrum of different approaches, but none address the multifactorial pathology of SCD with an oral once-a-day tablet. These approaches can be broadly categorized as follows:

Anti-Polymerization Agents: Oxbryta is designed to prevent polymerization of hemoglobin and sickling of RBCs by increasing hemoglobin's affinity for oxygen and maintaining hemoglobin in an oxygenated state. However, approaches that are solely focused on reducing polymerization may not address the complex symptomology of SCD and the clinical impact of Oxbryta on VOCs remains a question.

HbF Inducers: In addition to IMR-687, several other novel HbF inducers are in clinical development. Fulcrum Therapeutics, Inc. is in Phase 1 clinical development of FTX-6058, a small molecule embryonic ectoderm development inhibitor designed to induce expression of HbF. Novo Nordisk A/S (in collaboration with EpiDestiny, Inc.) is in Phase 1 clinical development of EPI-01, a DNA methyltransferase inhibitor.

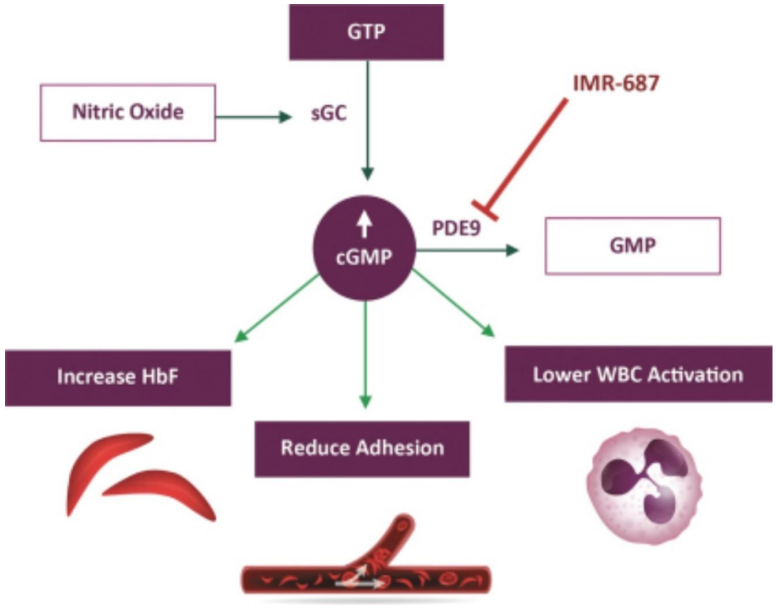
PKR Activators: Pyruvate kinase-R, or PKR, is an enzyme that is involved in the conversion of sugar into energy and is critical for the survival of RBCs. Mutations in PKR cause deficiencies in this process which results in a shortened lifespan for RBCs. This has led to the hypothesis that PKR activation can overturn this deficiency and may lead to a therapeutic benefit in patients with SCD (and potentially ß-thalassemia). Agios Pharmaceuticals, Inc. is developing mitapivat (AG-348), which is in Phase 1/2 clinical development, and Forma Therapeutics, Inc. is developing FT-4202, which is in Phase 3 clinical development.

Selectin Inhibitors: Pan selectin and specific P-selectin inhibitors, such as Adakveo, are designed to reduce adhesion of WBCs to the endothelial cell wall and reduce VOCs; however, selectin inhibitors do not ultimately prevent the sickling of RBCs in SCD. Furthermore, Adakveo requires lengthy infusion treatments every three to four weeks. Global Blood Therapeutics, Inc. is developing inclacumab, a specific P-selectin inhibitor that was previously under development for non-SCD indications. In preclinical studies, inclacumab demonstrated longer duration of exposure and greater inhibition of platelet-leukocyte aggregation as compared to Adakveo, which may create the potential for quarterly dosing, but inclacumab has yet to be tested in SCD patients (although Global Blood Therapeutics has reported that a Phase 3 clinical trial is planned for 2021).

Gene Therapy/Editing: Gene-based therapy is an innovative and potentially curative approach to SCD treatment. Like HSCT, gene therapy for SCD involves several pre-treatment steps that can include chemotherapy, which carry significant standalone risks. Recent data from a gene therapy trial indicated that chemotherapeutic pre-treatment resulted in a patient with SCD developing myelodysplastic syndrome, where the blood-forming cells in the bone marrow become abnormal. bluebird bio, Inc. and Aruvant Sciences, Inc. are each developing gene therapies which aim to deliver a functional copy of the human beta-globin gene (LentiGlobin, which is in Phase 3 clinical development, and ARU-1801, which is in Phase 2 clinical development, respectively). Gene editing, including CRISPR-Cas9, is an alternative approach to gene modification that has recently advanced in clinical development. Examples of gene editing approaches include CTX-001, currently in Phase 2 clinical development by CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals, Incorporated), BIVV-003, currently in Phase 1/2 clinical development by Sangamo Therapeutics, Inc. (in collaboration with Sanofi), and OTQ923, currently in Phase 1/2 clinical development by Intellia Therapeutics, Inc. (in collaboration with Novartis). Numerous questions remain with respect to the gene editing approach, including off-target mutagenesis and the ultimate potential reach of such therapeutics. More studies are needed to establish durability and safety of these potential treatments.

The Role of Phosphodiesterase-9 in SCD

IMR-687 is being developed to inhibit PDE9. PDE9 decreases cyclic GMP, an active signaling molecule that plays an important role in vascular biology. Lower levels of cyclic GMP, as found in patients with SCD, are associated with reduced blood flow, increased inflammation, greater cell adhesion and reduced nitric oxide mediated vasodilation. The figure below illustrates the role of PDE9 inhibition and its potential benefits on SCD pathophysiology. Nitric oxide, a chemical that supports blood vessel health, drives increases in a broadly expressed enzyme, soluble guanyl cyclase, or sGC, which drives the conversion of Guanosine-5'-triphosphate, or GTP, into cyclic GMP. Cyclic GMP levels are decreased by the PDE9 enzyme, which actively converts cyclic GMP to GMP. Increasing cyclic GMP by inhibiting PDE9 has several potential advantageous downstream impacts, including to increase HbF, reduce cell adhesion, decrease WBC activation and ultimately increase nitric oxide levels.



Novel cyclic GMP Degrader: PDE9 belongs to a family of 11 cyclic nucleotide phosphodiesterases, or PDEs. In general, PDEs degrade both cyclic GMP and cyclic adenosine monophosphate, or cAMP. However, PDE9 solely degrades cyclic GMP, has the highest affinity for cyclic GMP of all PDEs, and does not degrade cAMP. Inhibiting PDE9 offers a novel way to increase cyclic GMP levels by limiting cyclic GMP degradation. We believe that other approaches that increase cyclic GMP levels without addressing its degradation, such as HU, are unlikely to confer persistent and robust increases in cyclic GMP. Conversely, preventing degradation of cyclic GMP by targeting PDE9 may enable long-term benefits that include sustained HbF induction, reduced activation of WBCs, positive effects on other cell types and reduced cell adhesion.

High Expression in SCD Cells of Interest: PDE9 is highly expressed in cells of interest in SCD, specifically reticulocytes, which are an important cell type for HbF induction. Furthermore, PDE9 has high expression in WBCs and in areas where RBCs are formed. A potential drawback of inhibiting PDE9 for the treatment of SCD is that PDE9 is also highly expressed in the brain, which in part explains why PDE9 inhibitors have been extensively studied in neurodegenerative diseases. While several PDE9 inhibitors have been shown to be well-tolerated in adults, preclinical data suggests that brain penetrant PDE9 inhibition causes mice to have changes in fear response, which may reflect memory impairment. This could be concerning in pediatric patients with SCD who continue to have ongoing brain development. Thus, any PDE9 inhibitor broadly targeting SCD should minimally cross the blood-brain barrier.

Multimodal Method of Action: In preclinical studies, PDE9 inhibitors have been shown to increase cyclic GMP concentrations, induce HbF and F-cells, reduce WBC activation and adhesion across other cell types and modulate adhesion mediators. A brain penetrant PDE9 inhibitor developed by Bayer known as BAY73-6691, which was originally developed for the treatment of neurodegenerative diseases, was observed to increase cyclic GMP and HbF transcription in a representative human cell line for SCD. Furthermore, BAY73-6691 was observed to reduce WBC activation and adhesion to endothelial cells in patient-derived WBCs, however development was subsequently discontinued and we are not aware of any further development of this compound. Another brain penetrant PDE9 inhibitor developed by Pfizer known as PF-04447943

was originally developed for Alzheimer's disease and tested in patients with SCD. In Pfizer's Phase 1b clinical trial in patients with SCD, there were some reductions in adhesion markers but no significant HbF induction was observed. Development of PF-04447943 was subsequently discontinued and we are not aware of any further development of this compound.

Our Solution for Sickle Cell Disease: IMR-687 as a Differentiated PDE9 Inhibitor

Our approach to address SCD is fundamentally distinct from other therapies. IMR-687 is being developed to directly and potently inhibit PDE9, which represents a differentiated approach to increase cyclic GMP levels, with a selectivity for PDE9 that we believe will make it amenable for long-term use. We recently completed a Phase 2a randomized, double blinded, placebo-controlled clinical trial of IMR-687 in adult patients with SCD and we are currently conducting a Phase 2b clinical trial in this patient population. We believe IMR-687 may have advantages over other therapies, including speed of onset of HbF induction, a multimodal approach and a once daily dosing regimen. In addition, IMR-687 has been shown to be stable at high temperatures and in humid conditions, potentially enabling worldwide access, including in areas where SCD and ß-thalassemia are endemic.

We believe IMR-687 has several differentiating features relative to other PDE9 inhibitors:

Highly Potent PDE9 Inhibitor: IMR-687 is a highly potent PDE9 inhibitor, as measured by induction of cyclic GMP across various doses. We have specifically studied the potency of PDE9 inhibition of IMR-687 as compared to HU and analogues of BAY73-6691 and PF-04447943 by analyzing cyclic GMP levels across various doses in an *in vitro* assay. We studied analogues of BAY73-6691 and PF-04447943 because BAY73-6691 and PF-04447943 are proprietary compounds to which we did not have direct access. The analogues we used were based on the well-defined crystal structures of BAY73-6691 and PF-04447943 that are publicly available in published patent filings. When compared to these agents, IMR-687 was observed to be more potent across all dose groups.

Differentiated Selectivity and Tolerability Profile: IMR-687 is a highly selective PDE9 inhibitor. We compared the selectivity of IMR-687 and an analog of PF-04447943 against a panel of related PDEs. We chose not to test BAY73-6691 or an analog thereof because BAY73-6691's lack of potency led us to conclude there was little merit to further testing. For the isoform PDE9A1, IMR-687 was observed to be more than eight times more selective than the PF-04447943 analog and for the isoform PDE9A2, IMR-687 was observed to be more than four times more selective than the same compound. Isoforms are functionally similar proteins within each PDE family that have slightly different genetic coding. We believe the selectivity of IMR-687 will allow us to optimize dose while minimizing off-target effects. IMR-687 has exhibited lower interaction with other PDE family members compared to the PF-04447943 analog, or did not have measurable inhibition.

We also conducted toxicology studies of IMR-687. In a 26-week female rat infertility study and in early embryonic development studies, once-daily dosing of IMR-687 was observed to be well tolerated with no effects on fertility or embryonic development at any dose level studied. In addition to standard adult animal toxicology studies, a juvenile rat study was completed where once daily administration of IMR-687 was observed to be well tolerated with no indication of toxicity.

Minimal Brain Penetration: We are developing IMR-687 specifically because it was observed to have low brain penetration in animal models. We believe this will reduce the potential impact of PDE9 inhibition on central nervous system, or CNS, development and function. Historically, most early PDE9 inhibitors were developed for potential CNS indications and thus were specifically designed to cross the blood-brain barrier. We observed in a mouse model that while plasma concentrations were similar, brain exposure to levels of IMR-687 were observed to be five times lower than those seen with the PF-04447943 analog at 10mg/kg.

Additionally, IMR-687 showed no effect on locomotor activity or in a classical fear conditioning mouse model of learning and memory. In contrast, the brain penetrant PF-04447943 analog was observed to significantly increase conditioned fear responses in mice at an equivalent dose.

Drug Product Stability: IMR-687 has been observed to exhibit a durable shelf life at both standard and elevated room temperature and humidity conditions. For example, at standard room temperature and humidity conditions, we have observed consistent stability results at doses of 50 mg, 100 mg, and 200 mg at the 24-month time point. In addition, we have observed consistent stability results under accelerated stress conditions that mimic the high heat (40° Celsius, 104° Fahrenheit) and increased humidity (75%) of the tropics. We believe this observed stability of IMR-687 provides us with a potential opportunity to treat patients in areas where other treatments may not be accessible, including in the tropical climates where SCD and β-thalassemia are endemic.

Preclinical and Phase 1 Data

In preclinical SCD models, we observed that IMR-687 is a potent cyclic GMP inducer and had a multimodal mechanism of action, acting to increase RBC HbF expression, reduce RBC sickling and decrease expression of WBC adhesion molecules.

In an SCD *in vitro* model, we measured the ability of IMR-687 to increase cyclic GMP levels in an RBC cell line as compared to HU. In this study, we observed that IMR-687 induced cyclic GMP production in a dose-dependent manner at an approximately 30-fold lower drug concentration than HU. In addition, at an equivalent drug concentration of 10 µM of IMR-687, we observed an approximately ten-fold increase in cyclic GMP levels as compared to HU. We also evaluated IMR-687 in a mouse model of SCD that expresses human sickle hemoglobin. We observed that IMR-687 demonstrated statistically significant increases in HbF-positive RBCs, statistically significant decreases in the percentage of sickled RBCs and decreases in markers of hemolysis, or destruction of RBCs, and WBC adhesion.

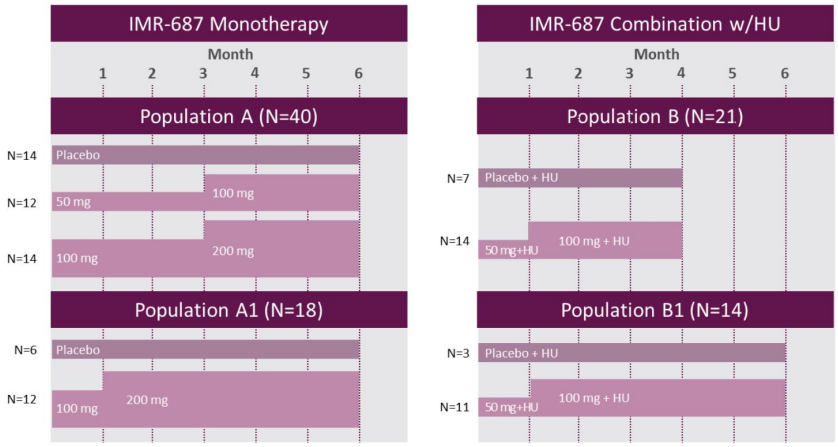
In our Phase 1 randomized, double-blind, placebo-controlled clinical trial in healthy volunteers, single and multiple ascending doses of IMR-687 were reported to be well tolerated to a maximum dose of 4.5 mg/kg per day and no serious adverse events were reported.

IMR-SCD-102: SCD Phase 2a Clinical Trial

Our Phase 2a clinical trial was a randomized, double-blind, placebo-controlled clinical trial in adult patients with the HbSS and HbS/ß-0 thalassemia genotypes of SCD and was conducted at clinical centers in the United States and the United Kingdom. The trial evaluated the safety, tolerability, PK and exploratory PD and clinical outcomes of IMR-687 in two groups of SCD patients: patients receiving IMR-687 administered as a monotherapy agent once daily for 24 weeks and patients receiving IMR-687 administered at lower doses in combination with HU for 16 weeks. The design of the Phase 2a trial separated out the monotherapy and combination arms into separate sub-studies. The combination sub-study was purposefully designed in consultation with the FDA, taking into account HU and IMR-687's overlap in the nitric oxide-cyclic GMP pathway, which ultimately drives cyclic GMP expression. This low-dose, short duration sub-study was thus created to test how the two drugs interact when dosed in combination. Patients in the combination sub-study were required to have been receiving HU for at least 60 days prior to screening and then continue to receive the same dose of HU throughout the duration of the trial. A total of 93 patients were dosed in the trial, of which 58 patients were dosed in the monotherapy sub-study and 35 patients were dosed in the combination sub-study.

We initially commenced the monotherapy sub-study with patients receiving IMR-687 at doses of 50 mg or 100 mg through 12 weeks and then escalating to higher doses of 100 mg or 200 mg, respectively, through 24 weeks if approved by the Safety Review Committee, or SRC, after review of vital signs and treatment emergent adverse events, or TEAEs. After dosing 40 monotherapy patients (referred to as Pop A), in the second quarter of 2019 we amended the trial protocol for the monotherapy sub-study to (i) accelerate the time of dose escalation for the 100 mg/200 mg dose group from week 13 to the end of the first month, (ii) allow for patients to be administered the higher dose for five months instead of three months and (iii) eliminate the 50 mg/100 mg dose group. Following the amendment of the protocol, we dosed a further 18 patients (referred to as Pop A1) in the monotherapy sub-study. All patients in the monotherapy sub-study who were dosed with placebo continued to receive placebo for the duration of the trial.

We initially commenced the combination sub-study with patients receiving IMR-687 at an initial dose of 50 mg on top of a stable dose of HU, with escalation after one month to 100 mg for the remaining portion of the trial (through week 16) upon SRC approval. After dosing 21 combination patients (referred to as Pop B), in the second quarter of 2019, we amended the trial protocol for the combination sub-study to extended dosing for an additional month. Following the amendment of the protocol, we dosed a further 14 patients (referred to as Pop B1) in the combination sub-study. All patients in the combination sub-study who were dosed with placebo continued to receive placebo for the duration of the trial. The design of the Pop A/A1 and B/B1 sub-studies are shown in the graphics below.



We conducted two planned interim analyses of data from our Phase 2a clinical trial as described below.

November 2018 Interim Analysis

The first interim analysis was blinded at the individual patient level and consisted of an evaluation of low dose IMR-687 in at least 18 patients that had completed one month of treatment in the Pop A monotherapy sub-study and was carried out as pre-specified in the protocol. The data cut-off for this interim analysis was October 8, 2018. At 13 weeks, we observed an increase of approximately 110% from baseline in the percentage of F-cells in the group receiving 100 mg of IMR-687 as monotherapy. We also observed decreases in absolute reticulocytes and percent reticulocytes in the 100 mg IMR-687 monotherapy group. The data for WBC and adhesion markers were inconclusive. Blinded safety and tolerability data as of the data cutoff date showed that treatment with IMR-687 was reported to be generally well tolerated, with no clinically significant changes in WBC counts and no evidence of neutropenia.

August 2019 Interim Analysis

The second interim analysis was triggered when at least 18 patients completed the 24 weeks of dosing in this trial in the Pop A monotherapy sub-study and had a cut-off date of July 8, 2019. Patients in the Pop B combination sub-study were evaluated for the first time to measure safety and PK related to HU being dosed in combination with IMR-687. In the second interim analysis, IMR-687 was generally reported to be well tolerated across all doses in the monotherapy and combination sub-studies.

All Comers Analysis (n=37)

The first analysis involved all Pop A monotherapy patients, regardless of where they were in the trial, referred to as all comers. We observed a statistically significant (p=0.022) increase in F-cells for the IMR-687 high dose cohort (100 mg/200 mg) compared to placebo after 24 weeks of dosing. We observed a relative increase in F-cell percentage of 18.1 percentage points, with the mean values for the absolute percentage of F-cells observed in patients increasing from 13.6% to 31.7%. We observed a mean absolute increase in HbF% of 1.7 percentage points in the IMR-687 high dose cohort (100 mg/200 mg) after 24 weeks of dosing. Patients in the IMR-687 high dose cohort had a mean baseline HbF% of 6.7%, which increased to 8.4% after 24 weeks of dosing.

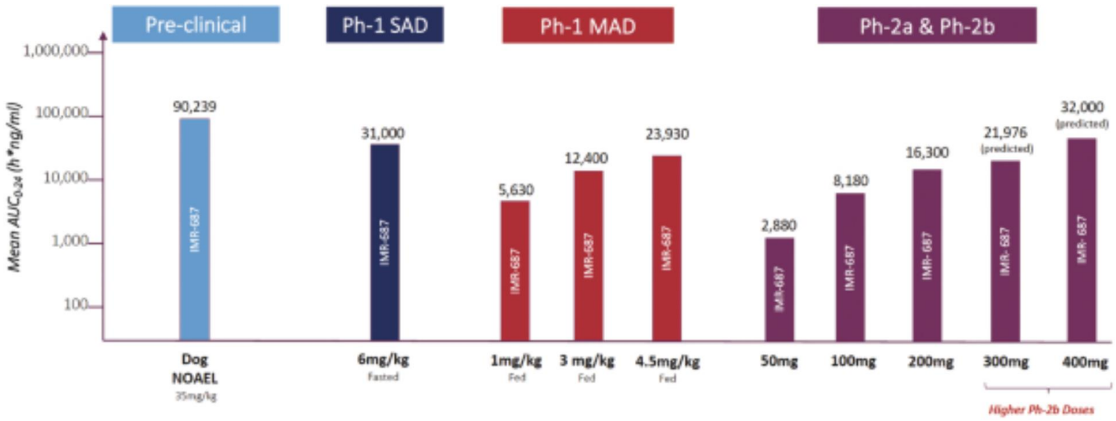
In addition, we observed a mean increase in mean corpuscular volume of 4.3 femtoliters in the IMR-687 high dose cohort. While we saw individual changes in other related downstream RBC biomarkers (including variable responses in reticulocytes, LDH, indirect bilirubin and hemoglobin) and white cell adhesion biomarkers (including sP-selectin, sE-selectin, iVCAM-1 and iCAM-1), we did not see consistent trends across the mean values.

Completer Analysis (n = 18)

The second analysis was a pre-specified protocol-driven analysis of the efficacy parameters for the 18 completers. For the measurements of F-cells, 100% of completers showed an increase in F-cells and no completer saw a decrease in F-cells in the high dose arm (100 mg/200 mg). While there was more variability in the lower dose arm (50 mg/100 mg), most completers saw F-cell increases, though they did not have the magnitude of increases as observed for the higher dose (100 mg/200 mg). Placebo completers, as expected, showed the most variability in changes in F-cells, with 50% showing increases in F-cells and 50% showing decreases, netting out to an overall slight decrease in F-cells. These data allowed us to create a relevant PK/PD model to potentially provide greater understanding of how dose impacts efficacy markers, including F-cells and HbF%.

Pharmacokinetics (PK) Summary

PK data from the monotherapy sub-study were analyzed to compare IMR-687 exposure for patients in the Phase 2a trial to exposure observed in preclinical studies and in healthy volunteers in the multiple ascending dose stage of our Phase 1 trial, in each case through an analysis of Area Under the Curve$_{0\text{-}24}$, or AUC$_{0\text{-}24}$, which measures drug concentration in blood plasma over the first 24 hours following dosing. As shown in the far-left column of the figure below, a preclinical female dog model established a No Observed Adverse Effect Level, or NOAEL, which is the highest experimental point that does not have adverse effects, of 90,239 hours x ng/mL, or h x ng/mL. As shown in the second-from-left column of the figure below, the 6 mg/kg highest dose in the fasted single ascending dose stage of our Phase 1 trial resulted in a mean exposure of 31,000 h x ng/mL. As shown in the set of middle columns of the figure below, exposure in the fed multiple ascending dose stage of the trial ranged from 5,630 h x ng/mL at a dose of 1 mg/kg to 23,930 h x ng/mL at a dose of 4.5 mg/kg, which was the maximum tolerated dose, or MTD. As shown in the far-right columns of the figure below, mean exposure in the interim analysis of the Phase 2a trial ranged from 2,880 h x ng/mL at the 50 mg dose to 16,300 h x ng/mL at the 200 mg dose. Also as reflected in the far-right columns in the figure below, we generated a PK model based on these values that predicted exposure of 21,976 h x ng/mL and 32,000 h x ng/mL for possible future higher doses of 300 mg and 400 mg, respectively. The observed mean exposure for 200 mg dosing of IMR-687 in the interim analysis of the Phase 2a trial and the predicted exposure for 300 mg dosing of IMR-687 are below the mean exposure at the 4.5 mg/kg MTD in the multiple ascending dose stage of our Phase 1 trial and are less than 25% of the NOAEL observed in preclinical dog experiments. While the predicted exposure for 400 mg dosing of IMR-687 surpasses the mean exposure at the 4.5mg/kg MTD in the multiple ascending dose stage of our Phase 1 trial, it is substantially lower than the established female dog NOAEL. We believe the exposure data we have observed to date and the exposure data predicted by our PK modeling support our decision to increase dosage to 300 mg, and potentially 400mg, in our ongoing Phase 2b clinical trial in SCD.



The second interim analysis also included analyses of additional PK exposure metrics from the monotherapy sub-study, including C_{max} values, which are the peak concentrations achieved by a drug, and concentrations of a drug after 24 hours, or C_{24} values. The C_{24} parameter provides an understanding of target coverage over a 24-hour period and is particularly

important when matched with the measure of inhibitory concentrations above 90%, or IC_{90}. We estimated an IC_{90} value of 160 ng/mL for IMR-687 from the *in vitro* dose-response curve using IMR-687 in combination with the isolated PDE9 enzyme. Patients in the 50 mg/100 mg group of the monotherapy sub-study were, on average, above this estimated IC_{90} for approximately six to 12 hours, depending on dose, and patients in the 100 mg/200 mg group were, on average, above this estimated IC_{90} for approximately 12 to 17 hours, depending on dose. Our PK modeling predicts that a 300 mg dose of IMR-687 will result in concentrations above the estimated IC_{90} for approximately 22 hours and a 400 mg dose will result in concentrations above the estimated IC_{90} for over 24 hours. In addition, the C_{max} and C_{24} levels observed for 200 mg dosing and predicted for 300 mg dosing of IMR-687 were below those observed at the 4.5 mg/kg MTD dose in the multiple ascending dose stage of our Phase 1 trial. Our PK modeling predicts that the C_{max} and C_{24} levels for 400 mg dosing of IMR-687 will be higher than those observed at the 4.5 mg/kg MTD in the multiple ascending dose stage of the Phase 1 trial.

Examination of the of the PK for the combination of IMR-687 + HU as compared to HU alone was the key objective for the combination sub-study of the Phase 2a trial and was recommended by the FDA in our pre-IND discussions. We measured HU PK on its own prior to the commencement of combination dosing as well as HU PK following the commencement of combination dosing at weeks five and 17. The PK data in the second interim analysis indicated that treatment with IMR-687 + HU did not result in changes in the HU PK observed prior to combination dosing and that there were no drug-drug interactions between IMR-687 and HU, which we believe supports our use of higher doses of IMR-687 in combination with HU in our Phase 2b clinical trial of IMR-687 in SCD. These findings also allowed us to combine monotherapy and combination dosing into a single trial population for our ongoing Phase 2b clinical trial of IMR-687 in SCD.

PK/PD Modeling with Completer Data

Noncompartmental PK results were combined with the completer data from the second interim analysis to establish PK/PD correlations for use in connection with our Phase 2b trials. There were two key correlations that helped us better understand HbF response in light of the PK data. The first of these was the correlation between F-cell response data and PK data. We defined responders as patients that had a ≥7% increase from baseline, which included all patients from the 100 mg/200 mg dose group and one patient from the 50 mg/100 mg dose group (total n=6). PK/PD analysis showed that completers that responded to IMR-687 had both higher median $AUC_{0\text{-}24}$ and C_{max} values with respect to IMR-687 as compared to completer non-responders. Although the median C_{24} values were similar for all completers, the 25th and 75th percentile values were higher for responders.

The second correlation we examined was between HbF response data and PK data. We defined responders as patients that had a ≥1% absolute increase in HbF from baseline, which included three patients from the 100 mg/200 mg dose group and one patient from the 50 mg/100 mg dose group (n =4). Similar to what we observed in our analysis of the F-cell data, PK/PD analysis showed that completers that responded to IMR-687 had higher median $AUC_{0\text{-}24}$ levels as compared to non-responders. While the median C_{24} and C_{max} values were similar for all completers, the 25th and 75th percentile values for C_{24} were higher for responders.

Future dose modeling predicts that exposure in $AUC_{0\text{-}24}$, C_{max} and C_{24} for IMR-687 should increase with dose levels above 200 mg and should achieve drug concentration levels above the estimated IC_{90} for approximately 22 hours at a 300 mg dose and over 24 hours at a 400 mg dose. We believe this PK/PD modeling further justifies our evaluation of higher doses of IMR-687 in our Phase 2b clinical trials.

January 2021 Topline Results

In January 2021, we disclosed topline results of the Phase 2a clinical trial, which are summarized below. We are continuing to conduct additional analyses with respect to this data, including final PK data, and expect to report results from these additional analyses at a future medical meeting in 2021.

As described above, in the second quarter of 2019 we amended the trial protocol for the monotherapy sub-study to create Pop A1, which was comprised of patients who received either placebo or IMR-687 at a once-daily dose of 100 mg through 4 weeks and then 200 mg for an additional 20 weeks (24 weeks total). At the same time, we amended the trial protocol for the combination sub-study to create Pop B1, which was comprised of patients who received either placebo or IMR-687 once-daily at 50 mg on top of a stable dose of standard of care HU, with escalation after 4 weeks to 100 mg for an additional 20 weeks (24 weeks total). None of the patients enrolled in Pop A1 or Pop B1 were included as part of the August 2019 interim analysis described above.

Summary of Safety and Tolerability Data

Overall, the data demonstrated that IMR-687 was well tolerated as a monotherapy and in combination with HU at all dose levels. In the monotherapy sub-studies (Pop A and Pop A1), the most frequent adverse events in the IMR-687 treatment arm included sickle cell anemia with crisis, nausea, headache and back pain. In the combination sub-studies (Pop B and Pop B1), the most frequent adverse events in the IMR-687 + HU treatment arm included headache, sickle cell anemia with crisis, nausea, fatigue and ocular icterus. There were no observed clinically significant shifts in vital signs or electrocardiogram data, including no hypotension or neutropenia in either the monotherapy or combination arms.

A 30% lower rate of VOCs/SCPCs, as part of the safety analysis, was observed in the Pop A1 IMR-687 treatment group when compared to placebo. 58% of patients (7 of 12 patients, 9 events total) experienced at least one VOC/SCPC in the Pop A1 IMR-687 treatment group as compared to 83% (5 of 6 patients, 14 events total) in the placebo population. Furthermore, the rate of VOC-related hospitalizations was lower in the Pop A1 IMR-687 treatment group when compared to placebo. 33% of patients (4 of 12) experienced one VOC-related hospitalization in the Pop A1 IMR-687 treatment group as compared to 66% (4 of 6) in the placebo population. There were no meaningful differences in VOCs/SCPCs or VOC related hospitalizations, between the Pop B1 IMR-687 + HU and HU + placebo groups.

Population A1 Monotherapy (n=18)

Biomarker results showed minimal changes in F-cells, HbF levels and total Hb levels from baseline through week 24. However, a dose-dependent increase in HbF (1.3% absolute increase) was seen when patients dose escalated from 100 mg to 200 mg, starting after 4 weeks (n=10) and through 24 weeks (n=7). One of seven evaluable patients (14%) in Pop A1 recorded an absolute increase in HbF percentage from baseline of greater than 1% (increase of 3.2%). Placebo patients from Pop A1 did not have evaluable week 24 PD biomarker results due in part to missing study visits and are therefore not included in the table below. Biomarkers related to hemoglobin, hemolysis, inflammation, and cardiac stress are summarized below for the IMR-687 treatment arm:

Parameter		**Baseline Value (n=12)***	**Week 24 Value (n=7)***	**Percent Difference**
HbF percentage (%)		8.8	8.7	-1.1%
F-cell percentage (%)		28.1	28.5	1.4%
Hb (g/dL)		8.8	8.6	-2.3%
Markers of Hemolysis				
Percent reticulocytes (%)		10.4	7.4	-28.8%
Absolute reticulocyte count ($\times 10^9$/L)		296	240	-18.9%
Indirect bilirubin (µmol/L)		47.8	31.9	-33.2%
LDH (IU/L)		397	346	-12.8%
Markers of Inflammation & Cardiac Stress				
hsCRP (mg/L)		10.4	2.5	-75.9%
NTproBNP (ng/L)		685	414	-39.6%

* With respect to F-cell percentage, n=9 at baseline and n=6 at Week 24.

Population B1 Combination Therapy (n=14)

Biomarker results in IMR-687+HU treated patients showed an overall increase in F-cells and HbF levels from baseline to week 24, while Hb levels did not meaningfully change. Three of the eight evaluable patients (33%) had absolute increases in HbF percentage of greater than 1%, with a mean absolute increase in HbF percentage of 4.3% in that subset of patients. There was a single placebo patient from Pop B1, as other patients did not have evaluable week 24 pharmacodynamics biomarker data due in part to missing study visits. Therefore, this single patient is not included in the table below.

Biomarkers related to hemoglobin, hemolysis, inflammation, and cardiac stress are summarized below for the IMR-687+HU treatment arm:

Parameter	Baseline Value (n=10)*	Week 24 Value (n=8)*	Percent Difference
HbF percentage (%)	18.6	19.8	6.5%
F-cell percentage (%)	58.8	61.4	4.4%
Hb (g/dL)	9.5	9.4	-1.1%
Markers of Hemolysis			
Reticulocytes (%)	7.5	5.3	-29.3%
Absolute reticulocyte count ($\times 10^9$/L)	185	137	-25.9%
Indirect bilirubin (µmol/L)	34.9	37.9	8.6%
LDH (IU/L)	351	340	-3.1%
Markers of Inflammation & Cardiac Stress			
hsCRP (mg/L)	11.5	12.5	8.7%
NTproBNP (ng/L)	284	317	11.6%

* With respect to F-cell percentage, n=8 at baseline and n=7 at Week 24.

Population A Monotherapy (n=40)

Subsequent to the August 2019 interim analysis described above, four additional patients completed 24 weeks of dosing in the Pop A monotherapy arm. A completers analysis in this group showed that the high dose of IMR-687 (100 mg/200 mg) resulted in an absolute increase in F-cell percentage of 13.3% from baseline (p=0.025) and a mean absolute increase in HbF percentage from baseline of 0.9%. Three of the eight evaluable patients (38%) in Pop A recorded absolute HbF percentage increases of greater than 1%, with a mean absolute increase in HbF percentage of 3.1% in that subset of patients.

We are in the process of conducting multiple post-hoc analyses of the Phase 2a clinical trial data that include, amongst other analyses, reviewing pooled data across the sub-studies from the trial. Preliminary review of certain of these analyses demonstrate potential benefits from IMR-687 with respect to certain SCD biomarkers, including F-Cells. We expect to report results from these analyses at a future medical meeting.

Phase 2a Open Label Extension

We are conducting a four-year OLE clinical trial which allows patients from the Phase 2a clinical trial to enroll in a long-term safety and tolerability study of IMR-687 following completion of the Phase 2a clinical trial. The OLE clinical trial was initially designed so that patients were administered a daily dose of 100 mg of IMR-687, and in the second quarter of 2020, a protocol amendment increased the daily dose to 200 mg. Patients from the combination sub-study continue to receive the same dose of HU that they received while on the Phase 2a clinical trial throughout the duration of the OLE clinical trial. Based on the tolerability profile of IMR-687 observed thus far in the OLE clinical trial, the safety review committee, or SRC, has approved, subject to the contingency below, dose escalation in the OLE clinical trial to a minimum daily dose of 300mg, with certain patients being eligible for a daily dose of 400mg based upon their weight. This weight-based approach is similar to that being used in our ongoing Ardent Phase 2b clinical trial in SCD. The SRC approved the dose adjustments contingent on the independent data monitoring committee, or DMC, for the Ardent Phase 2b clinical trial in SCD opening the higher-dose IMR-687 arm of that trial. We expect the Ardent Phase 2b clinical trial DMC to make a decision on opening the higher dose arm in March 2021.

We conducted a preliminary review of 24 patients enrolled in the OLE clinical as of December 31, 2020. As of data cutoff date, approximately 12 of these patients had evaluable PD biomarker data for at least four months of treatment on the OLE clinical trial. We organized the patients with evaluable PD biomarkers into two sub-groups. The first sub-group, which we refer to as the treatment interrupted sub-group, was comprised of approximately 8 patients who initiated treatment on the OLE clinical trial more than 12 weeks after completing treatment for the Phase 2a clinical trial. The second sub-group, which we refer to as the direct roll-over sub-group, was comprised of approximately 4 patients who initiated treatment on the OLE clinical trial within 12 weeks of completing treatment for the Phase 2a clinical trial. For purposes of analyzing PD biomarker results, patients in the direct roll-over sub-group were analyzed using the baseline value from the Phase 2a clinical trial, while patients in the treatment interrupted sub-group were analyzed using a new baseline established upon initiation of the OLE clinical trial.

Four-Month Data Review

Overall, data from the 24 patients enrolled in the OLE clinical trial as of December 31, 2020 demonstrated that IMR-687 was well tolerated. The most common adverse events (in more than 5% of subjects) were sickle cell anemia with crisis, headache, pain in extremity, nausea, upper abdominal pain and back pain, and were generally consistent with those observed in the Phase 2a clinical trial. 16 of the 24 patients (67%) experienced at least one adverse event, with a majority of the adverse events being mild or moderate in severity. There were no observed clinically significant shifts in vital signs, safety laboratory data, or electrocardiogram data.

Biomarker results demonstrated increases in both HbF and F-cells after four-months of treatment in both the treatment interrupted sub-group and the direct roll-over sub-group. Specifically, there was a mean absolute increase in HbF percentage of 1.7% and 2.3% in the treatment interrupted sub-group and direct roll-over sub-group, respectively, and a mean absolute increase in F-cells of 5.9% and 10.2% in the treatment interrupted sub-group and the direct roll-over sub-group, respectively, in each case after four months of treatment. There were minimal changes in total Hb in both sub-groups. Patients in the treatment interrupted sub-group also demonstrated improvements in several markers of hemolysis after four months of treatment, whereas the direct roll-over sub-group showed variable changes in these measures.

The preliminary biomarker results for the OLE clinical trial are shown in the table below.

Parameter	Treatment Interrupted Sub-Group		Direct Roll-Over Sub-Group	
	Mean (median) absolute change (4-month vs baseline)	**Mean percent change (4-month vs baseline)**	**Mean (median) absolute change (4-month vs baseline)**	**Mean percent change (4-month vs baseline)**
F-cells (%)	5.9 (4.8) (n=8)	48.7% (n=8)	10.2 (6.6) (n=4)	35.2% (n=4)
HbF (%)	1.7 (0.3) (n=6)	19.6% (n=6)	2.3 (1.7) (n=4)	16.9% (n=4)
Hb (g/dL)	-0.2 (-0.3) (n=9)	-1.7% (n=9)	-0.03 (0.15) (n=4)	0.7 (n=4)
	Mean percent change (4-month vs baseline)		**Mean percent change (4-month vs baseline)**	
Reticulocytes (%)	-6.0% (n=9)		19.0% (n=4)	
Absolute reticulocyte count ($\times 10^9$/L)	-8.2% (n=9)		11.5% (n=4)	
Indirect bilirubin (µmol/L)	-25.5% (n=8)		23.0% (n=4)	
LDH (U/L)	-4.8% (n=9)		6.3% (n=4)	
NTproBNP (ng/L)	-55.0% (n=3)		N/A*	
CRP (mg/L)	27.9% (n=3)		N/A*	

* Patients in the direct roll-over sub-group did not have data for NTproBNP or CRP as of December 31, 2020.

We are in the process of analyzing outcomes with respect to VOCs from the OLE clinical trial and expect to report this information at a future medical meeting.

Case Narratives

In the third quarter of 2020, we presented case narratives on the first two patients in the OLE clinical trial to complete at least six-months of treatment. Below we have provided an update on each of these two patients who remain on the OLE clinical trial as of the filing of this Annual Report on Form 10-K.

Patient #1 was part of the Pop A monotherapy sub-study of the Phase 2a clinical trial and enrolled in the OLE clinical trial shortly following completion of the Phase 2a clinical trial and was therefore a direct roll-over patient. As of December

31, 2020, Patient #1 had been on the OLE clinical trial for approximately 18 months (and on IMR-687 for 24 months) and has shown continued increases in levels of HbF and F-cells, as well as improvements in several SCD disease biomarkers.

The table below presents biomarker results for this patient at baseline, 12 months on study (as presented in the third quarter of 2020) and 18 months on study (the most recent OLE visit for this patient):

Parameter	Baseline Ph-2a*	12-month OLE	18-month OLE	Absolute change (18-month vs baseline)	Percent change (18-month vs baseline)
F-cells (%)	26.1	46.3	66.9	40.8	156%
HbF (%)	12.3	16.2	17.1	4.8	39%
Hb (g/dL)	7.6	8.6	7.7	0.1	1%
MCV (fL)	86.8	90.3	87.7	0.9	1%

* As Patient #1 was a direct roll-over patient, baseline was established using the baseline of the Phase 2a clinical trial (mean of screening and randomization values).

In addition, a comparison of VOC data for the 24-month period that Patient #1 has been on IMR-687 (six months on the Phase 2a and 18 months on the OLE) versus information from a retrospective review of the patient's medical records for the 24-month period prior to initiation of IMR-687 indicate potential benefits of IMR-687. In the 24-month period on IMR-687, the patient had a 64% reduction (55 to 20 events) in reported VOCs, as compared to the 24-month period prior to IMR-687 administration.

Patient #2 was part of the HU combination sub-study in the Phase 2a clinical trial and was randomized to the placebo dose group, and therefore never received IMR-687 during the Phase 2a clinical trial. The patient started the OLE clinical trial 14 months after completing the Phase 2a clinical trial, and was therefore a treatment interrupted patient, but remained on a stable HU dose (3000mg daily) during this interim period and while on the OLE clinical trial. As of December 31, 2020, we had data on Patient #2 through eight months of treatment, reflecting the most recent OLE visit for this patient. Patient #2 has shown sustained increases in levels of HbF and F-cells over baseline, however this patient has also shown increasing variability in other SCD biomarkers subsequent to the original case narrative presented in August 2020.

The table below presents biomarker results for this patient at baseline, four months on study (as presented in the third quarter of 2020) and eight months on study (the most recent OLE visit for this patient):

Parameter	Baseline OLE*	12-month OLE	18-month OLE	Absolute change (18-month vs baseline)	Percent change (18-month vs baseline)
F-cells (%)	59.7	81	71.3	11.6	19%
HbF (%)	20.7	29.7	25.2	4.5	22%
Hb (g/dL)	10	10.7	9.5	-0.5	-5%
MCV (fL)	107	122	115	8	7%

* As Patient #2 was a treatment interrupted patient, baseline was reestablished upon initiation of the OLE clinical trial (to the extent each are available, mean of baseline at screening and initiation of treatment).

In addition, a comparison of VOC data for Patient #2 for the eight-month OLE clinical trial period versus information from a retrospective review of the patient's medical records for the eight-month period prior to initiation of the OLE clinical trial indicate potential benefits of IMR-687 being administered in combination with HU. In the eight-month period on IMR-687, the patient had a 69% reduction (16 to 5 events) in reported VOCs, as compared to the eight-month period prior to IMR-687 administration.

We caution that the case narratives reflect data from only two patients at specified intervals in the OLE clinical trial and reported VOC comparisons involve retrospective reviews of the patients' medical records. As a result, we cannot assure you that future data on these patients will continue to be favorable or that data on other patients in the OLE clinical trial will demonstrate potential benefit of IMR-687. We plan to present more data on these patients at future medical meetings.

Ardent Phase 2b Clinical Trial of IMR-687 in SCD

In the second quarter of 2020, we initiated a Phase 2b clinical trial, which we refer to as the Ardent trial, of IMR-687 in SCD and enrollment is ongoing. The Ardent trial is designed as a randomized, double-blind, placebo-controlled, multicenter study of approximately 99 patients, aged 18 to 65 years with SCD and one to 12 VOC episodes within the 12 months preceding enrollment. Patients concomitantly receiving a stable dose of HU according to the patient's established treatment plan are eligible for enrollment. Patient randomization will be stratified by use of HU as well as by region. We plan to utilize weight-based dosing due to the possible wide range of patient weights in the trial and the increased drug exposure resulting from our use of 300 mg and 400 mg doses. We believe this use of weight-based dosing will more precisely manage drug exposure and tolerability, so that patients with below average weights do not receive too high of a dose and patients with above average weight do not receive too low of a dose. The lower-dose IMR-687 arm will test a range of 3.0 mg/kg up to 4.5 mg/kg (including up to a 300 mg dose) and patients will be randomly assigned in a 2:1 ratio to receive either IMR-687 or placebo. The higher-dose IMR-687 arm will test a range of 4.5mg/kg up to 6.7 mg/kg (including up to a 400 mg dose). Prior to enrolling the higher-dose IMR-687 arm, the independent DMC will review the then-available safety and tolerability data and, if the DMC recommends inclusion of the higher dose, randomization will then proceed in a 1:2:1 ratio (IMR-687 lower dose, IMR-687 higher dose or placebo). We expect the DMC to make a decision on opening the higher-dose IMR-687 arm in March 2021. The dose levels to be administered in the Ardent trial are designed to provide meaningful exposure to IMR-687 that could be up to two-fold that employed in the Phase 2a trial and utilize the 300 mg and potentially 400 mg dose for the first time.

The planned primary efficacy objective of the Ardent trial is to evaluate the proportion of patients with HbF response, defined as an increase of ≥3% in HbF from baseline to week 24, compared to placebo, and the trial is powered for statistical significance with respect to this endpoint. Planned secondary objectives include the evaluation of the effect of IMR-687 versus placebo on (i) HbF-associated biomarkers, (ii) indices of red cell hemolysis, (iii) indices of WBC adhesion, (iv) the incidence of VOCs in relation to HbF levels, and (v) quality of life measures. In addition, the Ardent trial will examine exploratory clinical endpoints, based in part, on the published *FDA-ASH Guide to Clinical Development of Sickle Cell Disease Therapies*. While the primary efficacy endpoint for the trial will assess results after 24 weeks of treatment, patients will continue on treatment through 52 weeks to provide data for additional exploratory endpoints and to measure the incidence of VOCs over the course of a one-year period. Following the completion of 52 weeks of dosing in the trial, patients will be eligible to enroll in an open-label extension study. In addition, there are pre-specified interim analyses planned in the trial, with the first such interim analysis being conducted when 33 patients have reached 24 weeks of dosing. We expect to report data from this first interim analysis in the second half of 2021.

Our systematic literature review and series of meta-analyses support our belief that HbF has the potential to predict clinical benefit and thus could serve as a surrogate endpoint for accelerated approval in SCD. Drugs that could qualify for accelerated approval are those that treat a serious or life threatening condition, generally provide a meaningful advantage over available therapies, and demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit.

In the first quarter of 2020, we held a face-to-face Type B meeting with the FDA under our Fast Track designation for IMR-687 to discuss both the potential for HbF to serve as a surrogate endpoint for accelerated approval as well as the design of later stage SCD trials seeking to establish the effect of HbF on important clinical outcomes in SCD. In the preliminary meeting comments, the FDA recommended that we conduct a Phase 2b dose finding trial instead of a Phase 2b/3 trial design that we proposed. At the Type B meeting, the FDA commented that our revised Phase 2b trial design and approach to data collection to support HbF as a potential surrogate endpoint was acceptable. The FDA also stated that it would welcome further discussion as the data from the Phase 2b trial matures to discuss the concept of the acceptability of HbF and a potential threshold of 3% from baseline as an acceptable surrogate endpoint. The FDA stressed the importance of defining clear and strong assumptions and having robust results, which would be evaluated by the FDA to test if 3% HbF or higher would provide meaningful clinical benefit and therefore constitute an acceptable surrogate endpoint for a future pivotal trial of IMR-687 in SCD.

Pediatric Development Program of IMR-687 in SCD

We currently anticipate initiating our pediatric clinical program of IMR-687 in SCD in the first half of 2021. We expect to conduct a Phase 1/2 clinical trial in adolescents (12-17 years old) comprised of a single ascending dose, followed by a 36-week multiple dose expansion phase. In December 2020 we held a Type C meeting with the FDA, during which the agency expressed general alignment with the overall clinical trial design and indicated the study could be submitted with the adult study data in the same NDA.

SAD/MAD Clinical Study in Health Volunteers

In the first half of 2021, we expect to initiate a single ascending dose, or SAD, followed by a multiple dose clinical trial of IMR-687 to explore the safety, tolerability, and PK of higher doses of IMR-687. This short duration study in healthy volunteers under fed conditions will sequentially assess doses of IMR-687 up to 800 mg per day administered once daily or twice daily. Based on the safety, tolerability and PK profile observed in the SAD portion of the trial, the multi-dose portion of the trial will evaluate multiple doses of IMR-687 at the maximum tolerated dose observed for both the once daily and twice daily administrations from the SAD portion of the trial.

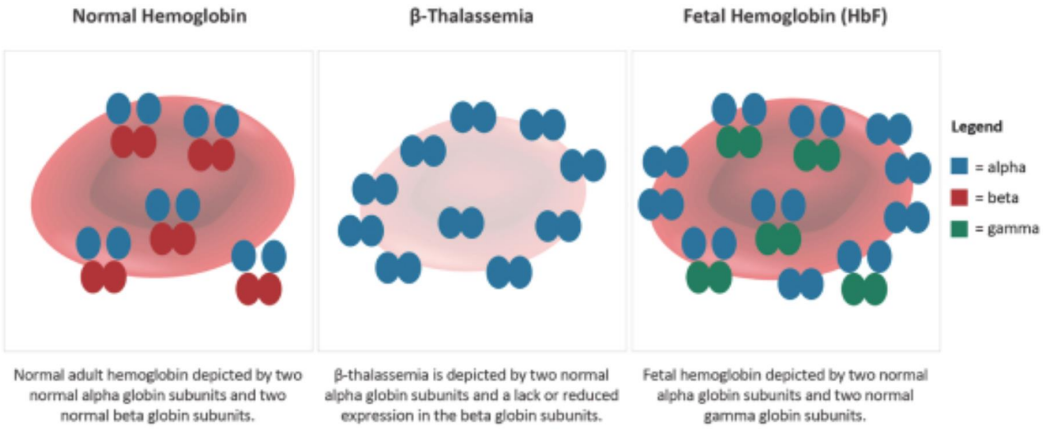
β-thalassemia Disorder Overview

β-thalassemia, which is part of the second group of hemoglobinopathies, is a rare inherited RBC disorder. Unlike patients with SCD, patients with β-thalassemia have a mutation that causes the absence or decreased synthesis of the beta globin subunit of hemoglobin, thereby creating an over-abundance of the alpha globin subunit. This causes the formation and aggregation of insoluble clumps that lead to ineffective RBC production and a reduction in the number of functioning RBCs. Furthermore, the RBCs that do survive have shorter lifespans and are smaller, paler and less efficient at transporting oxygen throughout tissues of the body. Oftentimes, RBCs of smaller size, measured as mean corpuscular volume, is a first indication of β-thalassemia prior to genotyping. If left untreated, β-thalassemia causes severe anemia, splenomegaly, skeletal abnormalities, organ failure and early death.

β-thalassemia presents as a spectrum of disease, with patients categorized based on hemoglobin levels and clinical manifestations. Although β-thalassemia can be classified as “major,” “intermedia,” and “minor,” a more recent classification is based on a patient’s dependency on blood transfusion. Most β-thalassemia major patients are classified as TDT, while intermedia and minor patients are classified as NTDT. TDT patients have a transfusion regimen that is well established and generally lifelong. NTDT patients are a clinically diverse group, with transfusions required intermittently during periods of RBC stress, such as pregnancy, infection, surgery, times of rapid growth and sometimes later in life.

As in SCD, a promising way to address the missing or decreased presence of the beta globin subunit is to induce HbF production. In addition to resolving persistent anemia, HbF induction rectifies the missing or mutated beta globin subunit and thereby reduces the overabundance of free-floating alpha globin subunits. These benefits have the potential to result in increased functional RBC production, higher hemoglobin levels, reduced hemolysis and the reduction of adhesion and inflammation. Like in SCD, infants with β-thalassemia major do not present clinical symptoms of their disorder until age six to 24 months, and sometimes later, when their HbF is replaced by mutated adult hemoglobin. Natural history data show that patients with β-thalassemia who have high HbF levels, due to hereditary persistence of HbF, have less severe forms of the disorder. In addition, genetic variations associated with increased HbF production have been shown to correlate with reduced β-thalassemia severity.

The image below depicts how RBCs and hemoglobin can change as a result of gene mutations in β-thalassemia. In healthy individuals, there are equal amounts of alpha globin and beta globin subunits, which form normal hemoglobin. In β-thalassemia, the absence and/or mutation of beta globin subunits cause excessive alpha subunits that often aggregate into clusters. In cells with reactivated HbF, the gamma subunit reduces the effects of free-floating alpha chains and may improve hemoglobin efficiency and RBC health.



The potential of HbF induction has been observed through off-label use of HU to treat patients with β-thalassemia and has been explored in numerous clinical trials in both NTDT and TDT patients. Most of these efforts were not randomized controlled trials, and many of them lacked a placebo comparator. Nevertheless, HbF induction by HU showed promising early response in TDT and NTDT patients. In fact, there are numerous documented cases both in clinical trials and in off-label real world use where TDT patients have a reduced need for transfusions with continued HU treatment. Despite these observed benefits, and similar to SCD, there continue to be limitations with HU as a therapy in β-thalassemia, including its toxicity, dosing schedule and potential long-term effects.

In addition to HbF induction, independent research suggests activation of the nitric oxide-cyclic GMP signaling pathway may induce RBC production, which is associated with increases in RBC counts and hemoglobin levels. We believe this is an important mechanism of action to that could be relevant in reducing disease burden. Furthermore, adhesion mediators are also highly upregulated in patients with β-thalassemia and may contribute to the increased number of clots in their blood vessels, known as a hypercoagulability state. Specifically, data show that two adhesion markers, ICAM-1 and VCAM-1, are over-expressed in patients with β-thalassemia as compared to controls. Furthermore, there is evidence that WBCs in patients with β-thalassemia express higher levels of CD11b and CD18, two important biomarkers in the WBC activation cascade. In preclinical SCD studies, we observed that IMR-687 reduced levels of CD11a and CD11b and CD18.

Addressable Patient Population

The prevalence of β-thalassemia globally is estimated to be 288,000, with an incidence of 60,000 births per year. The total combined prevalence of β-thalassemia in the United States and European Union is estimated to be approximately 19,000 patients. Of the patients currently treated in the United States and European Union, we believe approximately 50% and 10%, respectively, are transfusion dependent. β-thalassemia is especially prevalent in developing countries of Africa, South Asia, Southeast Asia, the Mediterranean region and the Middle East. Although historically prevalent in Mediterranean North Africa and South Asia, thalassemias are now encountered in other regions as a result of changing migration patterns. As such, there is a growing focus on developing new therapeutics aimed at improving quality of life for this significant unmet medical need.

Approved and Emerging Modalities and Their Limitations

Approved Treatments

Blood transfusions have been the standard of care treatment for β-thalassemia. The risks associated with transfusions are similar to those seen in the SCD population, but higher frequency of use often results in iron overload toxicities, a secondary complication of this treatment. Over time, iron becomes trapped in the tissues of vital organs, which can lead to diabetes, cirrhosis, osteoarthritis, heart attack and hormone imbalances. If not addressed, excess iron can result in organ failure and death. There are several approved agents that remove iron from the body, known as iron chelators, but they have significant challenges including high costs, the requirement for frequent monitoring, therapy complications and patient incompatibility.

HSCT is a potential curative therapy for β-thalassemia and has demonstrated successful outcomes across patient types. However, as in SCD, there are numerous barriers to use, including increased mortality risk, that have limited its broader adoption. Recently, the European Commission granted conditional marketing authorization for ZYNTEGLO, a gene therapy approach to β-thalassemia for patients 12 years and older with TDT and for whom HSCT is appropriate, but a donor has not yet been matched or been made available. The long-term efficacy of the therapy remains unknown, as do many of the associated risks.

In November 2019, the FDA approved REBLOZYL (luspatercept-aamt) for the treatment of anemia in adult patients with β-thalassemia who require regular RBC transfusions. REBLOZYL is a modified receptor protein that promotes RBC maturation and increases overall RBC production, but does not address other cell types implicated in β-thalassemia. REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia. REBLOZYL is the first and only FDA-approved erythroid maturation agent, representing a new class of therapy which works by regulating late-stage RBC maturation to help patients reduce their RBC transfusion burden.

Emerging Modalities

There has been increased development of new treatments for β-thalassemia, but no clinical-stage program addresses the full spectrum of the disease in an oral once-a-day tablet. These treatments can be broadly categorized into the following approaches:

RBC Maturation. Clinical stage programs in this category generally are aimed at promoting RBC maturation and/or increasing overall RBC production, but do not address other cell types implicated in b-thalassemia. Several molecules targeting this pathway, which includes the key regulators hepcidin and ferroportin, are in Phase 2 clinical development in patients with b-thalassemia to treat chronic anemia associated with ineffective erythropoiesis and iron overload. These include IONIS-TMPRss6-LRx, an antisense drug under development by Ionis Pharmaceuticals, andVIT-2763, a ferroportin inhibitor under development by Vifor Pharma.

Gene Therapy/Editing: As with SCD, gene therapy and gene editing approaches are also being developed as potential curative therapies for b-thalassemia. Lentiglobin is a gene therapy treatment in Phase 3 clinical development by bluebird bio, while CTX-001 and ST-400 are gene editing therapies currently in Phase 2 clinical development by CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals, Incorporated) and Sangamo Therapeutics, Inc. (in collaboration with Sanofi), respectively. Gene therapy involves pretreatment regimens associated with standalone risk which may limit its use in broad patient populations, and gene editing approaches still have many unanswered questions, including off-target mutagenesis.

PKR Activators. Drug candidates are being developed that activate PKR, an enzyme that is involved in the conversion of sugar into energy and is critical for the survival of RBCs. Agios Pharmaceuticals, Inc. is evaluating mitapivat in a Phase 2 clinical trial in non-transfusion-dependent patients with ß-thalassemia. Forma Therapeutics has reported that it plans to initiate clinical development of its PKR activator, FT-4202, in patients with ß-thalassemia.

Our Solution for β-thalassemia: IMR-687 as a Differentiated PDE9 Inhibitor

PDE9 is a potent and highly selective mechanism that uniquely targets cyclic GMP degradation, making it a promising pathway to increase cyclic GMP, reactivate HbF, enhance RBC production, enable RBC maturation, and reduce WBC activation in β-thalassemia. We believe IMR-687 is a differentiated PDE9 inhibitor that is highly potent, selective for its target, minimally brain penetrating, and is delivered in an oral once-a-day therapy, which could be used globally.

Preclinical Data of IMR-687 in ß-thalassemia

We conducted preclinical studies in a ß-thalassemia mouse model that recapitulates the human NTDT condition. This mouse model lacks a functional beta globin subunit, leading to deficits in hemoglobin and RBCs, as well as slowed RBC maturation. After 30 days of treatment at two different doses, we observed that IMR-687 induced statistically significant increases in functional hemoglobin and total RBC counts in a dose dependent way, with the 60mg/kg dose outperforming the 30mg/kg dose. Allometric scaling to reflect dose conversion from mouse to human indicates that the 30mg/kg mouse dose is equivalent to a human dose of approximately 2.4mg/kg and the 60mg/kg mouse dose is equivalent to a human dose of approximately 4.9mg/kg.

Promotion of RBC maturation, a key mechanistic component in reducing ß-thalassemia pathology, was also observed in preclinical studies. After 30 days of once-a-day treatment with 30 mg/kg and 60 mg/kg of IMR-687, we observed that erythroblast maturation was significantly improved as a result of increasing the amount of Ery.C, which is the population of mature erythroblasts, in comparison to Ery.B, which are more immature erythroblasts. These changes were also associated with a decrease on the ratio of Ery.B to Ery.C, otherwise known as a maturation index, where lower ratio indicates progression to maturity.

We believe the NTDT mouse model provides promising *in vivo* proof of concept that IMR-687 can improve the RBC-mediated aspects of ß-thalassemia. In addition, we believe the preclinical activity observed in NTDT models will translate to TDT preclinical models and supports clinical development in both populations. While SCD and ß-thalassemia are distinct hemoglobinopathies, they share similar pathophysiology and symptomology which support our strategy of developing IMR-687 across these indications.

Forte Phase 2b Clinical Trial of IMR-687 in ß-thalassemia

In the second quarter of 2020, we initiated a randomized, double-blind, placebo-controlled Phase 2b clinical trial, which we refer to as the Forte trial, in adult patients with ß-thalassemia and enrollment is ongoing. The trial will evaluate the safety and tolerability of IMR-687 in approximately 60 TDT patients and approximately 60 NTDT patients. Additionally, for TDT patients, we plan to evaluate the effect of IMR-687 versus placebo in reducing the average number of days between red blood cell transfusions, or transfusion burden, and change in iron load rate as the result of transfusion, for the treatment period as compared to the 12 weeks prior to screening. Frequent transfusions in TDT patients lead to iron overload, which is a common complication often leading to the development of organ damage and increased mortality in these patients. Accordingly, improvement in iron load rate is an important measure of an effective therapy for TDT patients. For NTDT patients, we plan to evaluate the effect of IMR-687 versus placebo on HbF as well as on anemia. The Forte trial will also examine additional exploratory efficacy endpoints as well as additional safety and PK endpoints.

The Forte trial will consist of a retrospective data collection period, a screening period, a double-blind treatment period and a safety follow-up period. Similar to our Phase 2b trial of IMR-687 for SCD, we plan to utilize weight-based dosing. We believe this use of weight-based dosing will more precisely manage drug exposure and tolerability, so that patients with below average weights do not receive too high of a dose and patients with above average weight do not receive too low of a dose. The lower-dose IMR-687 arm will test a range of 3.0mg/kg up to 4.5mg/kg (including up to a 300 mg dose) and patients will be randomly assigned in a 2:1 ratio to receive either IMR-687 or placebo. The higher-dose IMR-687 arm will test a range of >4.5mg/kg up to 6.7mg/kg (including up to a 400 mg dose). In January 2021, an independent DMC reviewed available safety and tolerability data and recommended inclusion of the higher dose arm. Going forward, randomization will proceed in a 1:2:1 ratio (IMR-687 lower dose, IMR-687 higher dose, or placebo). Safety and tolerability will be assessed after 24 weeks of dosing. There are pre-specified protocol-driven interim analyses planned in the trial, with the first such interim analysis being conducted when 30 patients have reached 24 weeks of dosing and an additional interim analysis being conducted when 30 patients have reached 36 weeks of dosing. We expect to report data from the first interim analysis in the second half of 2021.

Preclinical Pipeline

We are advancing a pipeline of development-stage programs utilizing IMR-687 targeting additional indications, including HFpEF, for which we began preclinical research in the second quarter of 2020. Heart failure affects approximately 26 million people worldwide. HFpEF represents almost half of all cases of heart failure with approximately 2.5-3 million affected adults in the United States alone. Pathophysiologic characteristics of HFpEF include ventricular hypertrophy, diastolic dysfunction, endothelial dysfunction, insulin resistance and inflammation and many of these have also been described in SCD. Cyclic GMP is known to play a pivotal role in cardiovascular and metabolic health. For example, increased cyclic GMP signaling promotes vasodilation, natriuresis, diuresis, insulin sensitivity and lipolysis, and can inhibit cardiac hypertrophy, inflammation and adverse platelet-leukocyte-endothelial interactions, the latter of which have also been implicated in SCD. Therefore, increasing cyclic GMP by PDE9 inhibition may be an attractive target for the treatment of HFpEF and a natural extension from our lead program in SCD. To investigate this hypothesis, we leveraged our existing clinical program in SCD and tested IMR-687 in preclinical models of HFpEF.

In October 2020, the results of an exploratory analysis co-led by VUMC on data from the second interim analysis from our Phase 2a clinical trial of IMR-687 in adult patients with SCD were presented. The exploratory analysis examined the potential of IMR-687 to reduce cardiovascular risk in patients with SCD. We measured plasma concentrations of NT-proBNP, a well-established biomarker of cardiovascular risk (higher levels associate with greater risk). We found patients treated with IMR-687 in combination with HU saw a mean decrease in NT-proBNP of 27.3% from baseline over four months. In contrast, patients on background HU alone saw a mean increase in NT-ProBNP levels of 27% from baseline over four months. The magnitude of this difference in treatment effect was more pronounced among patients with higher baseline NT-proBNP levels. Specifically, among patients with baseline NT-proBNP values greater than 400 pg/ml, treatment with IMR-687 in combination with HU led to a mean reduction of 67.9% from baseline in NT-proBNP over four months, as compared with a mean increase of 28.0% from baseline in patients who received HU alone. As SCD is a condition characterized by acute and chronic vasculopathy as well as high cardiovascular morbidity and mortality, this exploratory analysis by VUMC provides exploratory human data supporting our belief that PDE9 inhibition with IMR-687 may serve as an attractive target for the prevention and treatment of cardiovascular disease, such as HFpEF.

To compliment the observed human data, we also entered into an agreement with the Necker Institute of Paris, France in the second quarter of 2020 to conduct *in vivo* studies with IMR-687 in three different established mouse models for HFpEF. In the first model we tested whether IMR-687 could prevent the development of HFpEF induced by unilateral nephrectomy and six-week continuous infusion of d-aldosterone. IMR-687 was administered at doses of 60 mg/kg or 100

mg/kg concurrently with d-aldosterone for six weeks. The results showed that IMR-687 significantly attenuated the development of cardiac and cardiomyocyte hypertrophy and limited the increase in biomarkers of myocardial inflammation and fibrosis. Congruent findings were obtained in the second model, in which mice received continuous infusion of angiotensin II for six weeks to produce the HFpEF phenotype. IMR-687 was administered at doses of 60 or 100 mg/kg concurrently with angiotensin II infusion for six weeks. The results showed that IMR-687 attenuated cardiac and cardiomyocyte hypertrophy and limited the increase in biomarkers of myocardial inflammation and fibrosis. In addition to these two preventive models, a third model was employed to test the therapeutic potential of IMR-687 to treat prevalent HFpEF. In this study, twenty-week-old diabetic prone obese mice that previously displayed the HFpEF phenotype were assigned to receive vehicle or IMR-687 at 60- or 100-mg/kg for eight weeks. The mice treated with IMR-687 displayed significantly less cardiomyocyte hypertrophy and lower levels of biomarkers of myocardial inflammation and fibrosis. In the control arms of all three models, we found increased myocardial transcript levels of PDE9, atrial natriuretic peptide, or ANP, and B-type natriuretic peptide, or BNP, providing possible evidence for HFpEF being a condition of PDE9 excess. In all three models, we found IMR-687 significantly reduced PDE9, ANP and BNP transcript levels in a dose-dependent manner.

We are collaborating with VUMC and have engaged additional key opinion leaders in heart failure, with the aim of developing a Phase 2 protocol with the potential to establish proof-of-concept of IMR-687 in the treatment of patients with HFpEF. Additionally, we have begun work on a new formulation of IMR-687 that potentially could be used in this indication.

Exclusive License Agreement

In April 2016, we entered into an agreement with H. Lundbeck A/S, or Lundbeck, for a worldwide license under certain patent rights and certain know-how owned or otherwise controlled by Lundbeck within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies, which we refer to as the field. This agreement was amended in July 2016 and October 2017.

The agreement grants us an exclusive license under the licensed technology, including the right to grant sublicenses with certain restrictions, to research, develop, make, have made, use, sell, have sold, offer to sell, import, export and commercialize any product comprising or containing certain PDE9 inhibitors, in the field. We call such products licensed products. Subject to certain restrictions, under the agreement, we grant Lundbeck a non-exclusive, irrevocable, perpetual, worldwide, sub-licenseable, and fully paid-up right and license under patent rights we control to the extent necessary for Lundbeck to research, develop, make, have made, use, sell, have sold, offer to sell, import, export and commercialize licensed products outside of the field.

The agreement also grants us a non-exclusive license under the licensed technology to research and develop, and make, have made, use, import and export for purposes of enabling such research and development, enhancements, improvements, modifications or derivatives to licensed products, until but not beyond a specified pre-commercialization developmental stage with respect to each such enhancement, improvement, modification or derivative. We have the right to request that Lundbeck grant us an exclusive development and commercialization license to one or more compounds identified through these activities as a back-up compound.

As partial consideration for the licenses granted under the agreement, we issued 167,523 shares of our common stock to Lundbeck in April 2016. We issued 127,002 shares of our common stock to Lundbeck in December 2016 and 148,746 shares of our common stock in August 2017 as a result of antidilution provisions contained in the exclusive license agreement triggered by subsequent closings of our series A preferred stock financing. We are also obligated to make milestone payments to Lundbeck aggregating up to (i) $23.5 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any licensed product and (ii) $11.8 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any Imara product that is or comprises a PDE9 inhibitor but is not a licensed product, which is referred to as a PDE9 product, if any. We are obligated to pay tiered royalties of low-to-mid single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of licensed products, and tiered royalties of low single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of PDE9 products, if any. The royalties are payable on a product-by-product and country-by-country basis. Our obligation to make royalty payments extends with respect to a licensed product in a country until the later of ten years after the first commercial sale of that licensed product in that country and the expiration of the last-to-expire valid claim of a patent or patent application licensed from Lundbeck covering the licensed product or any constituent licensed compound in that country. Our obligation to make royalty payments extends with respect to a PDE9 product in a country until the ten years

after the first commercial sale of such PDE9 product in that country. To date pursuant to this agreement, we have made cash payments to Lundbeck of $1.8 million consisting of an upfront payment and ongoing milestone payments.

The agreement obligates us to use commercially reasonable efforts to develop, seek regulatory approval for, manufacture, market and otherwise commercialize at least one licensed product, in accordance with a development plan and a development milestone timetable specified in the agreement. We have the option to extend the development milestone timetable up to two times by agreeing to additional payment obligations.

Both we and Lundbeck have the right to terminate the agreement if the other party materially breaches the agreement and fails to cure such breach within specified cure periods or in the event the other party undergoes certain bankruptcy events. Lundbeck may terminate the agreement if we or any of our affiliates, sublicensees or subcontractors bring specified patent challenges against Lundbeck or assist others in bringing such a patent challenge against Lundbeck and fail to cease such challenge within a specified period of time. We have the right to terminate the agreement for our convenience at any time on six months' prior written notice to Lundbeck.

Competition

The biopharmaceutical industry is characterized by rapidly advancing technologies, intense competition and strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and government agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors may also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, and establishing clinical trial sites and patient registration for clinical trials. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

If our lead product candidate, IMR-687, is approved for the indications that we are currently targeting, it will likely compete with the currently marketed drugs and, if approved, the therapies in development discussed below.

Sickle Cell Disease

Approved drug treatments for SCD focus primarily on the management of anemia and reduction of VOCs. Until November 2019, there were only two drug treatments approved in the United States: HU and Endari. HU, marketed under trade names including DROXIA by Bristol-Myers Squibb Company, as well as in generic form, is approved for the treatment of anemia related to SCD, to reduce the frequency of VOCs and the need for blood transfusions. Endari, marketed by Emmaus Life Sciences, Inc., is an oral powder form of L-glutamine approved to reduce severe complications associated with the disorder.

In November 2019, the FDA granted accelerated approval for Oxbryta (voxelotor) for the treatment of SCD in adults and children 12 years of age and older. Oxbryta is an oral therapy taken once daily and is the first approved treatment that directly inhibits sickle hemoglobin polymerization. In addition, in November 2019, the FDA approved Adakveo (crizanlizumab), to reduce the frequency of VOCs in adult and pediatric patients aged 16 years and older with SCD. Adakveo is administered intravenously and binds to P-selectin, which is a cell adhesion protein that plays a central role in the multicellular interactions that can lead to vaso-occlusion.

These two recent approvals represent important milestones for patients with SCD. We believe that IMR-687's differentiated mechanism of action that seeks to increase HbF in patients with SCD, and the association between increases in HbF and reductions in disease risk, have the potential to provide IMR-687, if approved, with competitive advantages over Oxbryta, where the correlation between increases in hemoglobin and disease risk is being tested in a post-approval confirmatory trial, and Adakveo, which is administered intravenously and does not target RBC sickling. Further, IMR-687 acts primarily on red blood cells and has the potential to act on white blood cells, adhesion markers and other cell types that are implicated in SCD. We believe that IMR-687's multimodal mechanism-of-action has the potential to demonstrate significant benefit to patients with SCD.

Blood transfusions are also used to treat SCD, and can transiently bolster hemoglobin levels by adding functional RBCs. There are a number of limitations associated with this therapeutic approach, including limited patient access and serious complications such as iron overload. The only potentially curative treatment currently approved for severe SCD is HSCT. However, this treatment option is not commonly used given the difficulties of finding a suitable matched donor and the risks associated with the treatment, which include an approximately 5% mortality rate. HSCT is more commonly offered to pediatric patients with available sibling-matched donors.

IMR-687 could face competition from a number of different therapeutic approaches in development for patients with SCD. For example, bluebird bio has reported that it plans to submit a biologic license application, or BLA, for LentiGlobin for the treatment of SCD in 2022 based on the results of its ongoing Phase 2 clinical trial. Aruvant Sciences, Inc. is developing ARU-1801, a gene therapy treatment in Phase 2 clinical development. There are also several gene editing approaches to treating SCD under evaluation, including CTX-001, currently in Phase 2 clinical development by CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals, Incorporated), BIVV-003, currently in Phase 1/2 clinical development by Sangamo Therapeutics, Inc. (in collaboration with Sanofi), and OTQ923, currently in Phase 1/2 clinical development by Intellia Therapeutics, Inc. (in collaboration with Novartis). There are also several therapeutic approaches under development outside of gene editing/therapy. Novo Nordisk A/S (in collaboration with EpiDestiny, Inc.) is evaluating EPI-01, a small molecule designed to increase production of HbF, in Phase 1 clinical trials. Fulcrum Therapeutics, Inc. is developing FTX-HbF, a small molecule designed to upregulate HbF. Agios Pharmaceuticals, Inc. is developing the PKR activator mitapivat (AG-348), which is in Phase 1/2 clinical development, and Forma Therapeutics, Inc. is developing the PKR activator FT-4202, which is in Phase 3 clinical development. In addition, Syros Pharmaceuticals, Inc., in collaboration with Global Blood Therapeutics, is using its gene control platform to discover and develop product candidates to activate gamma globin expression to induce the production of HbF for the treatment of SCD.

ß-thalassemia

Until November 2019, there were no approved drug therapies for ß-thalassemia in the United States. The current standard of care for many patients with ß-thalassemia has been frequent blood transfusions to manage anemia. A potentially curative therapy for ß-thalassemia is HSCT, which is associated with serious risk and is limited to patients with a suitable donor.

In November 2019, the FDA approved REBLOZYL (luspatercept-aamt) for the treatment of anemia in adult patients with ß-thalassemia who require regular RBC transfusions. REBLOZYL is a modified receptor protein that promotes RBC maturation and increases overall RBC production, but does not address other cell types implicated in ß-thalassemia. REBLOZYL is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia. REBLOZYL is dosed subcutaneously and is administered every three weeks in an outpatient setting.

In June 2019, the European Commission granted conditional marketing authorization for ZYNTEGLO, a gene therapy developed by bluebird bio for the treatment of adult and adolescent patients with transfusion-dependent ß-thalassemia and with certain genotypes. Bluebird bio submitted its rolling BLA to the FDA which it has announced that it plans to complete in 2021.

IMR-687 could face competition from a number of different therapeutic approaches that are in development as a therapeutic option for patients with transfusion-dependent or non-transfusion-dependent ß-thalassemia.

For example, Ionis Pharmaceuticals and Vifor Pharma have ongoing Phase 2 trials to evaluate therapies targeting RBC maturation (IONIS-TMPRss6-LRx andVIT-2763, respectively). Agios Pharmaceuticals, Inc. is evaluating mitapivat, a PKR activator, in a Phase 2 clinical trial in non-transfusion-dependent patients with ß-thalassemia. Forma Therapeutics has reported that it plans to initiate clinical development of its PKR activator, FT-4202, in patients with ß-thalassemia. Sangamo (in collaboration with Sanofi) is conducting a Phase 1/2 clinical trial of ST-400, which uses a genome-edited cell therapy approach designed to produce functional RBCs using HbF. CRISPR Therapeutics AG, in collaboration with Vertex, is conducting a Phase 1/2 clinical trial of CTX-001, which uses a gene editing approach to upregulate the expression of HbF, in patients with transfusion-dependent ß-thalassemia. Syros Pharmaceuticals, Inc., in collaboration with Global Blood Therapeutics, is using its gene control platform to identify and develop product candidates to activate gamma globin expression to induce the production of HbF for the treatment of ß-thalassemia.

We believe that IMR-687's differentiated mechanism of action and oral route of administration have the potential to provide IMR-687, if approved, with competitive advantages over approved therapies for ß-thalassemia, including REBLOZYL.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including by seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field.

Our future commercial success depends, in part, on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce in our intellectual property rights, in particular our patent rights; preserve the confidentiality of our trade secrets; and operate without infringing, misappropriating or violating the valid and enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing any products we develop may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of biopharmaceutical companies like ours are generally uncertain and can involve complex legal, scientific and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will issue with respect to any patent applications that we or our licensors may file in the future, nor can we ensure that any of our owned or licensed patents or future patents will be commercially useful in protecting our product candidates and methods of manufacturing the same. In addition, the coverage claimed in a patent application may be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any products we develop will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented or invalidated by third parties. See “Risk Factors—Risks Related to Our Intellectual Property” for a more comprehensive description of risks related to our intellectual property.

We generally file patent applications directed to our key programs in an effort to secure our intellectual property positions vis-a-vis these programs. As of December 31, 2020, we owned, co-owned, or held exclusive license rights to numerous patent and patent applications, including at least six issued or allowed U.S. patents, five U.S. pending non-provisional patent applications, 29 issued or allowed non-U.S. patents, including four European patent applications which have been validated among individual European Patent Convention nations, 76 non-U.S. pending patent applications, and three pending Patent Cooperation Treaty, or PCT, applications.

The intellectual property portfolio for our most advanced program as of December 31, 2020, is summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office may be significantly narrowed before issuance, if issued at all. We expect this may be the case with respect to some of our pending patent applications referred to below.

IMR-687

The patent portfolio for our IMR-687 program includes at least six published patent families. As of December 31, 2020, we owned, co-owned, or held exclusive license rights to numerous patent and patent applications, including at least six issued or allowed U.S. patents, five U.S. pending non-provisional patent applications, 29 issued or allowed non-U.S. patents, including four European patent applications which have been validated among individual European Patent Convention nations, 76 non-U.S. pending patent applications, and three pending PCT applications relating to our IMR-687 program. These patents and patent applications comprise the following patent families:

The issued patents include coverage of the IMR-687 composition of matter. The issued patents include US 9,643,970 (exclusively licensed to us from Lundbeck A/S), which issued May 2017. This U.S. patent and related international family members are directed to the IMR-687 composition of matter, including racemic mixtures. The expected expiry date of US 9,643,970, including 63 days of Patent Term Adjustment, based on a 20-year term, of US 9,643,970, is December 2032, absent any other patent term extensions available.

The issued patents also include US 9,434,733 (exclusively licensed to us from Lundbeck A/S), which issued September 2016. This U.S. patent and related international family members are directed to the alternative PDE9 inhibitor compositions of matter, including racemic mixtures. The expected expiry date, based on a 20-year term, of US 9,434,733, is January 2033, absent any patent term extensions available.

The issued patents also include US 10,513,524 (exclusively licensed to us from Lundbeck A/S), which issued December 2019. This U.S. patent and related international family members provide further protection for the IMR-687 composition of matter, including the enantiomer, in addition to coverage of therapeutic methods of treating sickle cell disease with IMR-687. The expected expiry date, based on a 20-year term, of US 10,513,524 is July 2036, absent any patent term extensions available.

The pending applications include an additional patent family directed to therapeutic methods with a priority filing date of July 2016. A patent in Morocco has been allowed in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is June 2037, absent any patent term extensions available.

The pending applications also include a patent family directed to process chemistry for manufacturing with a priority date of May 2017. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2038, absent any patent term extensions available.

The PCT applications include a patent family directed to polymorphs of IMR-687 with a priority filing date of May 2018. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2039, absent any patent term extensions available.

The pending PCT applications also include a PCT application directed to solid dose formulations of IMR-687 with a priority filing date of August 2018. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is August 2039, absent any patent term extensions available.

The pending PCT applications also include a PCT application directed to liquid solution formulations of IMR-687 with a priority filing date of April 2019. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is April 2040, absent any patent term extensions available.

The pending PCT applications also include a PCT application directed to therapeutic methods of treating thalassemia with a priority date of May 2019. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2040, absent any patent term extensions available.

While we believe that the specific and generic claims contained in our owned and licensed pending U.S., non-U.S., and PCT applications provide protection for the claimed pharmaceutical compositions and methods of use, third parties may nevertheless challenge such claims.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering IMR-687 may be entitled to patent term extensions. If our use of drug candidates or the drug candidate itself receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved use or drug candidate. We also intend to seek patent term extensions in any jurisdictions where available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we rely upon unpatented trade secrets and confidential know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. We seek to protect our proprietary information, in part, using confidentiality agreements with any collaborators, scientific advisors, employees and consultants and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. These agreements may not provide meaningful protection. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and/or confidential know-how may become known or be

independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. See "Risk Factors—Risks Related to Our Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated clinical-trial scale demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our relationships with contract manufacturers.

Sales and Marketing

In light of our stage of development, we have not yet established a commercial organization or distribution capabilities. We have retained worldwide commercial rights for our product candidates. If our product candidates receive marketing approval, we plan to commercialize them in the United States and Europe and potentially other international regions with our own sales force.

Government Regulation and Product Approvals

Government authorities in the United States at the federal, state and local level, and in other countries and jurisdictions, such as the European Union, or EU, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the United States, drug products are approved and regulated under the Federal Food, Drug and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions.

An applicant seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be approved by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;

- preparation and submission to the FDA of a new drug application, or NDA, for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with current good manufacturing practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of user fees and securing FDA approval of the NDA to allow marketing of the new drug product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity and long-term toxicity studies may continue after the IND is submitted.

The IND and IRB Processes

An IND is a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for the clinical trial, and any subsequent protocol amendments must be submitted to the FDA as part of the IND application. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30- day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has so notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides a recommendation as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or the competitive climate.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product. Sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) must make publicly available their policy for evaluating and responding to requests for expanded access for individual patients.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage and dosage schedule. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug. Such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials and are conducted either as post-marketing commitments or post-marketing requirements. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to confirm a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to fulfilling post-marketing commitments or post-marketing requirements could result in withdrawal of approval for products.

Progress reports detailing the status and a brief description of available results of the clinical trials must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and they must also develop additional information about the chemistry and physical characteristics of the investigational drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Rare Pediatric Disease Priority Review Voucher Program

With enactment of the FDASIA in 2012, and subsequent passage of the Advancing Hope Act of 2016, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application.

For the purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. A sponsor may choose to request rare pediatric disease designation, but the designation process is entirely voluntary; requesting designation is not a prerequisite to requesting or receiving a priority review voucher. In addition, sponsors who choose not to submit a rare pediatric disease designation request may nonetheless receive a priority review voucher if they request such a voucher in their original marketing application and meet all of the eligibility criteria.

In December 2016, the 21st Century Cures Act extended the Rare Pediatric Disease Priority Review Voucher Program, authorizing the FDA to award vouchers through September 30, 2022, limited to drugs with rare pediatric disease designation granted by September 30, 2020. On September 30, 2020, Congress provided a short-term extension of the Priority Review Voucher Program. On December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was further extended. Under the current statutory sunset provisions, after September 30, 2024, the FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug, and that designation was granted by September 30, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers.

Review and Approval of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by independent investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2021 is $336,432. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application, generally within 60 calendar days of its receipt, and strives to inform the sponsor within 74 days of the FDA's receipt of the submission whether the application is sufficiently complete to permit substantive review. If the FDA determines that the application is incomplete, it may request additional information rather than accept the application for filing. In this event, the application

must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs but the review process and the Prescription Drug User Fee Act, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. A REMS uses risk-minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, the seriousness of the disease, the expected benefit of the product, the expected duration of treatment, the seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Regenerative Advanced Therapy designation.

Specifically, the FDA may designate a new product for Fast Track review if it is intended for the treatment of a serious or life-threatening disease or condition and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interaction with the FDA, and the FDA may initiate review of sections of a Fast Track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information, and the sponsor must pay applicable user fees. However, the FDA's time-period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a new product may be designated as a Breakthrough Therapy if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over available therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for Priority Review if it treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A Priority Review

designation is intended to direct overall attention and resources to the evaluation of such applications and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as Regenerative Advanced Therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and if preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a Regenerative Advanced Therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for Priority Review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of

this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a new product, it may limit the approved indications for use of the product. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including a REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit to the FDA samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information as part of bona fide scientific exchange.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Pediatric Exclusivity

The Best Pharmaceuticals for Children Act provides an incentive of additional marketing exclusivity in the United States to sponsors who voluntarily complete certain pediatric clinical studies. If granted, pediatric exclusivity provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a pediatric written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Health Care Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws, and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019.

Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020, and a ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden

Administration. Further on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers.

The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities as part of a national authorization procedure, or to the EMA as part of a centralized procedure, before the product can be marketed and sold in the EU.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual member states of the European Union, or EU Member States, govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014, or Clinical Trials Regulation, was adopted. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The Clinical Trials Regulation was published on June 16, 2014 but has not yet become effective. As of January 1, 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. In late

2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

As in the United States, parties conducting certain clinical trials must post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the European Union

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is also responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related “droit de regard”. The European Parliament’s role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called “marketing authorization under exceptional circumstances”. Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

Regulatory Data Protection in the European Union

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator’s data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator’s data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid.

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the EU, applicants must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements After a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU stringent pharmacovigilance or safety reporting rules must be ensured.
- The manufacturing of authorized medicinal products, for which a separate manufacturer’s license is mandatory, must also be conducted in strict compliance with the EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or

reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Employees

As of December 31, 2020, we had 27 full-time employees, including a total of 3 employees with M.D., Pharm.D. or Ph.D. degrees. Of these full-time employees, 18 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Corporate Information

We were incorporated under the laws of the State of Delaware on January 26, 2016. Our principal executive offices are located at 116 Huntington Avenue, 6th Floor, Boston, Massachusetts 02116, and our telephone number is (617) 206-2020. Our website address is www.imaratx.com. Our website and the information contained on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and in our other filings with the Securities and Exchange Commission, before deciding to invest in our common stock. Such risks and uncertainties may be amplified by the COVID-19 pandemic and its potential impact on our business and the global economy. The risks described below are not the only risks facing our company. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us, could cause our business, prospects, operating results and financial condition to suffer materially. In such event, the trading price of our common stock could decline, and you might lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, and we expect to incur losses over the next several years.

Since inception, we have incurred significant operating losses. Our net loss was $23.5 million for the year ended December 31, 2019 and $41.4 million for the year ended December 31, 2020. As of December 31, 2020, we had an accumulated deficit of $96.1 million. To date, we have financed our operations primarily through the sale of common stock in our initial public offering, or IPO, and the sale of convertible preferred stock. We have devoted substantially all of our financial resources and efforts to research and development, including clinical trials and preclinical studies of IMR-687. We are still in the early stages of development of our only product candidate, IMR-687. We expect to continue to incur significant expenses and operating losses over the next several years. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- navigate the impacts of COVID-19 and our response to it;
- continue to advance clinical development of IMR-687, including our ongoing open label extension, or OLE, clinical trial in patients with sickle cell disease, or SCD, and our ongoing Phase 2b clinical trials in patients with SCD and β-thalassemia;
- expand our planned research and development efforts for IMR-687 and potentially pursue clinical activities for IMR-687 in heart failure with preserved ejection fraction, or HFpEF;
- continue to incur third-party manufacturing costs to support our clinical trials of IMR-687 and, if approved, commercialization;
- seek regulatory and marketing approvals for IMR-687;
- establish a sales, marketing and distribution infrastructure to commercialize IMR-687, if approved;
- commence development activities for any additional product candidates we may identify;
- acquire or in-license products, product candidates, technologies and/or data referencing rights;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control, manufacturing and other scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company; and
- make any milestone payments to H. Lundbeck A/S, or Lundbeck, under our exclusive license agreement with Lundbeck, or the Lundbeck Agreement, upon the achievement of specified clinical or regulatory milestones.

We have never generated revenue from product sales and may never achieve or maintain profitability.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of IMR-687 and any other product candidates we may identify and pursue, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We are heavily dependent on the success of IMR-687, our only product candidate.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next several years will be devoted to IMR-687, which is currently our only product candidate. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of IMR-687. We cannot be certain that IMR-687 will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of IMR-687 or if IMR-687 does not receive regulatory approval or fails to achieve significant market acceptance, we would be delayed by many years in our ability to achieve profitability, if ever, and may not be able to generate sufficient revenue to continue our business.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, including our OLE and Phase 2b clinical trials of IMR-687 in patients with SCD and our Phase 2b clinical trial in patients with β-thalassemia. We expect our expenses to increase substantially in connection with our ongoing and planned activities, particularly as we advance our preclinical activities and clinical trials of and seek regulatory approval for IMR-687 and other product candidates we may identify. In addition, if we obtain regulatory approval for IMR-687 and any other product candidates we may identify and pursue, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, any product candidates, if approved, may not achieve commercial success. Commercial revenues, if any, will not be derived unless and until we can achieve sales of products, which we do not anticipate for many years, if at all. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

As of December 31, 2020, we had cash, cash equivalents and investments of $88.2 million. We believe that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into mid-2022. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the impact of the COVID-19 pandemic and our response to it;
- the time and cost necessary to complete our ongoing OLE and Phase 2b clinical trials of IMR-687 in patients with SCD, to initiate and complete one or more pivotal clinical trials of IMR-687 in SCD, and to pursue regulatory approvals for IMR-687 in SCD, and the costs of post-marketing studies that could be required by regulatory authorities;
- the time and cost necessary to complete our Phase 2b clinical trial of IMR-687 in patients with β-thalassemia, to initiate and complete one or more pivotal clinical trials of IMR-687 in β-thalassemia, and to pursue regulatory approvals for IMR-687 in β-thalassemia, and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to advance IMR-687 in HFpEF into and through clinical development, and the timing and scope of these development activities;
- the costs of obtaining clinical and commercial supplies of IMR-687 and any other product candidates we may identify and develop;

- our ability to successfully commercialize IMR-687 and any other product candidates we may identify and develop;
- the manufacturing, selling and marketing costs associated with IMR-687 and any other product candidates we may identify and develop, including the cost and timing of establishing our sales and marketing capabilities;
- the amount and timing of sales and other revenues from IMR-687 and any other product candidates we may identify and develop, including the sales price and the availability of coverage and adequate third-party reimbursement;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;
- our ability to attract, hire and retain qualified personnel; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

We will continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. For example, the global COVID-19 pandemic created significant uncertainty in the global financial markets, which may reduce our ability to raise additional capital. In addition, we may seek additional capital when market conditions are favorable, or for strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis or on terms acceptable to us, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more product candidates or discovery stage programs or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize any product candidates.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed or on terms acceptable to us, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.

We commenced activities in 2016 and are a clinical-stage company. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, and undertaking preclinical studies and early-stage clinical trials of our sole product candidate, IMR-687. We have not yet demonstrated our ability to successfully develop any product candidate, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our ability to use our net operating losses, or NOLs, and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our NOLs or research and development tax credit carryforwards. As of December 31, 2020, we had federal NOLs of $91.7 million and state NOLs of $85.5 million.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described below in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the Tax Cuts and Jobs Act, or the TCJA, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. Additionally, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers.

In December 2019, a novel strain of coronavirus, called COVID-19, emerged in Wuhan, Hubei Province, China, which has now spread globally, including to the United States, the United Kingdom and the European Union. The pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

The spread of COVID-19 has affected our operations to date, including by causing delays in the conduct of our clinical trials. While we have not experienced any significant disruptions with the third parties on which we rely, the spread of COVID-19, or another infectious disease, could also negatively affect the operations of our third-party manufacturers, which could result in disruptions in the supply of IMR-687. In addition, most of our employees are currently working remotely, and we are temporarily restricting travel and attendance at industry events by our employees. The COVID-19 pandemic continues to rapidly evolve and could more significantly impact our operations in the future.

We have enrolled and seek to enroll patients in our ongoing clinical trials at sites located both in the United States and internationally. The COVID-19 pandemic has delayed and may continue to delay or otherwise adversely affect these clinical development activities, including our ability to recruit and retain patients in our ongoing clinical trials, as a result of many factors, including:

- diversion of healthcare resources away from the conduct of our clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, availability of hospital staff supporting the conduct of our clinical trials and the reluctance of patients enrolled in our clinical trials to visit clinical trial sites;

- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples and other supplies used in our clinical trials;
- the impact of further limitations on travel that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by our employees, contractors or patients to clinical trial sites, or the ability of employees at any of our contract manufacturers or contract research organizations, or CROs, to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials, and limit the amount of clinical data we will be able to report;
- any future interruption of, or delays in receiving, supplies of clinical trial material from our contract manufacturing organizations, or CMOs, due to staffing shortages, production slowdowns or stoppages or disruptions in delivery systems; and
- availability of future capacity at contract manufacturers to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers elect or are required to divert attention or resources to the manufacture of other pharmaceutical products.

For example, the COVID-19 pandemic has resulted in disruptions to our clinical trial operations, including some missed and incomplete patient visits in our recently completed Phase 2a clinical trial of IMR-687 in SCD and site activation and enrollment delays and delays in review of our regulatory submissions with respect to our Phase 2b clinical trials of IMR-687 in SCD and β-thalassemia. In addition, the COVID-19 pandemic may affect the operations of the U.S. Food and Drug Administration, or FDA, and other health authorities, which could result in delays of regulatory actions related to our programs, including with respect to IMR-687. Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause additional delays which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital and have a material adverse effect on our financial results. In addition, if any of our clinical trial patients contract COVID-19, they may have adverse health outcomes that could impact the results of our clinical trials.

Additionally, while the potential economic impact and the duration of the COVID-19 pandemic is difficult to assess or predict, the impact of the COVID-19 pandemic on the global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity.

While we expect the impacts of COVID-19 will continue to have some adverse effect on our business, the extent to which COVID-19 impacts our clinical trials, research and development activities and operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, new information which may emerge concerning the severity of COVID-19, the actions to contain COVID-19 or treat its impact and changes in government spending or priorities, among others. The COVID-19 pandemic is a widespread health crisis that continues to adversely affect the global economy and financial markets of many countries, resulting in an economic downturn that could also affect our operations, our ability to conduct our clinical trials, our ability to raise additional funds through public offerings and the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has subsided, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

We are early in our development efforts and heavily dependent on the success of our sole product candidate, IMR-687. If we are unable to successfully complete clinical development, obtain regulatory approval for, or commercialize IMR-687, or experience delays in doing so, our business will be materially harmed.

To date, we have invested a majority of our efforts and financial resources in the preclinical and clinical development of IMR-687. Our future success is heavily dependent on our ability to successfully develop, obtain regulatory approval for and commercialize IMR-687. IMR-687 is currently our only product candidate and we are currently testing it as part of our OLE clinical trial in SCD and our Phase 2b clinical trials in SCD and β-thalassemia. It may be a significant time before IMR-687 can advance into a pivotal trial, if at all. We cannot be certain that IMR-687 will be successful in clinical trials or receive regulatory approval.

The success of IMR-687 will depend on several factors, including the following:

- our ability to effectively manage any adverse impact of COVID-19;
- successfully completing clinical trials;

- acceptance by the FDA or other regulatory agencies of regulatory filings for IMR-687;
- expanding and maintaining a workforce of experienced clinical-stage drug development professionals and others to continue to develop IMR-687;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for IMR-687;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- establishing sales, marketing and distribution capabilities and successfully launching commercial sales, if and when approved, whether alone or in collaboration with others;
- acceptance of IMR-687, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies, including Oxbryta (voxelotor) and Adakveo (crizanlizumab) in SCD and ZYNTEGLO (INN autologous CD34+ cells encoding βA-T87Q-globin gene) (currently only approved in Europe and for which FDA approval is currently being sought), as well as REBLOZYL (luspatercept-aamt) for the treatment of ß-thalassemia;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- patients' willingness to pay out-of-pocket for IMR-687 in the absence of coverage and/or adequate reimbursement from third-party payors; and
- maintaining a continued acceptable safety profile following receipt of any regulatory approvals.

Many of these factors are beyond our control, including clinical outcomes, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize IMR-687, or if we experience delays as a result of any of these factors or otherwise, we may need to spend significant additional time and resources to identify other product candidates, advance them through preclinical and clinical development and apply for regulatory approvals, which would adversely affect our business, prospects, financial condition and results of operations.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.

The risk of failure for IMR-687 and any other product candidates we may develop is high. It is impossible to predict when or if IMR-687 and any other product candidates we may develop will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of such product candidate in humans. We have not yet begun or completed a pivotal clinical trial of IMR-687, which is currently our only product candidate. Clinical trials may fail to demonstrate that IMR-687 and any other product candidates we may develop are safe for humans and effective for indicated uses. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned investigational new drug applications, or INDs, and other regulatory filings in the United States and abroad. We cannot be certain of the timely completion or outcome of our preclinical testing and studies, and cannot predict if the FDA or other regulatory agencies will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of any product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrent with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including,

but not limited to, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize IMR-687 and any other product candidates we may develop, including:

- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may decide the design of our clinical trials is flawed, for example if our trial protocol does not evaluate treatment effects in trial subjects for a sufficient length of time;
- clinical trials of IMR-687 and any other product candidates we may develop may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, or, if we seek accelerated approval, biomarker efficacy endpoints that applicable regulatory authorities would consider likely to predict clinical benefit;
- the number of patients required for clinical trials of IMR-687 and any other product candidates we may develop may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or IRBs may require us, to suspend or terminate clinical trials of IMR-687 and any other product candidates we may develop for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- regulators or IRBs may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain regulatory approval;
- regulators may revise the requirements for approving IMR-687 and any other product candidates we may develop, or such requirements may not be as we anticipate;
- the cost of clinical trials of IMR-687 and any other product candidates we may develop may be greater than we anticipate;
- the supply or quality of IMR-687 and any other product candidates we may develop or other materials necessary to conduct clinical trials of such product candidates may be insufficient or inadequate;
- IMR-687 and any other product candidates we may develop may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials; and
- regulators may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a risk evaluation and mitigation strategy, or REMS.

We face additional important risks related to the enrollment and completion of our clinical trials of IMR-687 as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic as may the operations of our suppliers and manufacturers and other third-party service providers."

If we are required to conduct additional clinical trials or other testing of IMR-687 beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing of IMR-687 or any other product candidates we may develop, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for any product candidates;

- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling or a REMS that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses and/or delays. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize any product candidates and may harm our business and results of operations.

Because we are developing IMR-687 using new endpoints and methodologies, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.

There are currently limited therapies approved to treat SCD. To date, we have concentrated a significant portion of our product research and development efforts on developing a novel therapeutic for the treatment of SCD, and our future success depends on the success of this therapeutic approach. The clinical trial requirements of the FDA and other comparable regulatory agencies and the criteria these regulators use to determine the safety and efficacy of any product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. To date, there are only four FDA-approved drugs for SCD: voxelotor (marketed as Oxbryta), crizanlizumab (marketed as Adakveo), hydroxyurea and L-glutamine (marketed as Endari), and there are no approved therapies that target phosphodiesterase 9, or PDE9. As a result, the design and conduct of clinical trials for a therapeutic product candidate such as IMR-687 that targets PDE9 in SCD patients is subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of IMR-687 in SCD because of the limited clinical experience with its mechanism of action in these patients.

In particular, regulatory authorities in the United States and the European Union have not issued definitive guidance as to how to measure and achieve efficacy in treatments for SCD. As a result, the design and conduct of clinical trials of IMR-687 may take longer, be more costly or be less effective as part of the novelty of development in SCD. We may use new or novel endpoints or methodologies, such as both red and white blood cell biomarkers in our IMR-687 clinical trials, and the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results. Even if applicable regulatory authorities do not object to our proposed endpoints in an earlier stage clinical trial, such regulatory authorities may require evaluation of additional or different clinical endpoints in later-stage clinical trials. Additionally, if we pursue accelerated approval or other expedited regulatory approval mechanisms for IMR-687, the FDA or another regulatory authority may determine that the biomarker efficacy endpoint we select for evaluation is not sufficiently predictive of clinical benefit to support accelerated approval. For example, while the FDA commented at our face-to-face Type B meeting that our revised Phase 2b trial design and approach to data collection to support HbF as a potential surrogate endpoint was acceptable, the FDA stressed the importance of defining clear and strong assumptions and having robust results, which would be evaluated by the FDA to test if an increase of at least 3% in HbF would provide meaningful clinical benefit and therefore constitute an acceptable surrogate endpoint for a future pivotal trial of IMR-687 in SCD. If we are not able to demonstrate clinical benefit related to this endpoint to the FDA's satisfaction, we will have to consider other endpoints for the pivotal program, which may include greater levels of HbF increases.

Even if the FDA does find our clinical trial success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance deemed approvable in any pivotal or other clinical trials we may conduct for IMR-687. Further, even if we do achieve the pre-specified criteria, our trials may produce results that are unpredictable or inconsistent with the results of the more traditional efficacy endpoints in the trial. The FDA also could give overriding weight to other efficacy endpoints over a primary endpoint, even if we achieve statistically significant results on that primary endpoint, if we do not do so on our secondary or other efficacy endpoints. The FDA also weighs the benefits of a product against its risks and the FDA may view the efficacy results in the context of safety as not being supportive of approval. Other regulatory authorities in the European Union and other countries may make similar findings with respect to these endpoints.

The outcome of preclinical studies and earlier-stage clinical trials may not be predictive of the success of later-stage clinical trials.

The outcome of preclinical testing and earlier-stage clinical trials may not be predictive of the success of later-stage clinical trials. IMR-687 and any other product candidates we may develop may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. For example, in clinical trials, IMR-687 may not be effective at increasing red blood cell biomarkers that include HbF, F-cells, hemoglobin, and reducing reticulocytes, indirect bilirubin, and LDH. Furthermore, in clinical trials, IMR-687 may not impact adhesion/white blood cell markers such as P-selectin, E-selectin, or VCAM. Even if IMR-687 successfully increases or decreases, as applicable, these biomarkers in clinical trials, such increase or decrease may not result in overall clinical benefit. A lack of clinical benefit may be due to insufficient dosing or for other reasons. Additionally, any positive results generated in our Phase 2a, OLE or Phase 2b clinical trials of IMR-687 in adults with SCD would not ensure that we will achieve similar results in larger, pivotal clinical trials or in clinical trials of IMR-687 in adolescent and pediatric populations with SCD. Several companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any product candidate to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of any other product candidates then under development and/or cause the FDA or other regulatory authorities to require additional testing before approving any other product candidates.

Interim top-line and preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures, which could result in material changes in the final data.

From time to time, we may publish interim top-line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for IMR-687 or any other product candidates we may develop.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, the European Medicines Agency, or EMA, or other regulatory agencies to market IMR-687 or any future product candidate. Carrying out later-stage clinical trials is a complicated process. As an organization, we have not previously conducted any later stage or pivotal clinical trials. In order to do so, we will need to expand our clinical development and regulatory capabilities, and we may be unable to recruit qualified personnel. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to approval of IMR-687 or future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Identifying and qualifying patients to participate in clinical trials for IMR-687 and any other product candidates we may develop is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. We may not be able to initiate or continue clinical trials for IMR-687 and any other product candidates we may develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. For example, the prevalence of patients with SCD and β-thalassemia in the United States and Europe is estimated to be low. Accordingly, there are limited patient pools from which to draw for clinical trials of IMR-687. We may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical trials of IMR-687 because of the perceived

risks and benefits of IMR-687, the availability of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective subjects and the subject referral practices of physicians, among other factors.

Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;
- the requirements of the trial protocols;
- the availability of existing commercially-available treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;
- the conduct of clinical trials by competitors for product candidates that treat the same indications as IMR-687 and any other product candidates we may develop;
- the ability to identify specific patient populations for biomarker-defined trial cohort(s); and
- the cost to, or lack of adequate compensation for, prospective patients.

In addition, the COVID-19 pandemic has impacted, and is likely to continue to directly or indirectly impact the pace of enrollment in our clinical trials for at least the next several months and possibly longer as patients may avoid, may not be allowed to, or may not be able to travel to healthcare facilities and physicians' offices unless due to a health emergency.

Our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for IMR-687 and any other product candidates we may develop, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. As an example, we expect to utilize an oral solution formulation of IMR-687 for clinical development in pediatric populations with SCD that will differ from the oral tablet formulation of IMR-687 we have used in our clinical trials to date. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause IMR-687 to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of IMR-687 and jeopardize our ability to commence sales and generate revenue.

If serious adverse events or unacceptable side effects are identified during the development of IMR-687 and any other product candidates we may develop, we may need to abandon or limit our development of those product candidates.

Clinical trials by their nature utilize a sample of the potential patient population. We have only begun to evaluate IMR-687 in a limited number of subjects at a limited duration of exposure. Accordingly, any rare and severe side effects of IMR-687 may be uncovered only in later stages of our current and future clinical development. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. If IMR-687 and any other product candidates we may develop are associated with undesirable side effects in clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon their

development or limit development to more narrow uses or subpopulations in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In pharmaceutical development, many compounds that initially show promise in early-stage or clinical testing are later found to cause side effects that delay or prevent further development of the compound.

Additionally, if results of our clinical trials reveal unacceptable side effects, we, the FDA or similar regulatory authorities outside of the United States, or the IRBs or Ethics Committees at the institutions in which our studies are conducted could suspend or terminate our clinical trials or the FDA or similar foreign regulatory authorities could order us to cease clinical trials or deny approval of IMR-687 and any other product candidates we may develop for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials. In addition, while not considered adverse events, in our Phase 1 clinical trial of IMR-687 in healthy volunteers, individual subjects were noted to have sporadic heart rates of greater than 100 bpm, including placebo subjects. One subject at 4.5 mg/kg per day had multiple readings greater than 100 bpm, including at study start, prior to any administration of study drug. If we elect or are forced to suspend or terminate any clinical trial of IMR-687 and any other product candidates we may develop, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenue from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

We are also developing IMR-687 in combination with other therapies, which exposes us to additional risks.

We are developing IMR-687 both as a monotherapy and in combination with hydroxyurea, a currently approved therapy for SCD, and may develop future product candidates in combination with one or more currently approved therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

If any product candidate receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

We conduct, and intend to conduct in the future, clinical trials of product candidates in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If any product candidate receives regulatory approval, and we, or others, later discover that it is less effective than previously believed, or causes undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a “black box” warning or contraindication;
- decrease or elimination of third-party reimbursement;
- requirement that we implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and

- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may present a greater commercial opportunity or for which there is a greater likelihood of success.

If we do not successfully develop and eventually commercialize products, we will not obtain product revenue in future periods, resulting in significant harm to our financial position and adversely affecting our share price. We recently completed a Phase 2a clinical trial of IMR-687 in patients with SCD and are currently conducting an OLE clinical trial and Phase 2b clinical trial of IMR-687 in patients with SCD. In addition, a key element of our business plan is to expand the breadth of indications for IMR-687 for the treatment of β-thalassemia and HFpEF. We are currently conducting a Phase 2b clinical trial of IMR-687 in patients with β-thalassemia and recently completed pre-clinical research in HFpEF. A failure to establish IMR-687 as a viable treatment for β-thalassemia and/or HFpEF could harm our business prospects. In addition, we may explore IMR-687 in other indications or acquire additional product candidates for development. However, there can be no assurance that we will be successful in our efforts to identify or acquire other potential product candidates. Even if we identify or acquire other product candidates, there can be no assurance that our development efforts will be successful.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. For example, we currently intend to focus our capital resources primarily on the development of IMR-687. However, the development of IMR-687 may ultimately prove to be unsuccessful or less successful than another potential product candidate in our pipeline that we might have chosen to pursue on a more aggressive basis with our capital resources. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

We are conducting clinical trials of IMR-687 at clinical trial sites outside the United States, and the FDA may not accept data from trials conducted in such international locations.

In addition to our clinical sites in the United States, we are currently conducting clinical trials of IMR-687 at clinical sites outside of the United States. For example, our Phase 2b clinical trials of IMR-687 in SCD and β-thalassemia are currently being conducted or expected to be conducted at clinical sites in Europe, Asia and Africa. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical and Good Clinical Practice, or GCP, principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial conducted or from particular clinical trial sites located outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Even if any product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any product candidate receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Sales of medical products depend in part on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost effective as compared with competing treatments. Efforts to educate the medical

community and third-party payors on the benefits of IMR-687 and any other product candidates we may develop may require significant resources and may not be successful. If IMR-687 and any other product candidates we may develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of IMR-687 and any other product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments, such as, in the case of IMR-687, Oxbryta, Adakveo, hydroxyurea, ZYNTEGLO and REBLOZYL;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and to continue treatment over time and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products, if approved, together with other medications.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we expect that we would begin to build a sales and marketing infrastructure to market IMR-687 and any other product candidates we may develop in the United States and potentially in Europe, if and when approved by the applicable regulatory authority. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to educate adequate numbers of physicians on the benefits of any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute any product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing any product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to IMR-687, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the same disease indications we are pursuing. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

In the area of SCD, we expect to face competition from voxelotor (marketed as Oxbryta by Global Blood Therapeutics, Inc., or GBT), crizanlizumab (marketed as Adakveo by Novartis AG, or Novartis), HU (marketed under trade names including DROXIA by Bristol-Myers Squibb Company, as well as in generic form) and L-glutamine, which are currently the only FDA-approved therapies for the treatment of SCD. In the area of ß-thalassemia, we expect to face competition from ZYNTEGLO (marketed by bluebird bio, Inc.), which is currently only approved in Europe for the treatment of ß-thalassemia and for which FDA approval is currently being sought, as well as REBLOZYL (marketed by Bristol-Myers Squibb Co. and Acceleron Pharma Inc.), which is approved in the United States for the treatment of anemia in adult patients with ß-thalassemia who require regular RBC transfusions. In addition, with respect to SCD, we are aware of several product candidates in clinical development, including several product candidates for which FDA approval is currently being sought, which could be competitive with product candidates that we may successfully develop and commercialize. Novo Nordisk A/S (in collaboration with EpiDestiny, Inc.), Aruvant Sciences, Inc., Sangamo Therapeutics Inc., or Sangamo (in collaboration with Sanofi), Fulcrum Therapeutics, Inc., Agios Pharmaceuticals, Inc., Forma Therapeutics, Inc., Intellia Therapeutics, Inc. (in collaboration with Novartis), Editas Medicine, Inc., CRISPR Therapeutics AG, or CRISPR (in collaboration with Vertex Pharmaceuticals Incorporated, or Vertex) and Syros Pharmaceuticals, Inc. (in collaboration with GBT), among potentially other companies, are developing therapeutic approaches for patients with SCD. Novo Nordisk A/S (in collaboration with EpiDestiny, Inc.), Sangamo (in collaboration with Sanofi), CRISPR (in collaboration with Vertex), Agios Pharmaceuticals, Inc. and Syros Pharmaceuticals, Inc. (in collaboration with GBT), among potentially other companies, are developing therapeutic approaches for patients with transfusion-dependent or non-transfusion-dependent b-thalassemia. See “Business—Competition” for additional information regarding competing products and product candidates.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. If any product candidates achieve marketing approval, we expect that they would be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If the market opportunities for IMR-687 and any other product candidates we may develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer. Moreover, because the target patient populations we are seeking to treat are small, and the addressable patient population even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

We focus our research and product development on treatments for rare inherited genetic disorders of hemoglobin. The prevalence of SCD is approximately 100,000 individuals in the United States and 134,000 individuals in the European Union. Similarly, the prevalence of β-thalassemia globally is estimated to be 288,000 individuals and the aggregate prevalence of β-thalassemia in the European Union and United States is estimated to be 19,000 individuals. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with IMR-687 and any other product candidates we may develop, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for IMR-687 and any other product candidates we may develop may be limited or may not be amenable to treatment with IMR-687 and any other product candidates we may develop, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for IMR-687 and any other product candidates we may develop, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Our target patient populations are relatively small, and there are currently limited standard of care treatments directed at SCD. As a result, the pricing and reimbursement of IMR-687 and any other product candidates we may develop, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell IMR-687 and any other product candidates we may develop will be adversely affected.

We rely on CMOs to manufacture IMR-687 and expect to rely on CMOs to manufacture any other product candidates we may develop. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of IMR-687 and any other product candidates we may develop may be delayed.

We do not have any manufacturing facilities. We currently rely on a single manufacturer of active pharmaceutical ingredient, or API, for IMR-687 and a different single manufacturer for finished drug product, and we expect to continue to rely on third parties to manufacture clinical supplies of IMR-687 and any other product candidates we may develop and commercial supplies of our products, if and when approved for marketing by applicable regulatory authorities, as well as for packaging, sterilization, storage, distribution and other production logistics. If we are unable to enter into such arrangements on the terms or timeline we expect, development and/or commercialization of IMR-687 and any other product candidates we may develop may be delayed. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture any product candidates in accordance with regulatory requirements, if there are disagreements between us and such parties or if such parties are unable to expand capacities to support commercialization of any product candidates for which we obtain marketing approval, we may not be able to fulfill, or may be delayed in producing sufficient product candidates to meet, our supply requirements. These facilities may also be affected by natural disasters, such as floods or fire, or geopolitical developments, or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility. In such instances, we may need to locate an appropriate replacement third-party facility and establish a contractual relationship, which may not be readily

available or on acceptable terms, which would cause additional delay and increased expense, and may have a material adverse effect on our business.

Our third-party manufacturers are subject to regulatory inspection from time to time, including inspection and approval by the FDA and similar foreign regulators before we can commence the manufacture and sale of any product candidates, and thereafter. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the approval regimen with respect to IMR-687 and any other product candidates we may develop may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses.

We or our third-party manufacturers may also encounter shortages in the raw materials or API necessary to produce IMR-687 and any other product candidates we may develop in the quantities needed for our clinical trials or, if IMR-687 and any other product candidates we may develop are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others. Even if raw materials or API are available, we may be unable to obtain sufficient quantities at an acceptable cost or quality. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of IMR-687 and any other product candidates we may develop could delay, prevent or impair our development efforts and may have a material adverse effect on our business.

We face additional important risks related to our reliance on CMOs to meet our current and future supply needs of IMR-687 as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic as may the operations of our suppliers and manufacturers and other third-party service providers."

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. There can be no assurance that any product candidates, even if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of

the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Further, no uniform policy for coverage and reimbursement exists in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and process apart from Medicare determinations. As a result, obtaining and maintaining coverage and adequate reimbursement is often time-consuming and costly. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that, if they materialize, could harm our business.

Our future profitability will depend, in part, on our ability to commercialize IMR-687 in markets outside of the United States and the European Union. If we commercialize IMR-687 and any other product candidates we may develop in foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers, as well as other governmental controls and trade restrictions;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

If risks related to any of these uncertainties materializes, it could have a material adverse effect on our business.

Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of IMR-687 and any other product candidates we may develop in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical

companies or others selling such products. If we cannot successfully defend ourselves against claims that IMR-687 and any other product candidates or products we may develop caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for IMR-687 and any other product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we currently hold clinical trial liability insurance coverage in amounts we believe to be adequate, we may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of any product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may harm our business.

We currently rely on third-party clinical research organizations to conduct our ongoing Phase 2b clinical trials in SCD and in β-thalassemia. We do not plan to independently conduct clinical trials of any other product candidates. We expect to continue to rely on third parties, such as clinical research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize any product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may successfully develop and commercialization of our products, producing additional losses and depriving us of potential product revenue.

We face additional important risks related to our dependence on third parties as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic as may the operations of our suppliers and manufacturers and other third-party service providers."

We contract with a third-party for the manufacture of IMR-687, plan to contract with third parties for any other product candidates we may develop for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties entails risks, including that such third parties may not be able to comply with applicable regulatory requirements. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We rely on a third-party for the manufacture of IMR-687, and we expect to rely on third parties for the future manufacture of any other product candidates for preclinical and clinical testing. Reliance on third-party manufacturers entails additional risks, including:

- reliance on the third-party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third-party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third-party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

IMR-687 and any other product candidates or products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a source for bulk drug substance. If any of our future contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture IMR-687 and any other product candidates we may develop, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of IMR-687 and any other product candidates or products we may develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We face additional important risks related to our reliance on third parties for the manufacture of IMR-687 and other services as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic as may the operations of our suppliers and manufacturers and other third-party service providers."

We may enter into collaborations with third parties for the development or commercialization of product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

While we have retained all rights to and are developing IMR-687 on our own, we may in the future enter into development, distribution or marketing arrangements with third parties with respect to IMR-687 or future product candidates. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of IMR-687 and any other product candidates we may develop. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue commercialization of IMR-687 and any other product candidates we may develop that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with any product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of any product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of any product candidates could be delayed and we may need additional resources to develop any product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If we are not able to establish or maintain collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

For some product candidates we may develop, we may decide to collaborate with pharmaceutical or biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a

competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical and biotechnology companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop any product candidates or bring them to market.

Risks Related to our Intellectual Property

If we fail to comply with our obligations under our existing license agreement with Lundbeck, or under any future intellectual property licenses, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

We are party to a license agreement with Lundbeck pursuant to which we have been granted an exclusive worldwide license within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies. The agreement grants us an exclusive license under the licensed technology to, among other things, develop and commercialize any product comprising or containing certain PDE9 inhibitors, including IMR-687. For further information regarding our exclusive license agreement with Lundbeck, see "Business – Exclusive License Agreement." We may enter into additional license agreements in the future. We may enter into additional license agreements in the future. Our license agreement with Lundbeck imposes, and we expect that future licenses will impose, specified diligence, milestone payment, royalty and other obligations on us. Furthermore, Lundbeck has the right to terminate the agreement if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. Lundbeck may also terminate the agreement if we or any of our affiliates, sublicensees or subcontractors bring specified patent challenges against Lundbeck or assist others in bringing such a patent challenge against Lundbeck and fail to cease such challenge within a specified period of time. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates we develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to IMR-687 and any other product candidates we may develop that are important to our business and by in-licensing intellectual property related to our technologies and product candidates. If we are unable to obtain or maintain patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of non-U.S. countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensor are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to IMR-687 and any other product candidates we may develop. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing of the priority application, or in some cases not published at all. Therefore, neither we nor our licensor can know with certainty whether either we or our licensor were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensor were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned and in-licensed patent rights are highly uncertain. Moreover, our owned and in-licensed pending and future patent applications may not result in patents being issued that protect our technology and product candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value of, or narrow the scope of, our patent rights.

Currently, we have no issued U.S. patents directed to methods of treating SCD or β-thalassemia. However, we do have pending Patent Cooperation Treaty and U.S. non-provisional applications directed to methods of treating SCD and β-thalassemia. In order to continue to pursue protection based on provisional patent applications, we will need to file Patent

Cooperation Treaty applications, non-U.S. applications and/or U.S. non-provisional patent applications prior to applicable deadlines. Even then, as highlighted above, patents may never issue from our patent applications, or the scope of any patent may not be sufficient to provide a competitive advantage. With respect to IMR-687, the patents covering IMR-687 licensed from Lundbeck are expected to expire in 2036.

Moreover, we or our licensor may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Patent terms may be inadequate to protect our competitive position on any product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering any product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. For example, the composition of matter patents covering IMR-687, licensed from Lundbeck, are expected to expire in 2036. Given the expected expiration date of these patents, and the fact that safe harbor protections in many jurisdictions permit third parties to engage in development, including clinical trials, these patents may not provide us with a meaningful competitive advantage.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in non-U.S. countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for any product candidates we may develop, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when any product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any non-U.S. country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering any of any product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for our licensed patents, we may not have the right to control prosecution, including filing with the USPTO a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering any product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If a product candidate is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

We and our licensor, and any future licensors, may become involved in lawsuits to protect or enforce our patent or other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our current and future licensors' issued patents or other intellectual property. As a result, we or any current or future licensor may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke such parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we or our licensors have asserted are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in non-U.S. jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly and could put any of our owned or in-licensed patent applications at risk of not yielding an issued patent. A court may also refuse to stop the third-party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information or trade secrets could be compromised by disclosure during this type of litigation. Any of the foregoing could allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties, or brought by us or by our licensor, or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable

terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring any product candidates to market.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell any product candidates we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in non-U.S. jurisdictions such as oppositions before the European Patent Office. Numerous U.S. and non-U.S. issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as any product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third-party intellectual property is invalid or that our activities and product candidates do not infringe such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third-party's intellectual property.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations or methods, such as methods of manufacture or methods for treatment, related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may identify, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, be forced to indemnify our customers or collaborators or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third-party's intellectual property rights, we could also be required to obtain a license from such third-party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required

license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. A finding of infringement could prevent us from commercializing any product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign any product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and non-U.S. patent agencies in several stages or annually over the lifetime of our owned and in-licensed patents and patent applications. The USPTO and various non-U.S. governmental patent agencies also require compliance with a number of procedural, documentary and other similar provisions during the patent application process. In certain circumstances, we may rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our current or future licensors fail to maintain the patents and patent applications covering any product candidates, it may have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of non-U.S. countries may not protect our rights to the same extent as the laws of the United States. In addition, the laws of some non-U.S. countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in non-U.S. jurisdictions. The legal systems of certain countries do not favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in non-U.S. jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our current or future licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensor may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensor may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing any product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensor's ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensor fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to any product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Certain of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require that our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third-party, and we could be required to obtain a license

from such third-party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

In addition to seeking patents for any product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third-party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third-party, our competitive position may be materially and adversely harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make product candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;
- it is possible that our owned and in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensor, will include claims having a scope sufficient to protect any product candidates;
- we cannot ensure that any patents issued to us or our current or future licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize any product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;

- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain technology as a trade secrets or know-how, and a third-party may subsequently file a patent application covering such technology.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize any product candidates, and our ability to generate revenue will be materially impaired.

IMR-687 and any future product candidates we may identify and pursue and the activities associated with their development and commercialization, including design, testing, manufacture, packaging, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export, import and adverse event reporting, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of any such product candidates. For example, the development of IMR-687 for the treatment of SCD in pediatric patients is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

Marketing approval of drugs in the United States requires the submission of a new drug application, or NDA, to the FDA and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the NDA for that product. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, toxicology, and chemistry, manufacturing and controls. We have not submitted an application for or received marketing approval for IMR-687 and any other product candidates we may develop in the United States or in any other jurisdiction.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations or other third-party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing processes to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of any product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate in various countries. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Finally, disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse

effect on our business. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

If we experience delays in obtaining approval or if we fail to obtain approval of IMR-687 and any other product candidates we may develop, the commercial prospects for any product candidates may be harmed and our ability to generate revenues will be materially impaired.

We may not be able to obtain or maintain orphan drug designation or exclusivity for any product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

We received orphan drug designation for IMR-687 for SCD and β-thalassemia in the United States in February 2017 and June 2020, respectively. We also received orphan drug designation for IMR-687 for SCD in the European Union in August 2020. We may seek orphan drug designation in other indications or for any other future product candidates. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because competing drugs containing a different active ingredient can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the U.S. Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Although we have obtained Rare Pediatric Disease Designation, or RPDD, for IMR-687 for the treatment of SCD and β-thalassemia, we may not be eligible to receive a priority review voucher in the event that FDA approval does not occur prior to October 1, 2022.

The Rare Pediatric Disease Priority Review Voucher Program, or PRV Program, is intended to incentivize pharmaceutical sponsors to develop drugs for rare pediatric diseases. A sponsor who obtains approval of an NDA or BLA for a rare pediatric disease may be eligible for a Priority Review Voucher, or PRV, under this program, which may be redeemed by the owner of such PRV to obtain priority review for a marketing application. A PRV is fully transferrable and can be sold to any sponsor, who in turn can redeem the PRV for priority review of a marketing application in six months, compared to the standard timeframe of approximately 10 months.

In December 2016, extended the Rare Pediatric Disease Priority Review Voucher Program, authorizing the FDA to award vouchers through September 30, 2022, limited to drugs with rare pediatric disease designation granted by September 30, 2020. On September 30, 2020, Congress provided a short-term extension of the Priority Review Voucher Program. On December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was further extended. Under the current statutory sunset provisions, after September 30, 2024, FDA may only award a voucher for an approved rare pediatric disease

product application if the sponsor has rare pediatric disease designation for the drug, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any rare pediatric disease priority review vouchers. If we do not obtain approval of an NDA for IMR-687 for SCD or β-thalassemia by these dates, and if the PRV Program is not further extended by congressional action, we may not receive a PRV.

A Fast Track designation by the FDA may not lead to a faster development or regulatory review or approval process.

We have received Fast Track designation for IMR-687 from the FDA, and we may seek Fast Track designation for other product candidates we may develop. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot be certain that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

Accelerated approval by the FDA, even if granted for any product candidates does not increase the likelihood that any product candidates will ultimately receive full approval.

We may seek approval of IMR-687 and any other product candidates we may develop using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA makes the determination regarding whether to accept a biomarker as a proposed surrogate endpoint.

Prior to seeking such accelerated approval, we will request feedback from the FDA regarding the eligibility of the drug product candidate for accelerated approval and otherwise evaluate our ability to seek and receive such accelerated approval. As a condition of accelerated approval, the FDA will require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence and we may be required to evaluate different or additional endpoints in these post-marketing confirmatory trials. In addition, the FDA currently requires as a condition for accelerated approval pre-clearance of promotional materials prior to use, which could adversely impact the timing of the commercial launch of the product.

There can be no assurance that the FDA will agree with our surrogate endpoints or intermediate clinical endpoints, including red blood cell biomarkers and adhesion/white blood cell markers, or that we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all.

Moreover, as noted above, for drugs granted accelerated approval, the FDA requires post-marketing trials to confirm the benefit of the drug. These confirmatory trials must be completed with due diligence. We may be required to evaluate additional or different clinical endpoints in these post-marketing confirmatory trials. These confirmatory trials may require enrollment of more patients than we currently anticipate and will result in additional costs, which may be greater than the estimated costs we currently anticipate. The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate. A failure to obtain accelerated approval or any other form of expedited development, review or approval for IMR-687 and any other product candidates we may develop, or withdrawal of a product candidate, would result in a longer time period for commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we do receive accelerated approval, we may not ultimately be able to obtain full FDA approval.

Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other foreign jurisdictions, we or our potential third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the product be approved for reimbursement before the product can be made available for sale in that country. We or our potential third-party collaborators may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

In light of the large population of patients with SCD and β-thalassemia who reside in foreign countries, our ability to generate meaningful revenues in those jurisdictions may be limited due to the strict price controls and reimbursement limitations imposed by governments outside of the United States.

In some countries, including for example countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially, based on the large population of patients with SCD and β-thalassemia who reside in foreign countries.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the

distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS. If any product candidate receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure, among other things, that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other agencies impose and enforce stringent restrictions on manufacturers' communications regarding off-label use, and if we promote our products beyond their approved indications, we may be subject to enforcement action or prosecution arising from off-label promotion. Violations of the Federal Food, Drug and Cosmetic Act, or FDCA, and other statutes relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, including the False Claims Act, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have various consequences, including:

- suspension of or restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the

distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a REMS.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers and third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Potentially applicable U.S. federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare programs such as Medicare and Medicaid;
- The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or *qui tam* actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with specific exceptions) to report annually to the U.S. Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti- kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant lawsuits or fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding data subjects in the European Union, including personal health data, is subject to the European Union General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that such rules should apply to transfers of personal data from clinical trial sites located in the EEA to the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and an ongoing review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, or CCPA, which became effective on January 1, 2020, is creating similar risks and obligations as those created by GDPR, although the CCPA does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states have passed similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, investigations into these issues

typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain reimbursement for any of our candidate products that do receive marketing approval and our ability to generate revenue will be materially impaired.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020, and a ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Current and future legislative efforts may limit the costs for our products, if and when they are licensed for marketing, and that could materially impact our ability to generate revenues.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal

legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products. Several of these orders are reflected in recently promulgated regulations, and one of these regulations is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for any product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

If we or any third-party manufacturers we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could harm our business.

We and third-party manufacturers we engage now are, and any third-party manufacturers we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Liability under certain environmental laws governing the release and cleanup of hazardous materials is joint and several and could be imposed without regard to fault. We also could incur significant costs associated with civil or criminal fines and penalties or become subject to injunctions limiting or prohibiting our activities for failure to comply with such laws and regulations.

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or

experience a disruption in the manufacture and supply of any product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, be precluded from developing manufacturing and selling certain products outside the United States or be required to develop and implement costly compliance programs, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Compliance with the FCPA, in particular, is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. If we expand our operations outside of the United States, we will need to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our employees, independent contractors, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants and vendors. Misconduct by these partners could include intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or similar foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions

and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of any collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyberattacks by malicious third parties. Cyber incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. For example, we have experienced attempts at phishing and e-mail fraud with the goal of causing payments to be transmitted to an unintended recipient. Cyber incidents could also include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information.

While we have not experienced any material system failure, accident, cyber incidents or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position and reputation could be harmed and the further development and commercialization of IMR-687 and any other product candidates we may develop could be delayed.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment offer letters with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not continue to develop or be sustained.

Our shares began trading on the Nasdaq Global Select Market on March 12, 2020. Prior to March 12, 2020, there was no public market for our common stock, and we cannot be certain that an active trading market for our shares will continue to develop or be sustained. As a result, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or at all.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. We do not have control over these analysts. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. If one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price paid for their shares. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of IMR-687 and any other product candidates we may develop or those of our competitors or potential collaborators;
- timing of the results of our preclinical studies and clinical trials or those of our competitors;
- our success in commercializing any product candidates, if and when approved;
- the success of competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to IMR-687 and any other product candidates we may develop;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;

- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of common stock by us, our executive officers, directors or principal stockholders, or others;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including, without limitation, the current adverse impact of the COVID-19 pandemic; and
- the other factors described in this "Risk Factors" section.

COVID-19 has been spreading rapidly around the world since December 2019 and has created significant stock market volatility. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance. The price of our common stock may be disproportionately affected as investors may favor traditional profit-making industries and companies during the times of market uncertainty and instability.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and divert management's attention and resources.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

As of December 31, 2020, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock, in the aggregate, beneficially owned shares representing approximately 88% of our common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

This concentration of ownership may also adversely affect the market price of our common stock.

We have broad discretion in the use of our cash, cash equivalents and investments and may not use them effectively.

Our management has broad discretion in the application of our cash, cash equivalents and investments and could use such funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of IMR-687 and any other product candidates we may develop. Pending their use, we may invest our cash, cash equivalents and investments in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock, impair our ability to raise capital through the sale of additional equity securities, and make it more difficult for our stockholders to sell their common stock at a time and price that they deem appropriate. Persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

Moreover, holders of an aggregate of 11,005,600 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered all 3,505,468 shares of common stock that we may issue under our equity compensation plans and such shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, vesting arrangements and exercise of options.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until December 31, 2025, although if the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have annual gross revenues of $1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1.0 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some or all of the available exemptions. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an EGC.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that either (i) our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or (ii) our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations, such as an exemption from providing selected financial data and an ability to provide simplified executive compensation information and only two years of audited financial statements.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has devoted and will continued to be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly.

We continue to evaluate these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our filing of an Annual Report on Form 10-K with the SEC for the year ended December 31, 2021. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an "emerging growth company" for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

As a public company, we are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the TCJA, which significantly reformed the Code. The TCJA, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for NOLs arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of NOL carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such NOLs may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, the CARES Act was enacted on March 27, 2020 and COVID relief provisions were also included in the Consolidated Appropriations Act 2021, or CAA, which was enacted on December 27, 2020. The FFCR Act, the CARES Act, and the CAA contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of NOLs, which was enacted as part of the TCJA. It also provides that NOLs arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act, the CARES Act and the CAA is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic and as a result of the changes in the U.S. presidential administration and control of the U.S. Senate, additional tax legislation may also be enacted;

any such additional legislation could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act, the CARES Act or the CAA.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of proceedings: (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs

associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our principal facilities consist of office space. Our headquarters consists of approximately 4,210 square feet of office space in Boston, Massachusetts under a 62-month lease that we entered into in May 2019. This lease expires in October 2024, and we have an option to extend it for a term of five years through October 2029. In addition, we have a right of first option to lease an additional 2,069 square feet of the premises if such space becomes available during the term of the lease. We believe this office space will be sufficient to meet our needs for the foreseeable future and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock is publicly traded on The Nasdaq Global Market under the symbol "IMRA."

Holders

As of February 15, 2021, there were approximately 60 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Recent Sales of Unregistered Equity Securities

On February 25, 2020, we issued and sold 1,562,994 shares of Series B Preferred Stock to 12 investors for cash at a price per share of $10.9722 for an aggregate purchase price of $17.1 million. The securities were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

On March 16, 2020, in connection with the closing of our initial public offering of our common stock, or IPO, all of our outstanding shares of preferred stock were converted into an aggregate of 11,172,955 shares of common stock. The conversion of preferred stock into common stock occurred in accordance with the terms of our certificate of incorporation and did not constitute a sale for purposes of the Securities Act.

Use of Proceeds from Initial Public Offering

On March 16, 2020, we received aggregate net proceeds from the IPO, inclusive of the underwriters' option to purchase additional shares, of approximately $76.5 million, after deducting $6.1 million of underwriting discounts and commissions and $3.9 million of other offering expenses payable by us. The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-236465), which was declared effective by the Securities and Exchange Commission on March 11, 2020. We had not used any of the net proceeds from the IPO as of December 31, 2020, as we have continued to fund operations from proceeds received through our preferred stock financings. We have invested the unused net proceeds from the offering in money market accounts. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on March 12, 2020.

Item 6. Selected Financial Data.

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Form Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin, known as hemoglobinopathies. Our pipeline is built on the differentiated therapeutic potential of our initial product candidate, IMR-687, which is an oral, once-a-day, potentially disease-modifying treatment for sickle cell disease, or SCD, and ß-thalassemia. IMR-687 is a highly selective, potent small molecule inhibitor of phosphodiesterase-9, or PDE9, that has a multimodal mechanism of action that acts primarily on red blood cells, and has the potential to act on white blood cells, adhesion mediators and other cell types that are implicated in these disorders. We recently completed a Phase 2a clinical trial of IMR-687 in adult patients with SCD and are currently conducting an open label extension, or OLE, clinical trial, which allows patients from the Phase 2a clinical trial to continue into a long-term four-year trial to test safety and measure tolerability of IMR-687.

In the second quarter of 2020, we initiated a Phase 2b clinical trial of IMR-687 for the treatment of patients with SCD and a Phase 2b clinical trial of IMR-687 for the treatment of patients with ß-thalassemia. We are currently enrolling patients in each trial and expect to report interim data from each of these trials in the second half of 2021. We continue to evaluate the impact of the COVID-19 pandemic on these Phase 2b trials, as discussed below, and therefore, our estimated timelines for these clinical trials could be delayed. In addition, we recently completed preclinical research of IMR-687 in heart failure with preserved ejection fraction, or HFpEF, and are developing a Phase 2 protocol to support potential future clinical development of IMR-687 in this indication.

Since our inception in 2016, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of IMR-687. To date, we have funded our operations primarily through the sale of common stock in our initial public offering, or IPO, and the sale of convertible preferred stock.

In March 2020, we completed an IPO of our common stock and issued and sold 4,700,000 shares of common stock at a public offering price of $16.00 per share, resulting in gross proceeds of $75.2 million. In April 2020, the underwriters exercised their option to purchase additional shares in full to purchase 705,000 additional shares of common stock for aggregate gross proceeds of $11.3 million. Inclusive of the underwriters' option to purchase additional shares, we received approximately $76.5 million in net proceeds from the IPO after deducting $10.0 million of underwriting discounts and commissions and offering expenses. Upon completion of the IPO, all 70,378,661 shares of outstanding convertible preferred stock automatically converted into 11,172,955 shares of common stock.

In February 2020 we effected a 1-for-6.299 reverse stock split of our common stock. All historical share and per share information shown herein and in our consolidated financial statements and related notes have been retroactively adjusted to give effect to the reverse stock split.

We have incurred significant operating losses since inception. Our losses from operations were $24.1 million, and $41.7 million for the years ended December 31, 2019, and 2020, respectively. As of December 31, 2020, we had an accumulated deficit of approximately $96.1 million. We expect to continue to incur significant operating losses for the foreseeable future, as we advance IMR-687 and any product candidates we may develop in the future from discovery through preclinical development and clinical trials and seek regulatory approval of our product candidates. We expect to incur significant expenses related to maintaining and expanding our intellectual property portfolio, hiring additional research and development and business personnel and operating as a public company. In addition, our losses from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We do not have any products approved for sale. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for IMR-687 or any future product candidate. In addition, if we obtain regulatory approval for IMR-687 or any future product candidate and to the extent that we engage in

commercialization activities on our own, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing, manufacturing, and distribution activities.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We may be unable to raise additional funds or enter into other arrangements when needed on acceptable terms, or at all. Our failure to raise capital or enter into such agreements as, and when, needed, could have a material adverse effect on our business, results of operations, and financial condition. We will need to generate significant revenue to achieve profitability, and we may never do so.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2019 and December 31, 2020, we had $28.9 million and $88.2 million, respectively, in cash, cash equivalents and investments. We believe that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into mid-2022. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources."

Impact of COVID-19 Pandemic

On March 11, 2020, the World Health Organization declared the outbreak of COVID-19 a pandemic, and on March 13, 2020, the United States declared a national emergency with respect to COVID-19. The COVID-19 pandemic is ongoing and its impact continues to evolve as of the date of this Annual Report on Form 10-K. We are actively monitoring the impact of the COVID-19 pandemic on our financial condition, liquidity, operations, suppliers, industry and workforce.

Although we have not experienced any significant adverse impact from the COVID-19 pandemic on our financial condition, results of operations or liquidity as of the date of this Annual Report on Form 10-K, the COVID-19 pandemic has resulted in disruptions to our clinical trial operations, including some missed and incomplete patient visits in our recently completed Phase 2a clinical trial of IMR-687 in SCD as well as site activation and enrollment delays and delays in review of our regulatory submissions with respect to our Phase 2b clinical trials of IMR-687 in SCD and ß-thalassemia. In addition, most of our employees are currently working remotely, and we are temporarily restricting travel and attendance at industry events by our employees. The COVID-19 pandemic has also resulted in significant financial market volatility. A continuation of the volatility could have an adverse effect on our ability to access capital, on our business, results of operations and financial condition and on the market price of our common stock.

Our financial condition, results of operations and liquidity could be negatively impacted by the COVID-19 pandemic in future periods. The extent to which the COVID-19 pandemic impacts our business will depend on future developments, which remain uncertain and cannot be predicted, including new information that may emerge concerning the continued severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. As the COVID-19 pandemic continues, it may have an adverse effect on our results of future operations, financial position and liquidity, and even after the COVID-19 pandemic has subsided, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

Lundbeck License Agreement

In April 2016, we entered into an agreement with H. Lundbeck A/S, or Lundbeck, for a worldwide license under certain patent rights and certain know-how owned or otherwise controlled by Lundbeck within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies, which we refer to as the field. The agreement grants us an exclusive license under the licensed technology, including the right to grant sublicenses with certain restrictions, to research, develop, make, have made, use, sell, have sold, offer to sell, import, export and commercialize any product comprising or containing certain PDE9 inhibitors, in the field. The agreement also grants us a non-exclusive license under the licensed technology to research and develop, and make, have made, use, import and export for purposes of enabling such research and development, enhancements,

improvements, modifications or derivatives to licensed products, until but not beyond a specified pre-commercialization developmental stage with respect to each such enhancement, improvement, modification or derivative. Under the agreement, we have made cash payments totaling $1.8 million to date, consisting of an upfront payment and ongoing milestone payments, and also issued shares of our common stock as described in "Note 14 – Related Party Transactions" of the notes to our consolidated financial statements in this Annual Report on Form 10-K. We are obligated to make milestone payments to Lundbeck aggregating up to $23.5 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any licensed product and $11.8 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any IMARA product that is or comprises a PDE9 inhibitor but is not a licensed product, or a PDE9 product, if any. We are obligated to pay tiered royalties of low-to-mid single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of licensed products, and tiered royalties of low single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of PDE9 products, if any. See "Business – Exclusive License Agreement" for a further description of the license agreement with Lundbeck.

Financial Operations Overview

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. If our development efforts for IMR-687 or additional product candidates that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating Expenses

Research and Development. Research and development expenses consist primarily of costs incurred in connection with the preclinical and clinical development and manufacture of IMR-687, and include:

- personnel-related expenses, including salaries, benefits and stock-based compensation expenses, for individuals involved in research and development activities;
- external research and development expenses incurred under agreements with contract research organizations, or CROs, investigative sites, and consultants that conduct our preclinical studies and clinical trials and other scientific development services;
- costs incurred under agreements with contract manufacturing organizations, or CMOs, for developing and manufacturing material for our preclinical studies and clinical trials;
- costs related to compliance with regulatory requirements;
- milestone fees incurred in connection with our current license agreement with Lundbeck; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent, insurance and other operating costs.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as prepaid expenses or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

A significant portion of our research and development costs have been external costs, which we track after a clinical product candidate has been identified. Our internal research and development costs are primarily personnel-related costs and other indirect costs. Our research and development expenses to-date have been incurred in connection with our development of IMR-687 in SCD and β-thalassemia. We do not intend to track our internal research and development expenses on a program-by-program basis as our personnel are deployed across multiple projects under development.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to

the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as we continue the development of IMR-687 and any product candidates we may develop in the future. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of IMR-687 and any product candidates we may develop in the future, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development program and plans.

The following table summarizes our research and development expenses for the periods indicated:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
IMR-687	$ 25,902	$ 14,598
Personnel expenses (including stock-based compensation)	5,566	3,089
Other expenses	686	1,322
Total research and development expenses	$ 32,154	$ 19,009

The successful development of IMR-687 and any product candidates we may develop in the future is highly uncertain. Therefore, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development and commercialization of IMR-687 or any future product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from the sale of IMR-687 or potential future product candidates, if approved. This is due to the numerous risks and uncertainties associated with developing product candidates, including the uncertainty of:

- the impact of the ongoing COVID-19 pandemic and our response to it;
- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new ones;
- establishing an appropriate safety profile with investigational new drug application, or IND, enabling studies;
- successful patient enrollment in, and the initiation of, clinical trials;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority;
- the timing, receipt and terms of any regulatory approvals from applicable regulatory authorities;
- our ability to establish new licensing or collaboration arrangements;
- the performance of our future collaborators, if any;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- launching commercial sales of our product candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

Any changes in the outcome of any of these variables with respect to the development of IMR-687 or any future product candidates could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that product candidate. We may never obtain regulatory approval for any of our product candidates. Drug commercialization will take several years and millions of dollars in development costs.

General and Administrative. General and administrative expenses consist primarily of personnel-related expenses, including salaries, benefits, and stock-based compensation expenses for personnel in executive, finance, accounting, human resources and other administrative functions. Other significant general and administrative expenses include legal fees relating to patent, intellectual property and corporate matters, and fees paid for accounting, consulting and other professional services.

We anticipate that our general and administrative expenses will increase in the future as our business expands to support our continued research and development activities, including our future clinical programs. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, among other expenses. We also anticipate increased expenses associated with being a public company, including costs for audit, legal, regulatory, and tax-related services related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, listing standards applicable to companies listed on a national securities exchange, director and officer insurance premiums and investor relations costs. In addition, if we obtain regulatory approval for IMR-687 or any future product candidate and to the extent that we engage in commercialization activities on our own, we expect to incur significant expenses related to building a sales and marketing team to support product sales, marketing and distribution activities.

Total Other Income, Net

Total Other Income, Net. Total other income, net primarily consists of interest earned on our cash, cash equivalents and investments, offset by amortization and accretion on investments and foreign currency translation adjustments.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Operating expenses:		
Research and development	$ 32,154	$ 19,009
General and administrative	9,544	5,107
Total operating expenses	41,698	24,116
Loss from operations	(41,698)	(24,116)
Total other income, net	338	653
Net loss	$ (41,360)	$ (23,463)

Research and Development Expenses

Research and development expenses increased by approximately $13.1 million from $19.0 million for the year ended December 31, 2019 to $32.2 million for the year ended December 31, 2020. The increase in research and development expenses was primarily attributable to the following:

- a $11.3 million increase in costs related to the development and manufacturing of clinical materials, clinical research and oversight of our clinical trials and investigative fees for IMR-687;
- a $2.5 million increase in personnel-related costs, including a $0.4 million increase in stock-based compensation expense, primarily due to an increase in headcount to support the growth of our research and development efforts; and
- a $0.6 million decrease in other research and development operational costs, including facilities, supplies, and travel.

General and Administrative Expenses

General and administrative expenses increased by approximately $4.4 million from $5.1 million for the year ended December 31, 2019 to $9.5 million for the year ended December 31, 2020. The increase in general and administrative expenses was primarily attributable to the following:

- a $2.3 million increase in other general and administrative operational costs, including facilities, rent and increased insurance costs as a result of operating as a public company;
- a $1.7 million increase in personnel costs, including a $0.9 million increase in stock-based compensation expense, primarily due to an increase headcount; and
- a $0.4 million increase in legal and professional costs.

Total Other Income, Net

Total other income, net was $0.7 million for the year ended December 31, 2019, compared to total other income, net of $0.3 million for the year ended December 31, 2020. In June 2019, we invested our cash in money market funds and available-for-sale securities and in each of the years ended December 31, 2019 and December 31, 2020, our total other income, net consisted primarily of interest earned on our cash, cash equivalents and investments.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant losses in each period and on an aggregate basis. We have not yet commercialized IMR-687, which is in clinical development, and we do not expect to generate revenue from sales of IMR-687 or any product candidates we may develop in the future for several years, if at all.

Through December 31, 2020, we have funded our operations primarily through the sale of common stock in our IPO and sale of convertible preferred stock. On February 25, 2020, we raised $17.1 million in gross proceeds from the issuance of 1,562,994 shares of Series B Preferred Stock upon a waiver of specified milestone conditions from the holders of a majority of the shares then held by the holders of Series B Preferred Stock. On March 16, 2020, we completed an IPO of our common stock and issued and sold 4,700,000 shares of common stock at a public offering price of $16.00 per share, resulting in gross proceeds of $75.2 million. On April 13, 2020, the underwriters exercised their option in full to purchase 705,000 additional shares of common stock for aggregate gross proceeds of $11.3 million. Inclusive of the underwriters' option to purchase additional shares, we received approximately $76.5 million in net proceeds from the IPO after deducting $10.0 million of underwriting discounts and commissions and offering expenses.

As of December 31, 2019 and December 31, 2020, we had $28.9 million and $88.2 million, respectively, in cash, cash equivalents and investments.

While we do not currently expect that the COVID-19 pandemic will have a material adverse impact on our short-term or long-term liquidity, the impact of the COVID-19 pandemic on the global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity. For additional information see "—Impact of COVID-19 Pandemic."

Cash Flows

The following table provides information regarding our cash flows for the periods indicated:

	Year Ended December 31,	
	2020	**2019**
	(in thousands)	
Net cash used in operating activities	$ (37,398)	$ (21,877)
Net cash used in investing activities	(16,721)	(24,060)
Net cash provided by financing activities	96,881	43,579
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 42,762	$ (2,358)

Net Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2020 was $37.4 million primarily due to our net loss of $41.4 million, partially offset by stock-based compensation expense of $2.2 million, depreciation expense of $0.1 million, amortization of $0.1 million on our short-term investments, and net cash inflows from the change in working capital of $1.7 million.

Net cash used in operating activities for the year ended December 31, 2019 was $21.9 million primarily due to our net loss of $23.5 million, partially offset by stock-based compensation expense of $0.9 million and net cash inflows from the change in working capital of $0.7 million.

Net Cash Used in Investing Activities

Net cash used in investing activities for the year ended December 31, 2020 was $16.7 million primarily due to purchases of marketable securities of $64.2 million, partially offset by proceeds from sales and maturities of short-term investments of $47.5 million.

Net cash used in investing activities for the year ended December 31, 2019 was $24.1 million for purchases of property and equipment related to our operating lease, under which we commenced occupancy in August 2019, and for purchases of short-term investments.

Net Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $96.9 million, primarily due to $80.4 million of net proceeds received from our IPO, after deducting underwriting discounts and commissions, $17.1 million of cash inflow resulting from sale of Series B Preferred Stock in February 2020, and $1.0 million of proceeds from stock option exercises. The proceeds from our IPO were partially offset by payments of $1.7 million of issuance costs.

Net cash provided by financing activities for the year ended December 31, 2019 was $43.6 million, primarily due to $45.6 million of cash inflow resulting from the issuance of our Series B Preferred Stock in March and May of 2019, which was partially offset by payments of $2.0 million in deferred offering costs.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we continue research and development, initiate clinical trials, and seek marketing approval for IMR-687 and any of our future product candidates. In addition, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase if, and as, we:

- navigate the impacts of COVID-19 and our response to it;
- continue to advance clinical development of IMR-687, including our OLE clinical trial in patients with SCD and our ongoing Phase 2b clinical trials of IMR-687 in patients with SCD and β-thalassemia;
- expand our planned research and development efforts for IMR-687 and potentially pursue clinical activities for IMR-687 in HFpEF;
- continue to incur third-party manufacturing costs to support our clinical trials of IMR-687 and, if approved, commercialization;
- seek regulatory and marketing approvals for IMR-687;
- establish a sales, marketing and distribution infrastructure to commercialize IMR-687, if approved;
- commence development activities for any additional product candidates we may identify;
- acquire or in-license products, product candidates, technologies and/or data referencing rights;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control, manufacturing and other scientific personnel;

- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company; and
- make any milestone payments to Lundbeck under our exclusive license agreement with Lundbeck, upon the achievement of specified clinical or regulatory milestones.

Based on our current operating plan, we expect that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into mid-2022. However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the impact of the COVID-19 pandemic and our response to it;
- the time and cost necessary to complete our ongoing OLE and Phase 2b clinical trials of IMR-687 in patients with SCD, to initiate and complete one or more pivotal clinical trials of IMR-687 in SCD, and to pursue regulatory approvals for IMR-687 in SCD, and the costs of post-marketing studies that could be required by regulatory authorities;
- the time and cost necessary to complete our Phase 2b clinical trial of IMR-687 in patients with β-thalassemia, to initiate and complete one or more pivotal clinical trials of IMR-687 in β-thalassemia, and to pursue regulatory approvals for IMR-687 in β-thalassemia, and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to advance IMR-687 in HFpEF into and through clinical development, and the timing and scope of these development activities;
- the costs of obtaining clinical and commercial supplies of IMR-687 and any other product candidates we may identify and develop;
- our ability to successfully commercialize IMR-687 and any other product candidates we may identify and develop;
- the manufacturing, selling and marketing costs associated with IMR-687 and any other product candidates we may identify and develop, including the cost and timing of establishing our sales and marketing capabilities;
- the amount and timing of sales and other revenues from IMR-687 and any other product candidates we may identify and develop, including the sales price and the availability of coverage and adequate third-party reimbursement;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;
- our ability to attract, hire and retain qualified personnel; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

A change in the outcome of any of these or other variables with respect to the development of IMR-687 or any product candidate we may develop in the future could significantly change the costs and timing associated with the development of that product candidate. Further, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We currently have no credit facility or committed sources of capital. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect the rights of such stockholders. Additional debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research program or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt

financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Critical Accounting Policies and Estimates

This management's discussion and analysis is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reported periods. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our critical accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates. See Note 2 of the notes to our annual consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a description of our other significant accounting policies.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued third-party research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid balance accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

Stock-Based Compensation

We measure stock-based compensation issued to employees and non-employees based on the grant date fair value of the stock-based awards and recognize stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award. We have also granted stock-based awards with performance-based vesting conditions. We recognize compensation expense for awards with performance-based vesting conditions over the remaining service period using the accelerated attribution method when the performance condition is deemed to be probable. We account for forfeitures as they occur.

We classify stock-based compensation expense in our consolidated statements of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified. In future periods, we expect stock-based compensation expense to increase, due in part to our existing unrecognized stock-based compensation expense and as we grant additional stock-based awards to continue to attract and retain our employees.

We determine the fair value of stock-based awards based on the fair value of our common stock on the date of grant. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. Given our limited trading history as a public company, we determine the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies. We expect to continue to do so until we have adequate historical data regarding the volatility of our own traded stock price. The expected term of our stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Prior to our IPO, the expected term of our stock options granted to non-employees also used the "simplified" method. Following our IPO, the expected term of options granted to non-employees is determined by contractual term. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. We have not paid, and do not anticipate paying, dividends on our common stock; therefore, the expected dividend yield is assumed to be zero.

As there was no public market for our common stock prior to our IPO, the estimated fair value of our common stock for awards made prior to the IPO was approved by our board of directors, with input from management, as of the date of each award grant, considering our most recently available independent third-party valuations of common stock and utilizing the valuation of our company's enterprise value determined utilizing various methods including the back-solve method, OPM, or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM. The total enterprise value was then allocated to the various outstanding equity instruments, including the underlying common stock, utilizing the option-pricing model. We believed the assumptions underlying these valuations represented our best estimates. The independent third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

Following our IPO, we have determined the fair value of our common stock based on the quoted market price of our common stock on the Nasdaq Global Select Market.

Emerging Growth Company Status

We are an "emerging growth company," or EGC, under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Section 107 of the JOBS Act provides that an EGC can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as private entities.

As an EGC, we may take advantage of certain exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC:

- we may present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations within registration statements;
- we may avail ourselves of the exemption from providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act;
- we may avail ourselves of the exemption from complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis;

- we may provide reduced disclosure about our executive compensation arrangements; and
- we may not require nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments.

We will remain an EGC until the earliest of (i) December 31, 2025, (ii) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous rolling three-year period, or (iv) the date on which we are deemed to be a large accelerated filer under the Securities Exchange Act of 1934, as amended.

Off-balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are in the form of money market funds that are invested in U.S. Treasury securities. We also hold investments in corporate debt securities and commercial paper. As of December 31, 2020, we had cash, cash equivalents and investments of $88.2 million. Interest income is sensitive to changes in the general level of interest rates; however, due to the short-term maturities of our cash equivalents and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe and Asia, who we may pay in local currency. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the report of our independent registered public accounting firm, are presented beginning on page F-1 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer and Chief Operating Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Chief Financial Officer and Chief Operating Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Executive Officers and Directors

The following table sets forth the name, age as of January 31, 2021, and position of each of our executive officers and directors. There are no family relationships among any of our directors or executive officers.

Name	Age	Position
Executive Officers		
Rahul D. Ballal, Ph.D.	43	President and Chief Executive Officer, Director
Michael P. Gray	50	Chief Financial Officer, Chief Operating Officer
Kenneth Attie, M.D.	62	Senior Vice President, Chief Medical Officer
Non-Employee Directors		
David M. Mott(2)(3)	54	Chairman of the Board of Directors
Mette Kirstine Agger(3)	55	Director
David Bonita, M.D.(2)	44	Director
Mark Chin(1)	38	Director
Edward R. Conner, MD (3)	47	Director
Barbara J. Dalton, Ph.D.(2)	66	Director
Carl Goldfischer, M.D.(1)	61	Director
Sara Nayeem, M.D.(1)	42	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Rahul D. Ballal, Ph.D. has served as our President and Chief Executive Officer and as a member of our board of directors since June 2018. Prior to joining us, Dr. Ballal served as Chief Business Officer of Northern Biologics Inc., a biotechnology company, from May 2016 to June 2018, and as an Entrepreneur-in-Residence at Versant Ventures Management LLC, a life sciences venture capital firm, from May 2016 to June 2018. Previously, Dr. Ballal was Vice President, Business Development at Flexion Therapeutics, Inc., or Flexion, a public biopharmaceutical company, from March 2011 to May 2016. Prior to Flexion, he held a venture fellowship position at Novartis Venture Funds, a venture capital fund, as part of the Kauffman Fellowship, from June 2010 to June 2012, and overlapped in business development at the Broad Institute of Massachusetts Institute of Technology, a biomedical and genomic research center, from September 2009 to March 2011. Dr. Ballal was also the founder and CEO of Redmind LLC, a venture backed data analytics startup that was sold to Ikimbo Inc. in June 2002. Dr. Ballal received his Ph.D. in biochemistry and molecular biology from Georgetown University, his M.S. in biotechnology from Johns Hopkins University and his B.A. in biology from Brown University. We believe Dr. Ballal is qualified to serve on our board of directors based on his broad experience in the life sciences industry, including in various investment, operating and leadership roles.

Michael P. Gray has served as our Chief Financial Officer and Chief Operating Officer since April 2019. Prior to joining us, Mr. Gray held various leadership positions at Arsanis, Inc., now X4 Pharmaceuticals, Inc., a public biopharmaceutical company, including President and Chief Executive Officer from November 2018 to March 2019, Chief Financial Officer from March 2016 to March 2019, Chief Operating Officer from September 2017 to November 2018, and Chief Business Officer from March 2016 to September 2017. Mr. Gray also served in various leadership positions from January 1998 through February 2016 at Curis Inc., or Curis, a public oncology drug development company. He served as Curis' Chief Financial Officer and Chief Business Officer from February 2014 to February 2016 and as its Chief Financial Officer and Chief Operating Officer from December 2006 to February 2014. From December 2003 until December 2006, Mr. Gray served as Curis' Vice President of Finance and Chief Financial Officer and from August 2000 until December 2003, served as its Senior Director of Finance and Controller. Previously, Mr. Gray held positions including Controller at Reprogenesis Inc., a biotechnology company focused on the development of cell therapy drug candidates, and as an audit

professional for the accounting and consulting firm of Ernst & Young, LLP. Mr. Gray has served on the board of directors of Therapeutics Acquisition Corporation, a special purpose acquisition corporation, since May 2020. Mr. Gray received his M.B.A. in corporate finance and entrepreneurial management from the F.W. Olin Graduate School of Business at Babson College and a B.S. in accounting from Bryant University.

Kenneth Attie, M.D. has served as our Senior Vice President and Chief Medical Officer since January 2021. Prior to joining us, Dr. Attie served as Vice President of Medical Research at Acceleron Pharma Inc., a biopharmaceutical company, from November 2009 to January 2021. Prior to Acceleron, Dr. Attie held clinical development and medical affairs leadership roles of increasing responsibility at Altus Pharmaceuticals Inc., a biopharmaceutical company, from 2007 to 2009, Insmed, Inc., a biopharmaceutical company, from 2005 to 2007, and Genentech, Inc, a biotechnology company, from 1988 to 2000. Dr. Attie received his B.A in music from the University of Michigan and his M.D. from the New York University School of Medicine.

Non-Employee Directors

David M. Mott has served as a member of our board of directors since January 2016. Mr. Mott has been a private investor through Mott Family Capital since February 2020 and previously served as a General Partner of New Enterprise Associates, Inc., or New Enterprise Associates, an investment firm focused on venture capital and growth equity investments and, with its affiliates, a holder of more than 5% of our voting securities, from September 2008 to February 2020, where he led the healthcare investing practice. From 1992 until 2008, Mr. Mott worked at MedImmune, Inc., or MedImmune, a biotechnology company and subsidiary of AstraZeneca plc, or AstraZeneca, a public global, science-led biopharmaceutical company, and served in numerous roles during his tenure, including most recently as Chief Executive Officer from October 2000 to July 2008. During that time, Mr. Mott also served as Executive Vice President of AstraZeneca from June 2007 to July 2008 following AstraZeneca's acquisition of MedImmune in June 2007. Mr. Mott has served on the board of directors of several public companies, including Epizyme, Inc., or Epizyme, a public late-stage biopharmaceutical company, since 2009, Ardelyx, Inc., a public specialized biopharmaceutical company, since 2009, Adaptimmune Therapeutics plc, a public clinical-stage biopharmaceutical company, since September 2014 and Mersana Therapeutics, Inc., a public life sciences company, since July 2012, and previously served on the board of Tiburio Therapeutics, Inc., a biopharmaceutical company, from December 2018 to February 2020, Nightstar Therapeutics plc, a public gene therapy company that was acquired by Biogen in June 2019, from November 2015 to June 2019, Clementia Pharmaceuticals, Inc., a clinical-stage company, from June 2015 to February 2018, and Tesaro, Inc., an oncology-focused company, from May 2010 to January 2019. Mr. Mott also serves on the boards of several private biopharmaceutical companies. Mr. Mott received his B.A. in economics and government from Dartmouth College. We believe Mr. Mott is qualified to serve on our board of directors based on his experience as an executive officer at MedImmune and his role on several public and private boards of directors as well as his leadership position in healthcare investing.

Mette Kirstine Agger has served as a member of our board of directors since January 2016. Since 2009, Ms. Agger has served as a Managing Partner of Lundbeckfonden Ventures, a life science venture fund and, with its affiliates, a holder of more than 5% of our voting securities. Prior to joining Lundbeckfonden Ventures, Ms. Agger co-founded 7TM A/S, a biotech company engaged in therapeutic drug discovery and development, in 2000, and served as its Chief Executive Officer from founding to 2009. Prior to founding 7TM, Ms. Agger was part of the management team of NeuroSearch A/S, a drug research and development company. Ms. Agger served on the board of Trevi Therapeutics, Inc., a public life sciences company, from July 2017 to June 2019 and Veloxis Pharmaceuticals A/S, an emerging specialty pharmaceutical company from April 2010 to December 2019, and has served on the board of directors of scPharmaceuticals Inc., a public pharmaceutical company, since March 2014, and Tiburio Therapeutics, Inc., a biopharmaceutical company, since December 2018. She also serves on the boards of several private companies, including Cydan II, Inc., or Cydan. Ms. Agger received her M.Sc. in biology from the University of Copenhagen and received her M.B.A. from Henley Business School at the University of Reading. We believe Ms. Agger is qualified to serve on our board of directors based on her experience holding senior leadership positions within biotechnology companies and her role on public and private boards of directors, as well as her experience in investing in healthcare companies.

David Bonita, M.D. has served as a member of our board of directors since March 2019. Since February 2020, Dr. Bonita has been a member of OrbiMed Advisors LLC, or OrbiMed, a venture capital firm and, with its affiliates, a holder of more than 5% of our voting securities, where he previously served as a private equity partner from June 2013 to February 2020. From June 2004 to June 2013, Dr. Bonita held other positions at OrbiMed. Dr. Bonita has served on the board of directors of Tricida, Inc., a pharmaceutical company, since January 2014, Acutus Medical Inc, an arrhythmia management company, since March 2016, Prelude Therapeutics, Inc., an oncology company, since July 2016, and Repare Therapeutics Inc., a cancer-focussed biotechnology company, since September 2019. Dr. Bonita also previously served on the boards of directors of Clementia Pharmaceuticals Inc., a public pharmaceutical company, from April 2013 to April 2019, Loxo Oncology, Inc., a public biopharmaceutical company, from October 2013 to December 2017, Si-Bone, Inc., a public medical device company, from April 2014 to June 2019, and ViewRay Inc., a public medical device company from January 2008 to June 2018. Dr. Bonita currently serves, and has previously served, on the boards of directors of numerous private companies. Dr. Bonita worked as a corporate finance analyst in the healthcare investment banking groups of Morgan Stanley and UBS. He has published scientific articles in peer-reviewed journals based on signal transduction research performed at Harvard Medical School. He received his B.A. in biology from Harvard University and his joint M.D./M.B.A. from Columbia University. We believe that Dr. Bonita is qualified to serve on our board of directors based on his roles on several public and private boards of directors as well as his extensive experience in investing in healthcare companies.

Mark Chin has served as a member of our board of directors since March 2019. Mr. Chin served as an Investment Director at Arix Bioscience plc, a life science investment company and, with its affiliates, a holder of more than 5% of our voting securities, from August 2016 to April 2020. From September 2012 to July 2016, Mr. Chin served as a Principal at Longitude Capital Management Co. LLC, a healthcare venture capital firm. From January 2011 to September 2012, Mr. Chin served as a Consultant with the Boston Consulting Group, a global management consulting firm. Mr. Chin has served on the board of Harpoon Therapeutics Inc., a public clinical-stage immunotherapy company, since May 2017, and Iterum Therapeutics plc, a public clinical-stage pharmaceutical company, since May 2017. Mr. Chin earned his B.S. in management science from the University of California, San Diego, his M.B.A. from the Wharton School at the University of Pennsylvania and his M.S. in biotechnology from the University of Pennsylvania. We believe Mr. Chin is qualified to serve on our board of directors based on his roles on several public and private boards of directors and his extensive experience in investing in healthcare companies as well as his consulting experience.

Edward R. Conner, M.D. has served as a member of our board of directors since April 2020. Since July 2019, Dr. Conner has served as Senior Vice President and Chief Medical Officer at Audentes Therapeutics, Inc., an Astellas company and a genetic medicines company. From November 2016 to May 2019, he served as Senior Vice President and Chief Medical Officer at Sangamo Therapeutics, Inc., a biotechnology company. Dr. Conner served as Vice President, Clinical Development at Ultragenyx Pharmaceutical Inc., a pharmaceutical company, from January 2015 to October 2016, and in senior clinical and medical leadership positions at BioMarin Pharmaceutical Inc., a pharmaceutical company and at Genentech, Inc., a biotechnology company, prior to that. Dr. Conner earned his B.S. in Biology from Duke University and his M.D. from the University of California, San Francisco. We believe Dr. Conner is qualified to serve on our board of directors based on his significant industry experience leading medical and clinical development operations.

Barbara J. Dalton, Ph.D. has served as a member of our board of directors since January 2016. Dr. Dalton is the Vice President of Venture Capital for Pfizer Ventures, the venture capital group of Pfizer Inc. and, with its affiliates, a holder of more than 5% of our voting securities, since she joined Pfizer in 2007. She serves on the board of Artios Ltd., Cydan, Ixchelsis Ltd, AMRA Medical and Second Genome, which are all private independent biopharmaceutical companies. Barbara also serves on several other Pfizer Venture Investments portfolio companies as a board observer. Dr. Dalton began her pharmaceutical career as a Research Scientist in Immunology at SmithKline Beecham Ltd. (formerly SmithKline and French Laboratories), a pharmaceutical company that merged with Glaxo Holdings to become GSK, and joined their venture capital group, SR One, Ltd., in the early 1990s. She was also a founding member and Partner with EuclidSR Partners LP, a private venture capital firm, where SmithKline was a leading limited partner. She received her Ph.D. in microbiology and immunology from The Medical College of Pennsylvania (now the Drexel University College of Medicine) and received her B.S. in General Science from Pennsylvania State University. We believe Dr. Dalton is qualified to serve on our board of directors based on her research background, her past role on several public and private boards of directors, as well as her extensive experience in venture investing in healthcare companies.

Carl Goldfischer, M.D. has served as a member of our board of directors since January 2016. Dr. Goldfischer has served as an Investment Partner, Managing Director, member of the board of directors and member of the executive committee of Bay City Capital LLC, or Bay City Capital, a life sciences investment firm, since January 2000. Prior to joining Bay City Capital, Dr. Goldfischer was Chief Financial Officer and VP of Finance and Strategic Planning of ImClone Systems Inc., a biopharmaceutical company. Dr. Goldfischer has served on the board of directors of Epizyme since September 2009. He has previously served on the board of directors of EnteroMedics Inc., now ReShape Lifesciences Inc., a public medical

device company, from 2004 to September 2017, MAP Pharmaceuticals, Inc., a biopharmaceutical company, from 2004 to 2011 and Poniard Pharmaceuticals, Inc., a public biopharmaceutical company, from 2000 to 2012. Dr. Goldfischer received his B.A. in Liberal Arts from Sarah Lawrence College and his M.D. with honors in scientific research from Albert Einstein College of Medicine at Yeshiva University. We believe Dr. Goldfischer is qualified to serve on our board of directors based on his experience as chief financial officer at ImClone Systems and his role on several public and private boards of directors as well as his experience in investing in healthcare companies.

Sara Nayeem, M.D. has served as a member of our board of directors since January 2016. Dr. Nayeem has been a partner at Avoro Capital Advisors, an investment firm, since February 2021. From October 2015 to February 2021, Dr. Nayeem served as a Partner at New Enterprise Associates, a venture capital firm and, with its affiliates, a holder of more than 5% of our voting securities. From January 2009 to October 2015, Dr. Nayeem held other positions at New Enterprise Associates. Prior to joining New Enterprise Associates, Dr. Nayeem was an Associate with Merrill Lynch and Co. Inc.'s Global Healthcare Group from August 2006 to January 2009. Dr. Nayeem previously served on the board of directors of Mersana Therapeutics, Inc., a public life sciences company, from July 2012 to June 2018. Dr. Nayeem currently serves on the board of directors of several private biopharmaceutical companies, including Centrexion Therapeutics Corp., Cydan, Cydan LLC, Complexa Inc. and Tiburio Therapeutics, Inc. Previously, she served on the boards of Vtesse, Inc. from December 2014 to April 2017, Eperia Inc. from July 2016 to December 2018, and Therachon Holding AG, a clinical stage global biotechnology company, from July 2015 to October 2016. Dr. Nayeem received her M.D. and M.B.A. from Yale University and her B.A. in biology from Harvard University. We believe Dr. Nayeem is qualified to serve on our board of directors based on her experience in healthcare investment banking, her experience in investing in healthcare companies and her role as a member of the boards of directors for several biotechnology companies.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the code on the "Corporate Governance" section of the "Investors" section of our website, www.imaratx.com. In addition, we intend to post on our website all disclosures that are required by law or Nasdaq listing standards concerning any amendments to, or waivers from, any provision of the code.

Stockholder Nomination Process

Our nominating and corporate governance committee is responsible for identifying individuals qualified to serve as directors, consistent with criteria approved by our board, and recommending the persons to be nominated for election as directors, except where we are legally required by contract, law or otherwise to provide third parties with the right to nominate director candidates.

Stockholders may recommend individuals to the nominating and corporate governance committee for consideration as potential director candidates. Any such proposals should be submitted to our corporate secretary at our principal executive offices and should include appropriate biographical and background material to allow the nominating and corporate governance committee to properly evaluate the potential director candidate and the number of shares of our stock beneficially owned by the stockholder proposing the candidate.

If a stockholder wishes to propose a nomination of persons for election to our board of directors at an annual meeting but does not wish to have the proposal considered for inclusion in our proxy statement and proxy card, our amended and restated bylaws establish an advance notice procedure for such nominations and proposals. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely notice in proper form to our corporate secretary of the stockholder's intention to bring such business before the meeting.

The required notice must be in writing and received by our corporate secretary at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting. However, in the event that the date of the annual meeting is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the preceding year's annual meeting, or if no annual meeting was held in the preceding year, a stockholder's notice must be so received no earlier than the 120th day prior to such annual meeting and not later than the close of business on the later of (A) the 90th day prior to such annual meeting and (B) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs.

Assuming that biographical and background material has been provided on a timely basis, any recommendations received from stockholders will be evaluated in the same manner as potential nominees proposed by the nominating and corporate governance committee. If our board of directors decides to nominate a stockholder-recommended candidate and recommends his or her election, then his or her name will be included on our proxy card for the next annual meeting.

Audit Committee

The members of our audit committee are Mark Chin, Carl Goldfischer and Sara Nayeem. Dr. Goldfischer is the chair of the audit committee. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- overseeing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities and Exchange Commission, or SEC, rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Dr. Goldfischer is an "audit committee financial expert" as defined in applicable SEC rules. The composition of our audit committee satisfies the member independence requirements under current Nasdaq and SEC rules and regulations. Our board of directors has also determined that each member of our audit committee can read and understand fundamental financial statements, in accordance with applicable requirements. In arriving at these determinations, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

Item 11. Executive Compensation.

The following discussion relates to the compensation of our President and Chief Executive Officer, Rahul D. Ballal, Ph.D., and our Chief Financial Officer and Chief Operating Officer, Michael P. Gray, for the years ended December 31, 2020 and 2019. We also include discussion of the compensation of our former Chief Medical Officer, Willem Scheele, for the years ended December 31, 2020 and 2019 pursuant to the requirements of the Securities Act of 1933, or the Securities Act. These three individuals are collectively referred to in this Annual Report on Form 10-K as our named executive officers.

We have begun, and expect to continue in the coming months, a thorough review of all elements of our executive compensation program, including the function and design of our equity incentive programs. We have begun, and expect to continue in the coming months, to evaluate the need for revisions to our executive compensation program to ensure that our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers for the years ended December 31, 2020 and 2019.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option awards ($)(2)	All other compensation ($)	Total ($)
Rahul D. Ballal, Ph.D.(3)	2020	437,750	177,289	—	2,620(4)	617,659
President and Chief Executive Officer	2019	421,806	153,000	1,446,110	5,453(5)	2,026,369
Michael P. Gray(6)	2020	393,444	134,263	—	2,620(7)	530,327
Chief Financial Officer and Chief Operating Officer	2019	281,458	88,659	897,219	4,403(8)	1,271,739
Willem Scheele(9)	2020	110,265	—	—	258,137(10)	368,402
Former Chief Medical Officer	2019	282,386	67,900	708,330	4,578(11)	1,063,194

(1) Amounts represent a cash bonus award paid to our named executive officers under our bonus program.
(2) The amounts reported in the "Option awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718. See Note 11 of the notes to our consolidated financial statements in this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options. For 2019 options subject to performance-based vesting, the amounts reflect the grant date fair value of such awards based upon the probable outcome at the time of grant, in the amounts of $353,256, $134,238 and $105,977 for Dr. Ballal, Mr. Gray and Dr. Scheele, respectively, which amounts also equal what would have been the grant date fair value of the awards assuming achievement of the highest level of performance conditions.
(3) Dr. Ballal also serves as a member of our board of directors but does not receive any additional compensation for his service as a director.
(4) Amount represents compensation of $1,090 from premiums paid on behalf of Dr. Ballal for life insurance and $1,530 in reimbursements for monthly parking costs.
(5) Amount represents compensation of $533 from premiums paid on behalf of Dr. Ballal for life insurance and $4,920 in reimbursements for monthly parking costs.
(6) Mr. Gray commenced employment with us on April 8, 2019.
(7) Amount represents compensation of $1,090 from premiums paid on behalf of Mr. Gray for life insurance and $1,530 in reimbursements for monthly parking costs.
(8) Amount represents compensation of $533 from premiums paid on behalf of Mr. Gray for life insurance and $3,870 in reimbursements for monthly parking costs.
(9) Dr. Scheele commenced employment with us on March 15, 2019 and ceased to be an employee, effective April 22, 2020.
(10) Amount represents compensation of $356 from premiums paid on behalf of Dr. Scheele for life insurance, $1,530 in reimbursements for monthly parking costs, $246,528 in severance and $9,723 in vacation paid to Dr. Scheele.
(11) Amount represents compensation of $533 from premiums paid on behalf of Dr. Scheele for life insurance and $4,045 in reimbursements for monthly parking costs.

Narrative to Summary Compensation Table

Base Salary. In 2019, we paid Dr. Ballal an annualized base salary of $405,000 until April 1, 2019, when his annualized base salary was increased to $425,000. Effective January 1, 2020, his annualized base salary was increased to $437,750. In 2019, we paid Mr. Gray an annualized base salary of $385,000, which was pro-rated to reflect the number of days he served with our company following his hire in April 2019 and effective January 1, 2020 his annualized base salary was increased to $393,444. In 2019, we paid Dr. Scheele an annualized base salary of $355,000, which was pro-rated to reflect the number of days he served with our company following his hire in March 2019. Dr. Scheele's annualized base salary remained $355,000 during 2020 until his cessation of service on April 22, 2020. We use base salaries to recognize the

experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers are currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Annual Bonus. Our board of directors may, in its discretion, award bonuses to our executive officers, including our named executive officers, from time to time. Our letter agreements with Dr. Ballal, Mr. Gray and Dr. Scheele provide that they will be eligible for an annual discretionary bonus up to a specified percentage of their salaries based upon our achievements and their performance, as determined by our board of directors. Performance-based bonuses, which are calculated as a percentage of base salary, are designed to motivate our employees to achieve annual goals based on our strategic, financial and operating performance objectives. From time to time, our board of directors has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance. In 2019, Dr. Ballal was eligible to receive a discretionary bonus of up to 40% of his annualized base salary. In 2020, Dr. Ballal's annual discretionary bonus eligibility was increased up to 45% of his annualized base salary. We paid Dr. Ballal a discretionary bonus of $153,000 with respect to 2019 and $177,289 with respect to 2020. In 2019, Mr. Gray was eligible to receive a discretionary bonus of up to 35% of his annualized base salary, pro-rated to reflect the number of days he served with our company following his hire in April 2019. In 2020, Mr. Gray was eligible to receive a discretionary bonus of up to 35% of his annualized base salary. We paid Mr. Gray a discretionary bonus of $88,659 with respect to 2019 and $134,263 with respect to 2020. In 2019, Dr. Scheele was eligible to receive a discretionary bonus of up to 35% of his annualized base salary, pro-rated to reflect the number of days he served with our company following his hire in March 2019. We paid Dr. Scheele a discretionary bonus of $67,900 with respect to 2019.We did not pay Dr. Scheele a discretionary bonus with respect to 2020 due to his departure from our company.

Equity Incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our executive officers, including our named executive officers, and from time to time may grant equity incentive awards to them in the form of stock options.

We granted two options to purchase an aggregate of 421,434 shares of our common stock to Dr. Ballal in May 2019: one option to purchase 321,289 shares of our common stock, which award is subject solely to time-based vesting and which we refer to as the Initial Ballal 2019 Option, and a second option to purchase 100,145 shares of our common stock, which award is subject to both time-based and performance-based vesting and which we refer to as the Ballal Milestone Option. The Initial Ballal 2019 Option vests as to 25% of the shares underlying the option on the first anniversary of the applicable vesting commencement date (which vesting commencement date is March 12, 2019) and in equal quarterly installments for three years thereafter. The Ballal Milestone Option also vests as to 25% of the shares underlying the option on February 25, 2021, the first anniversary of the closing of the second tranche of our series B preferred stock financing, and in quarterly installments for three years thereafter. All of the shares underlying the unvested portion of the Initial Ballal 2019 Option and the Ballal Milestone Option will immediately vest if, within twelve months following a change in control, Dr. Ballal's service is terminated by us without cause or by Dr. Ballal with good reason (as each such term is defined in his letter agreement with us).

We granted two options to purchase an aggregate of 262,364 shares of our common stock to Mr. Gray in May 2019: one option to purchase 224,309 shares of our common stock, which award is subject solely to time-based vesting and which we refer to as the Initial Gray 2019 Option, and a second option to purchase 38,055 shares of our common stock, which award is subject to both time-based and performance-based vesting and which we refer to as the Gray Milestone Option. The Initial Gray 2019 Option vests as to 25% of the shares underlying the option on the first anniversary of the vesting commencement date (which vesting commencement date is April 8, 2019) and in equal quarterly installments for three years thereafter. The Gray Milestone Option also vests as to 25% of the shares underlying the option on February 25, 2021, the first anniversary of the closing of the second tranche of our series B preferred stock financing, and in quarterly installments for three years thereafter. All of the shares underlying the unvested portion of the Initial Gray 2019 Option and the Gray Milestone Option will immediately vest if, within twelve months following a change in control, Mr. Gray's service is terminated by us without cause or by Mr. Gray with good reason (as each such term is defined in his letter agreement with us).

We granted two options to purchase an aggregate of 207,129 shares of our common stock to Dr. Scheele in May 2019: one option to purchase 177,086 shares of our common stock, which award was subject solely to time-based vesting and which we refer to as the Initial Scheele 2019 Option, and a second option to purchase 30,043 shares of our common stock, which award was subject to both time-based and performance-based vesting and which we refer to as the Scheele Milestone Option. The Initial Scheele 2019 Option vested as to 25% of the shares underlying the option on the first anniversary of the vesting commencement date (which vesting commencement date was March 15, 2019) and ceased vesting thereafter in connection with the termination of Dr. Scheele's employment in April 2020. No shares underlying the Scheele Milestone Option vested prior to the termination of Dr. Scheele's employment.

We did not grant equity incentive awards to any of our named executive officers during 2020.

Prior to the completion of our initial public offering in March 2020, our executives were eligible to participate in our 2016 Stock Incentive Plan, as amended, or the 2016 Plan. During 2019, all stock options were granted pursuant to the 2016 Plan, and we did not grant any restricted stock awards during 2019 and 2020. Our employees and executives are now eligible to receive stock options and other stock-based awards pursuant to our 2020 Equity Incentive Plan, or the 2020 Plan.

We have used stock options and restricted stock awards to compensate our executive officers in the form of initial grants in connection with the commencement of employment and also at various times, often but not necessarily annually, if we have performed as expected or better than expected. The award of stock options and restricted stock to our executive officers have historically been made by our board of directors or compensation committee. None of our executive officers is currently party to an employment agreement that provides for automatic award of stock options or restricted stock. We have granted stock options and restricted stock to our executive officers with time-based and performance-based vesting. The options and restricted stock that we have granted to our executive officers typically vest as to 25% of the shares underlying the award on the first anniversary of the grant date and in equal quarterly installments for three years thereafter. We have also granted performance-based awards tied to the achievement of milestones. Vesting rights cease upon termination of employment and exercise rights for stock options cease shortly after termination, except that vesting is fully accelerated upon certain terminations in connection with a change of control and exercisability is extended in the case of death or disability. Prior to the exercise of a stock option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

We have historically awarded stock options and restricted stock with exercise prices or purchase prices, as applicable, that are equal to the fair market value of our common stock on the date of grant as determined by our board of directors.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information regarding all outstanding stock options held by each of our named executive officers as of December 31, 2020.

Name	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price ($)	Option expiration date
Rahul D. Ballal	163,124	100,875(1)	3.15	10/18/2028
	140,563	180,726(2)	4.92	5/15/2029
	—	100,145(3)	4.92	5/15/2029
Michael P. Gray	82,865	140,194(4)	4.92	5/15/2029
	—	38,055(3)	4.92	5/15/2029
Willem Scheele	—	—(5)	—	—

(1) This option was granted on October 19, 2018, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares vesting on May 29, 2019 and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Ballal's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

(2) This option was granted on May 16, 2019, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares vesting on March 12, 2020 and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Ballal's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

(3) Options vest as to 25% of the shares underlying the option on February 25, 2021, the first anniversary of the closing of the second tranche of our series B preferred stock financing, and in quarterly installments for three years thereafter. All of the shares underlying the unvested portion of the options will immediately vest if, within twelve months following a change in control, the recipient's service is terminated by us without cause or by the recipient with good reason (as each such term is defined in such recipient's letter agreement with us).

(4) This option was granted on May 16, 2019, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares vesting on April 8, 2020 and the remaining shares vesting in equal quarterly installments thereafter, subject to Mr. Gray's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Mr. Gray's employment within twelve months following a change in control.
(5) Dr. Scheele's unvested options expired in connection with his cessation of service in April 2020.

Employment Agreements

Letter Agreement with Rahul D. Ballal, Ph.D.

In connection with our initial hiring of Dr. Ballal as our President and Chief Executive Officer, we entered into a letter agreement with him dated April 17, 2018, which was amended and restated on August 12, 2019 and further amended and restated on September 23, 2019. We refer to the current amended and restated letter agreement as the Ballal letter agreement. Under the Ballal letter agreement, Dr. Ballal is an at-will employee, and his employment with us can be terminated by Dr. Ballal or us at any time and for any reason. Pursuant to the Ballal letter agreement, Dr. Ballal's annualized base salary is $425,000, and he is eligible to receive an annual discretionary bonus of up to 40% of his annualized base salary. We will also reimburse all of Dr. Ballal's monthly parking costs at a designated parking garage lot or his commuting costs for public transportation.

Under the Ballal letter agreement, Dr. Ballal is entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, in the event of the termination of his employment by us without cause or by him for good reason, each as defined in the Ballal letter agreement, to (i) continue receiving his then-current annual base salary for a period of twelve months following the date his employment with us is terminated, and (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to twelve months following the date that his employment with us is terminated.

In the event that Dr. Ballal's employment is terminated by us without cause or by Dr. Ballal with good reason within twelve months following a change of control, each as defined in the Ballal letter agreement, Dr. Ballal will be entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, to (i) continue receiving his then-current annual base salary for a period of twelve months following the date his employment with us is terminated, (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to twelve months following the date that his employment with us is terminated and (iii) one hundred percent of his annual bonus target amount for the year in which the termination occurs, payable as a lump sum. In addition, Dr. Ballal will be entitled to full acceleration of vesting of the option to purchase 268,999 shares of our common stock granted to Dr. Ballal in October 2018 in connection with the commencement of his employment with us, the Initial Ballal 2019 Option and the Ballal Milestone Option. Under the Ballal letter agreement, if payments and benefits payable to Dr. Ballal in connection with a change in control are subject to Section 4999 of the Code, then such payments and benefits will either be paid in full or be reduced so that the Section 4999 excise tax does not apply, whichever results in the better after-tax result for Dr. Ballal.

Letter Agreement with Michael P. Gray

In connection with our initial hiring of Mr. Gray as our Chief Financial Officer and Chief Operating Officer, we entered into a letter agreement with him dated February 26, 2019, which was amended and restated on June 27, 2019 and further amended and restated on September 23, 2019. We refer to the current amended and restated letter agreement as the Gray letter agreement. Under the Gray letter agreement, Mr. Gray is an at-will employee, and his employment with us can be terminated by Mr. Gray or us at any time and for any reason. Pursuant to the Gray letter agreement, Mr. Gray's annualized base salary is $385,000, and he is eligible to receive an annual discretionary bonus of up to 35% of his annualized base salary. We will also reimburse all of Mr. Gray's monthly parking costs at a designated parking garage lot or his commuting costs for public transportation.

Under the Gray letter agreement, Mr. Gray is entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, in the event of the termination of his employment by us without cause or by him for good reason, each as defined in the Gray letter agreement, to (i) continue receiving his then-current annual base salary for a period of nine months following the date his employment with us is terminated, and (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to nine months following the date that his employment with us is terminated.

In the event that Mr. Gray's employment is terminated by us without cause or by Mr. Gray with good reason within twelve months following a change of control, each as defined in the Gray letter agreement, Mr. Gray will be entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive

covenants, to (i) continue receiving his then-current annual base salary for a period of nine months following the date his employment with us is terminated, (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to nine months following the date that his employment with us is terminated and (iii) seventy-five percent of his annual bonus target amount for the year in which the termination occurs, payable as a lump sum. In addition, Mr. Gray will be entitled to full acceleration of vesting of the Initial Gray 2019 Option and the Gray Milestone Option. Under the Gray letter agreement, if payments and benefits payable to Mr. Gray in connection with a change in control are subject to Section 4999 of the Code, then such payments and benefits will either be paid in full or be reduced so that the Section 4999 excise tax does not apply, whichever results in the better after-tax result for Mr. Gray.

The severance payments that Mr. Gray is eligible to receive under the Gray letter agreement will be reduced, but not below $1,000, by the amount of garden leave pay received by Mr. Gray under the restrictive covenant agreement he entered into with us described further under "Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreements" below.

Letter Agreement with Willem H. Scheele, M.D.

In connection with our initial hiring of Dr. Scheele as our Chief Medical Officer, we entered into a letter agreement with him dated March 1, 2019, which was amended and restated on June 27, 2019 and further amended and restated on September 23, 2019. We refer to the most recently amended and restated letter agreement as the Scheele letter agreement. Under the Scheele letter agreement, Dr. Scheele was an at-will employee, and his employment with us was terminable by Dr. Scheele or us at any time and for any reason. Pursuant to the Scheele letter agreement, Dr. Scheele's annualized base salary was $355,000, and he was eligible to receive an annual discretionary bonus of up to 35% of his annualized base salary. Dr. Scheele was also entitled to reimbursement of all of his monthly parking costs at a designated parking garage lot or his commuting costs for public transportation.

In connection with his cessation of service in April 2020, Dr. Scheele is received severance benefits according to the terms of the Scheele letter agreement including (i) his annual base salary as of the date of termination for a period of nine months following the date of termination and (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to nine months following the date that date of termination.

Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreements

Each of our executive officers has entered into a standard form of agreement with respect to non-competition, non-solicitation, confidential information and assignment of inventions. Under this agreement, each executive officer has agreed not to compete with us during his employment and for a period ranging from six months to one year after the termination of his employment, not to solicit our employees, consultants, clients or customers during his employment and for a period ranging from six months to one year after the termination of his employment, and to protect our confidential and proprietary information indefinitely. In addition, under this agreement, each executive officer has agreed that we own all inventions that are developed by such executive officer during his employment with us that are related to our business or research and development conducted or planned to be conducted by us at the time such development is created. Each executive officer also agreed to provide us with a non-exclusive, royalty-free, perpetual license to use any prior inventions that such executive officer incorporates into inventions assigned to us under this agreement.

Stock Option and Other Compensation Plans

In this section we describe the 2016 Plan, the 2020 Plan and our 2020 Employee Stock Purchase Plan, or the 2020 ESPP. Prior to our initial public offering in March 2020, we granted awards to eligible participants under the 2016 Plan. We currently grant awards to eligible participants under the 2020 Plan.

2016 Stock Incentive Plan

The 2016 Plan was initially approved by our board of directors and stockholders in April 2016 and was subsequently amended in November 2016, May 2018, March 2019, June 2019 and December 2019, in each case solely to increase the total number of shares reserved for issuance under the 2016 Plan. The 2016 Plan provided for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. Our employees, officers, directors, consultants and advisors were eligible to receive awards under the 2016 Plan; however, incentive stock options could only be granted to our employees. The type of award granted under the 2016 Plan and the terms of such award were set forth in the applicable award agreement. Pursuant to the terms of the 2016 Plan, our board of directors (or a committee delegated by our board of directors) administered the plan and, subject to any limitations in the plan, selected the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options became exercisable;

- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, measurement price, issue price and repurchase price (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years).

The maximum number of shares of common stock authorized for issuance under the 2016 Plan was 2,091,969 shares. Our board of directors may amend, suspend or terminate the 2016 Plan at any time, except that stockholder approval may be required to comply with applicable law.

Effect of Certain Changes in Capitalization. Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, under the terms of the 2016 Plan, we are required to equitably adjust (or make substitute awards, if applicable), in the manner determined by our board of directors:

- the number and class of securities available under the 2016 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares subject to and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share-related provisions and the purchase price, if any, of each outstanding other stock-based award.

Effect of Certain Corporate Transactions. Upon the occurrence of a merger or other reorganization event (as defined in the 2016 Plan), our board of directors may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2016 Plan as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unexercised awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of the notice;
- provide that outstanding awards shall become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to the reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of the award;
- provide that, in connection with our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated under the 2016 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, the repurchase and other rights with respect to outstanding restricted stock awards will continue for the benefit of the succeeding company and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock was converted into or exchanged for in the reorganization event in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award. However, our board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between a participant and us, either initially or by amendment. Upon our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the plan participant and us, all restrictions and conditions on all restricted stock awards then outstanding will automatically be deemed terminated or satisfied.

Our board of directors may at any time provide that any award under the 2016 Plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

No further awards will be made under the 2016 Plan; however, awards outstanding under the 2016 Plan will continue to be governed by their existing terms.

2020 Equity Incentive Plan

Our 2020 Plan, which became effective on March 11, 2020, was adopted by our board of directors in October 2019 and approved by our stockholders in February 2020. The 2020 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares of our common stock that are reserved for issuance under the 2020 Plan is the sum of: (1) 1,220,283 shares of our common stock; plus (2) the number of shares (up to a maximum of 2,091,969 shares) equal to the sum of (x) 228,852 shares, which represents the number of shares of our common stock reserved for issuance under the 2016 Plan that remained available for grant under the 2016 Plan on March 11, 2020 and (y) the number of shares of our common stock subject to outstanding awards granted under the 2016 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing until, and including, the fiscal year ending December 31, 2030, equal to the lesser of (i) 4% of the number of shares of our common stock outstanding on the first day of such fiscal year and (ii) an amount determined by our board of directors. On January 1, 2021, 701,930 additional shares of common stock became available for future issuance under the 2020 Plan due to the first such annual increase. No more than 8,541,982 shares of common stock may be issued as incentive stock options under the 2020 Plan.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2020 Plan. Incentive stock options, however, may only be granted to our employees.

Pursuant to the terms of the 2020 Plan, our board of directors (or a committee delegated by our board of directors) administers the 2020 Plan and, subject to any limitations in the 2020 Plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards, including conditions for repurchase, measurement price, issue price and repurchase price (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years).

If our board of directors delegates authority to one or more of our officers to grant awards under the 2020 Plan, the officers will have the power to make awards to all of our employees, except executive officers (as such terms are defined in the 2020 Plan). Our board of directors will fix the terms of the awards to be granted by any such officer, the maximum number of shares subject to awards that such officer may grant, and the time period in which such awards may be granted.

The 2020 Plan contains limits on awards that may be made under the 2020 Plan to our non-employee directors. The maximum aggregate amount of cash and value (calculated based on grant date fair value for financial reporting purposes) of awards granted in any calendar year under the 2020 Plan to an individual non-employee director may not exceed $750,000, or $1,000,000 in the case of a new director during his or her first year of service. Fees paid by us on behalf of any non-employee director in connection with regulatory compliance and any amounts paid to a non-employee director as reimbursement of an expense will not count against the foregoing limit. Our board of directors may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation.

Effect of Certain Changes in Capitalization. Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, under the terms of the 2020 Plan, we are required to equitably adjust (or make substitute awards, if applicable), in the manner determined by our board of directors:

- the number and class of securities available under the 2020 Plan;
- the share counting rules under the 2020 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding award of restricted stock; and
- the share and per-share-related provisions and the purchase price, if any, of each outstanding restricted stock unit award and other stock-based award.

Effect of Certain Corporate Transactions. Upon the occurrence of a merger or other reorganization event (as defined in the 2020 Plan), our board of directors may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2020 Plan as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited immediately prior to the consummation of the reorganization event and/or unexercised awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of the notice;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of the award;
- provide that, in connection with our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated under the 2020 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, our repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the succeeding company (or any affiliate of the succeeding company) and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock was converted into or exchanged for pursuant to the reorganization event. However, our board of directors may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or in any other agreement between a participant and us, either initially or by amendment. Upon our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the participant and us, all restrictions and conditions on all restricted stock awards then outstanding will automatically be deemed terminated or satisfied.

At any time, our board of directors may provide that any award under the 2020 Plan will become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to certain actions requiring stockholder approval under the Code or Nasdaq Stock Market rules, our board of directors may amend, modify or terminate any outstanding award under the 2020 Plan, including but not limited to, substituting for the award another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a non-qualified stock option, subject to certain participant consent requirements. However, unless our stockholders approve such action, the 2020 Plan provides that we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2020 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding stock option or stock appreciation right (whether or not granted under the 2020 Plan) and grant a new award under the 2020 Plan in substitution for the cancelled award (other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock (valued in the manner determined by (or in the manner approved by) our board of directors); or
- take any other action that constitutes a “repricing” within the meaning of Nasdaq Stock Market rules or rules of any other exchange or marketplace on which our common stock is listed or traded.

No award may be granted under the 2020 Plan on or after March 11, 2030. Our board of directors may amend, suspend or terminate the 2020 Plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

2020 Employee Stock Purchase Plan

Our 2020 ESPP, which became effective on March 11, 2020, was adopted by our board of directors in October 2019 and approved by our stockholders in February 2020. The 2020 ESPP is administered by our board of directors or by a committee appointed by our board of directors. The 2020 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 193,216 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2020 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2021 and continuing until, and including, the fiscal year commencing on January 1, 2031, in an amount equal to the lowest of (i) 386,432 shares of our common stock, (ii) 1% of the number of shares of our common stock outstanding on the first day of such fiscal year and (iii) an amount determined by our board of directors.

All of our employees and employees of any designated subsidiary, as defined in the 2020 ESPP, are eligible to participate in the 2020 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2020 ESPP.

We retain the discretion to determine which eligible employees may participate in an offering under applicable regulations.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2020 ESPP, with the first such offering having commenced on June 15, 2020 and the first purchase having occurred on December 14, 2020. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors or a committee designated by the board of directors may, at its discretion, choose a different period of not more than 27 months for offerings.

On each offering commencement date, each participant will be granted the right to purchase, on the last business day of the offering period, up to a number of shares of our common stock determined by multiplying $2,083 by the number of full months in the offering period and dividing that product by the closing price of our common stock on the first day of the offering period. No employee may be granted an option under the 2020 ESPP that permits the employee's rights to purchase shares under the 2020 ESPP and any other employee stock purchase plan of ours or of any of our subsidiaries to accrue at a rate that exceeds $25,000 of the fair market value of our common stock (determined as of the first day of each offering period) for each calendar year in which the option is outstanding. In addition, no employee may purchase shares of our common stock under the 2020 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

Each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2020 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2020 ESPP, the purchase price shall be determined by our board of directors or the committee for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors or the committee does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may at any time prior to the close of business on the fifteenth business day prior to the end of an offering period (or such other number of days as is determined by us), and for any reason, permanently withdraw from participating in an offering and permanently withdraw the balance accumulated in the employee's account. Partial withdrawals are not permitted. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be taken and the balance in the employee's account will be paid to the employee.

We will be required to make equitable adjustments to the extent determined by our board of directors or a committee thereof to the number and class of securities available under the 2020 ESPP, the share limitations under the 2020 ESPP, and the purchase price for an offering period under the 2020 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2020 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2020 ESPP on such terms as our board of directors or committee thereof determines:

- provide that options will be assumed, or substantially equivalent options will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board of directors or committee thereof in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the cash payment for each share surrendered in the reorganization event is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2020 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or
- provide that, in connection with our liquidation or dissolution, options will convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2020 ESPP or any portion of the 2020 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board of directors may not make any amendment that would cause the 2020 ESPP to fail to comply with Section 423 of the Code. The 2020 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) Plan

We maintain a defined contribution employee retirement plan for our employees, including our named executive officers. The plan is intended to qualify as a tax-qualified 401(k) plan so that contributions to the 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan (except in the case of contributions under the 401(k) plan designated as Roth contributions). Under the 401(k) plan, each employee is fully vested in his or her deferred salary contributions and any qualified nonelective contributions made by us. Employee contributions are held and invested by the plan's trustee as directed by participants. The 401(k) plan provides us with the discretion to match employee contributions.

Limitation of Liability and Indemnification

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law, or the DGCL, and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the DGCL is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we entered into new indemnification agreements with all of our directors and executive officers prior to the completion of our initial public offering. These indemnification agreements may require us, among other things, to indemnify each such executive officer or director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our executive officers or directors.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. In addition, our directors and executive officers may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director Compensation

The table below shows all compensation to our non-employee directors during the year ended December 31, 2020.

Name	Fees earned or paid in cash ($)	Option awards ($)(1)(2)	Total ($)
David M. Mott	62,648	155,961	218,609
Mette Kirstine Agger(3)	34,099	155,961	190,060
Carl Goldfischer, M.D.	39,651	155,961	195,612
Barbara J. Dalton, Ph.D.	31,720	155,961	187,681
James McArthur, Ph.D.(4)	4,061	155,961	160,022
Sara Nayeem, M.D.	33,703	155,961	189,664
David Bonita, M.D.	31,720	155,961	187,681
Mark Chin	33,703	155,961	189,664
Edward R. Conner	26,975	159,980	186,955

(1) The amounts reported in the "Option awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC 718. See Note 11 of the notes to our consolidated financial statements in this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the directors upon the vesting of the stock options, the exercise of the stock options or the sale of the common underlying such stock options.

(2) As of December 31, 2020, the aggregate number of shares of our common stock subject to outstanding option awards for each non-employee director was as follows: Mr. Mott, 15,457 shares; Ms. Agger, 0 shares; Dr. Goldfischer, 15,457 shares; Dr. Dalton, 15,457 shares; Dr. McArthur, 126,544 shares; Dr. Nayeem, 15,457 shares; Dr. Bonita, 15,457 shares; Mr. Chin, 15,457 shares; and Mr. Conner, 15,457 shares.

(3) Ms. Agger earned $34,099 in fees related to her service as a director of the company and was granted an option on March 11, 2020, each of which Ms. Agger decided to voluntarily forego. Ms. Agger voluntarily surrendered her option in full on June 30, 2020 pursuant to a stock option termination agreement.

(4) Dr. McArthur resigned from our board of directors in April 2020. Upon his resignation, the board amended Dr. McArthur's stock option award agreement to extend the exercise period of any vested options to September 22, 2021. All unvested options expired in connection with his resignation.

Dr. Ballal, one of our directors who also serves as our President and Chief Executive Officer, does not receive any additional compensation for his service as director. Dr. Ballal is one of our named executive officers and, accordingly, the compensation that we pay to Dr. Ballal is discussed under "—Summary Compensation Table" and "—Narrative to Summary Compensation Table."

In October 2019, our board of directors approved a director compensation program that became effective on March 11, 2020. Under this director compensation program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of the board and the chairman of each committee will receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors, on such committee or in such position. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Member Annual Fee	Chairman Incremental Annual Fee	
Board of Directors	$ 35,000	$ 3,000	(1)
Audit Committee	$ 7,500	$ 15,000	
Compensation Committee	$ 5,000	$ 10,000	
Nominating and Corporate Governance Committee	$ 4,000	$ 8,000	

(1) $15,000 for a lead independent director, if any.

Notwithstanding the foregoing, each of our non-employee directors may elect, no later than December 31 of each year, to receive his or her annual base fees for service on the board of directors in the form of an option to purchase our common stock, which option will be granted on January 2 of the following year, have a Black- Scholes value equal to the annual base board of directors fees that are anticipated to be payable to the director for the entire calendar year, have an exercise price equal to the closing price of our common stock on the date of grant of the award, vest in four equal quarterly installments on the last day of each quarter, subject to the director's continued service as a director through each applicable vesting date (with such vesting prorated for any portion of the quarter that the director is not serving on our board of directors) and have a term of ten years from the date of grant. No such election may be made with respect to fees for serving as chairman (or lead independent director) of the board of directors, or as a member or chairman of a committee of our board of directors.

We also reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

In addition, under our director compensation program, each non-employee director receives under the 2020 Plan, upon his or her initial election or appointment to our board of directors, or in the case of our directors serving at the time of our initial public offering, received upon completion of our initial public offering, an option to purchase 15,457 shares of our common stock. Each of these options vest as to 33.3333% of the shares underlying such award on each of the first, second and third anniversaries of the date of grant of the award, subject to the non-employee director's continued service as a director, employee or consultant. Further, on the dates of each of our annual meetings of stockholders, each non-employee director that has served on our board of directors will receive, under the 2020 Plan, an option to purchase 7,728 shares of our common stock, provided that for a non-employee director who was initially elected to our board of directors within the 12 months preceding the annual meeting of stockholders, the number of shares subject to such option will be pro-rated on a monthly basis for time in service. Each of these options will vest on the twelve-month anniversary of the date of the date of grant of the award (or, if earlier, the date of the next annual meeting of stockholders following the date of grant of the award), subject to the non-employee director's continued service as a director, employee or consultant. All options issued to our non-employee directors under our director compensation program are issued at exercise prices equal to the fair market value of our common stock on the date of grant, will have a term of ten years and will become exercisable in full upon a change in control of our company.

Prior to our initial public offering in March 2020, we paid cash fees and granted shares of restricted stock to certain of our non-employee directors for their service on our board of directors; however, we did not have a written agreement with any of our directors or a formal non-employee director compensation policy.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The following table sets forth information with respect to the beneficial ownership of our common stock as of January 15, 2021 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock that an individual has a right to acquire within 60 days after January 15, 2021 are considered outstanding and beneficially owned by the person holding such right for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of each beneficial owner is c/o IMARA Inc., 116 Huntington Avenue, 6th Floor, Boston, Massachusetts 02116.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned (%)
Entities affiliated with New Enterprise Associates 14, L.P.(1)	4,017,170	22.9%
OrbiMed Private Investments VII, LP(2)	2,719,902	15.5%
FMR LLC(3)	2,611,116	14.9%
Entities affiliated with Pfizer Ventures (US) LLC(4)	1,557,722	8.9%
Entities affiliated with RA Capital Healthcare Fund, L.P.(5)	1,454,348	8.3%
Lundbeckfond Invest A/S(6)	1,432,722	8.2%
Arix Bioscience Holdings Limited(7)	1,068,255	6.1%
Directors and Named Executive Officers:		
Sara Nayeem, M.D.(1)(11)	4,022,321	22.9%
David Bonita, Ph.D.(2)(11)	2,725,053	15.5%
Barbara J. Dalton, Ph.D.(4)(11)	1,562,873	8.9%
Mette Kirstine Agger(6)	1,432,722	8.2%
Carl Goldfischer, M.D.(8)(11)	708,531	4.0%
Rahul D. Ballal, Ph.D.(9)	365,616	2.0%
Michael P. Gray(10)	106,398	*
David M. Mott(11)	5,151	*
Mark Chin(11)	5,151	*
Edward R. Conner	—	*
All current executive officers and directors as a group(11 persons)(12)	10,933,816	62.3%

* Less than one percent.

(1) Consists of (i) 4,013,995 shares of common stock held by New Enterprise Associates 14, L.P., or NEA, and (ii) 3,175 shares of common stock held by NEA Ventures 2016, L.P., or NEA Ventures. The shares held by NEA are indirectly held by NEA Partners 14, L.P., or NEA Partners, the sole general partner of NEA, NEA 14 GP, LTD, or NEA GP, the sole general partner of NEA Partners and each of the individual directors of NEA GP. The individual directors, or the Directors, of NEA GP are Forest Baskett, Anthony A. Florence, Jr., Patrick J. Kerins, Peter Sonsini and Scott Sandell. NEA, NEA Partners, NEA GP and the Directors share voting and dispositive power with regard to the shares directly held by NEA. With regard to the shares directly held by NEA Ventures, Mr. Mott and Dr. Nayeem have neither voting nor dispositive power, and disclaim beneficial ownership of such shares, except to the extent of their pecuniary interests therein, if any. With regard to the shares directly held by NEA, Dr. Nayeem has no voting or dispositive power over any of such shares directly held by NEA and disclaims beneficial ownership of such shares, except to the extent of her pecuniary interest therein, if any. Mr. Mott and Dr. Nayeem are also members of our board of directors. The address for NEA is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093.

(2) Based solely on a Schedule 13D filed with the SEC on March 20, 2020. Consists of (i) 2,532,402 shares of common stock held by OrbiMed Private Investments VII, LP, or OPI VII and (ii) 187,500 shares of common stock held by The Biotech Growth Trust PLC, or BIOG. OrbiMed Capital GP VII LLC, or OrbiMed GP, is the general partner of OPI VII and OrbiMed Advisors LLC, or OrbiMed Advisors, is the managing member of OrbiMed GP. As a result, OrbiMed Advisors and OrbiMed GP share power to direct the vote and disposition of the shares held by OPI VII and may be deemed to be

the beneficial owners of the shares held by OPI VII. OrbiMed Advisors exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein, each of whom disclaims beneficial ownership of the Shares held by OPI VII. OrbiMed Capital LLC, or OrbiMed Capital, is the investment advisor of BIOG. As a result, OrbiMed Capital has the power to direct the vote and disposition of the shares held by BIOG and may be deemed to be the beneficial owner of the shares held by BIOG. OrbiMed Capital disclaims any beneficial ownership over the shares. OrbiMed Capital exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein, each of whom disclaims beneficial ownership of the Shares held by BIOG. The business address for OPI VII is c/o OrbiMed Advisors LLC, 601 Lexington Avenue 54th Floor, New York, NY 10022.

(3) Based solely on a Schedule 13G/A filed with the SEC on February 8, 2021. Consists of 2,611,116 shares of common stock held by FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or Fidelity Funds, advised by Fidelity Management & Research Company LLC, or FMR Co. LLC, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co. LLC carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address of FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

(4) Based solely on a Schedule 13G filed with the SEC on March 26, 2020. Consists of (i) 1,481,719 shares of common stock held by Pfizer Ventures (US) LLC, or Pfizer Ventures, and (ii) 76,003 shares of common stock held by Pfizer Inc., or Pfizer. Pfizer Ventures is a wholly-owned subsidiary of Pfizer and Pfizer may be deemed to beneficially own the shares directly owned by Pfizer Ventures. The address of Pfizer and Pfizer Ventures is 235 East 42nd Street, New York, New York 10017.

(5) Consists of (i) 1,151,230 shares of common held by RA Capital Healthcare Fund, L.P., or RA Capital, (ii) 108,083 shares of common stock held by RA Capital Nexus Fund, L.P. and (iii) 195,035 shares of common stock held by a separately managed account, or the Account. Dr. Peter Kolchinsky is the managing member of RA Capital Management, L.P., the general partner of RA Capital and the investment advisor of the Account. Dr. Kolchinsky and RA Capital Management, L.P. may be deemed to beneficially own the shares held by RA Capital and the Account. Dr. Kolchinsky and RA Capital Management, L.P. disclaim beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein. The address for the entities listed above is 200 Berkeley Street, 18th Floor, Boston, MA 02116.

(6) Consists of 1,432,722 shares of common stock held by Lundbeckfond Invest A/S, or Lunbeckfonden. The board of directors of Lundbeckfonden consists of Jørgen Huno Rasmussen, Steffen Kragh, Lars Holmqvist, Susanne Krüger Kjær, Michael Kjær, Peter Schütze, Gunhild Waldemar, Ludovic Tranholm Otterbein, Vagn Flink Møller Pedersen, Henrik Villsen Andersen and Peter Adler Würtzen. No individual member of the Lunbeckfonden board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Lunbeckfonden. The board of directors of Lunbeckfonden and Lene Skole, the chief executive officer of Lunbeckfonden, may be deemed to share voting and investment authority over the shares held by Lundbeckfonden. Mette Kirstine Agger, a member of our board of directors, is a Managing Partner at Lundbeckfon Ventures, which is an affiliate of Lundbeckfonden. The address of Lundbeckfonden and the above-mentioned persons is Scherfigsvej 7, DK-2100 Copenhagen, Denmark.

(7) Based solely on a Schedule 13D/A filed with the SEC on January 8, 2021. Consists of 1,068,255 shares of common stock held by Arix Bioscience Holdings Limited, or Arix Ltd. Arix Bioscience Plc, or Arix Plc, is the sole owner and parent of Arix Ltd. and may be deemed to indirectly beneficially own the shares held by Arix Ltd. The address for Arix Ltd. And Arix Plc is 20 Berkeley Square, London, W1J 6EQ, United Kingdom.

(8) Consists of (i) 690,232 shares of common stock held by Bay City Capital Fund V, L.P., or Bay City Capital Fund V, and (ii) 13,148 shares of common stock held by Bay City Capital Fund V Co-Investment Fund, L.P., or Bay City Capital Fund V Co-Investment. Bay City Capital Management V, or GP V, is the General Partner of Bay City Capital Fund V and Bay City Capital Fund V Co-Investment, or collectively, BCC V. Bay City Capital LLC, or BCC LLC, is the Manager of GP V. BCC V has shared voting and dispositive power with respect to the shares held by BCC V. GP V has sole voting and dispositive power with respect to the shares held by BCC V. GP V disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. BCC LLC has sole voting and dispositive power with respect to the shares held by BCC V. BCC LLC disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Carl Goldfischer and Fred Craves are managing directors of Bay City Capital LLC and have voting and dispositive power with respect to shares held by Bay City Capital Funds. Dr. Goldfischer disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. The address for Bay City Capital Fund V is 750 Battery Street, Suite 400, San Francisco, CA 94111.

(9) Consists of 365,616 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2021 or will become exercisable within 60 days after such date.

(10) Consists of 106,398 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2021 or will become exercisable within 60 days after such date.

(11) Includes 5,151 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2021 or will become exercisable within 60 days after such date.

(12) Consists of 10,430,896 shares of common stock and 502,920 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2021 or will become exercisable within 60 days after such date.

Securities Authorized for Issuance under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2020:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders			
2016 Stock Incentive Plan	1,274,312	$ 4.49	—
2020 Equity Incentive Plan (1)	661,320	20.18	1,110,675
2020 Employee Stock Purchase Plan (2)	—	—	191,363
Equity compensation plans not approved by security holders	—	—	—
Total	1,935,632	$ 24.67	1,302,038

(1) Our 2020 Equity Incentive Plan, or 2020 Plan, has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2020 Plan to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2030, equal to the least of (i) 4% of the outstanding shares on such date and (ii) an amount determined by our board of directors. On January 1, 2021, 701,930 additional shares were reserved for issuance under the 2020 Plan pursuant to this provision.

(2) Our 2020 Employee Stock Purchase Plan, or 2020 ESPP, has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2020 Plan to be added on the first day of each fiscal year, commencing on January 1, 2021 and ending on January 1, 2031, equal to the least of (i) 386,432 shares of common stock, (ii) 1% of the outstanding shares on such date and (iii) an amount determined by the Board.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Since January 1, 2019, we have engaged in the following transactions in which the amounts involved exceeded $120,000 and any of our directors, executive officers, or holders of more than 5% of our capital stock, or any member of the immediate family of, or person sharing the household with, the foregoing persons, had or will have a direct or indirect material interest. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Cydan Business Services Agreement

In January 2016, we entered into a Business Services Agreement with Cydan, or the Business Services Agreement, pursuant to which Cydan provided office space, personnel assistance, and other business services to us on an as-needed basis. At the time the agreement was signed, Cydan was a holder of more than 5% of our capital stock, Dr. McArthur was our founder, President and Chief Executive Officer, a member of our board of directors and a holder of more than 5% of our capital stock and the Chief Scientific Officer of Cydan; Dr. Adams was our Treasurer and Secretary, a member of our board of directors and a holder of more than 5% of our capital stock and the Chief Executive Officer of Cydan; Dr. Bisker-Leib was a holder of more than 5% of our capital stock and the Chief Business Officer of Cydan; and certain other members of our board of directors, including Ms. Agger, Dr. Dalton, Mr. Mott and Dr. Nayeem, were also members of the board of directors of Cydan and continue to serve on both our board of directors and the board of directors of Cydan. We paid Cydan $1.0 million in 2017, $0.7 million in 2018 and $0.3 million in 2019, related to these services under the Business Services Agreement. We agreed with Cydan to terminate the Business Services Agreement and all related services rendered by Cydan to us effective as of August 17, 2019.

Lundbeck Exclusive License Agreement

In April 2016, we entered into an exclusive license agreement with H. Lundbeck A/S, or Lundbeck, pursuant to which Lundbeck granted us a worldwide license under certain patent rights and certain know-how owned or otherwise controlled by Lundbeck within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or diseases or disorders, including those directly or indirectly related to hemoglobinopathies. As partial consideration for the licenses granted under

the agreement, we issued 167,523 shares of our common stock to Lundbeck in April 2016. We issued 127,002 shares of our common stock to Lundbeck in December 2016 and 148,746 shares of our common stock in August 2017 as a result of antidilution provisions contained in the exclusive license agreement triggered by subsequent closings of our series A preferred stock, described below. In addition, pursuant to this exclusive license agreement, we have made cash payments to Lundbeck of $1.8 million to date consisting of an upfront payment and ongoing milestone payments. See "Business—Exclusive License Agreement" for additional information regarding the exclusive license agreement. Ms. Agger, a member of our board of directors, is also the Managing Partner of Lundbeckfond Invest A/S, the majority stockholder of Lundbeck. Lundbeckfond Invest A/S owns more than 5% of our capital stock.

Series B Preferred Stock Financing

Between March 2019 and February 2020, we issued and sold an aggregate of 36,166,661 shares of series B preferred stock, at a price per share of $1.7419 in cash, for an aggregate purchase price of $63.0 million.

The following table sets forth the aggregate number of shares of series B preferred stock that we issued and sold to our directors and 5% stockholders and their affiliates and the aggregate purchase price for such shares:

Purchaser(1)	Shares of Series B Preferred Stock	Aggregate Purchase Price
New Enterprise Associates 14, L.P.(2)	5,625,926	$ 9,799,800
OrbiMed Private Investments VII, LP(3)	10,046,294	17,499,640
Arix Bioscience Holdings Limited(4)	8,611,110	14,999,693
Entities affiliated with RA Capital Healthcare Fund, L.P.(5)	5,224,073	9,099,813
Pfizer Ventures (US) LLC(6)	1,894,444	3,299,932
Lundbeckfond Invest A/S(7)	1,894,444	3,299,932
Entities affiliated with Bay City Capital(8)	861,111	1,499,969

(1) See "Principal Stockholders" for additional information about shares held by certain of these entities.
(2) David M. Mott, the chairman of our board of directors, was a general partner of New Enterprise Associates and Sara Nayeem, M.D., a member of our board of directors, is a partner of New Enterprise Associates.
(3) David Bonita, M.D., a member of our board of directors, is a Partner of OrbiMed Advisors.
(4) Mark Chin, a member of our board of directors, was an Investment Director at Arix Bioscience until April 2020.
(5) RA Capital Healthcare Fund, L.P. is a 5% stockholder.
(6) Barbara J. Dalton, Ph.D., a member of our board of directors, is Vice President of Venture Capital of Pfizer, Inc., an affiliate of Pfizer Ventures (US) LLC.
(7) Mette Kirstine Agger, a member of our board of directors, is the Managing Partner of Lundbeckfonden Ventures.
(8) Carl Goldfischer, M.D., a member of our board of directors, is the Managing Director of Bay City Capital.

The series B preferred stock converted into common stock on a 6.299-for-1 basis upon the closing of our initial public offering on March 16, 2020.

Initial Public Offering

In March 2020, we closed our initial public offering, pursuant to which we issued and sold 4,700,000 shares of our common stock. In April 2020, we issued and sold an additional 705,000 shares of common stock pursuant to the full exercise of the underwriters' over-allotment option. The following table sets forth the aggregate number of shares of our common stock that we issued and sold to our directors and 5% stockholders and their affiliates and the aggregate purchase price for such shares. Such purchases were made through the underwriters at the initial public offering price of $16.00 per share.

Purchaser(1)	Shares of Common Stock	Aggregate Purchase Price
New Enterprise Associates 14, L.P.(2)	475,000	$ 7,600,000
OrbiMed Private Investments VII, LP(3)	1,125,000	18,000,000
Arix Bioscience Holdings Limited(4)	187,500	3,000,000
Entities affiliated with RA Capital Healthcare Fund, L.P.(5)	625,000	10,000,000
Pfizer Ventures (US) LLC(6)	312,500	5,000,000
Lundbeckfond Invest A/S(7)	187,500	3,000,000

(1) See "Principal Stockholders" for additional information about shares held by these entities.
(2) David M. Mott, the chairman of our board of directors, was a general partner of New Enterprise Associates and Sara Nayeem, M.D., a member of our board of directors, is a partner of New Enterprise Associates.
(3) David Bonita, M.D., a member of our board of directors, is a Partner of OrbiMed Advisors.
(4) Mark Chin, a member of our board of directors, was an Investment Director at Arix Bioscience until April 2020.
(5) RA Capital Healthcare Fund, L.P. and its affiliates is a 5% stockholder.
(6) Barbara J. Dalton, Ph.D., a member of our board of directors, is Vice President of Venture Capital of Pfizer, Inc., an affiliate of Pfizer Ventures (US) LLC.
(7) Mette Kirstine Agger, a member of our board of directors, is the Managing Partner of Lundbeckfonden Ventures.

Registration Rights

We are a party to an investors' rights agreement with certain holders of our common stock, including our 5% stockholders and their affiliates and entities affiliated with some of our directors. This investors' rights agreement provides these stockholders the right, subject to certain conditions, to demand that we file a registration statement or to request that their shares be covered by a registration statement that we are otherwise filing.

See "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Indemnification Agreements

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we entered into indemnification agreements with all of our directors and executive officers in connection with our initial public offering. These indemnification agreements may require us, among other things, to indemnify each such director or executive officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers.

Employment Arrangements

We have entered into employment agreements with certain of our executive officers. For more information regarding the agreements with Dr. Ballal and Mr. Gray, see "Executive Compensation."

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our chief financial officer. The

policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of the entity, that is a participant in the transaction where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee's charter.

The transactions described in this section occurred prior to the adoption of the policy.

Director Independence

The Nasdaq Stock Market LLC, or Nasdaq, Marketplace Rules, or the Nasdaq Listing Rules, require a majority of a listed company's board of directors to be composed of independent directors within one year of listing. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under the Nasdaq Listing Rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In October 2019, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director and in April 2020 undertook this review with respect to Edward Conner upon his appointment to our board of directors. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Rahul D. Ballal, are "independent directors" as defined under the Nasdaq Listing Rules. Our board of directors had also previously determined that James McArthur, a former director who served during the year ended December 31, 2019, was not an independent director as defined under applicable Nasdaq rules prior to his resignation from our board of directors in 2020. In making such determinations, our board of directors considered the relationships that each such director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each director. Dr. Ballal is not an independent director under these rules because he is our President and Chief Executive Officer. Dr. McArthur was not an independent director under these rules because he served as our President and Chief Executive Officer until May 2018.

Item 14. Principal Accountant Fees and Services.

The following table summarizes the fees of Ernst & Young LLP, our independent registered public accounting firm, billed us for each of the last two fiscal years (in thousands):

	Year Ended December 31,	
	2020	2019
Audit Fees (1)	$ 556	$ 1,046
Audit-Related Fees	—	—
Tax Fees (2)	12	10
All Other Fees	4	—
	$ 572	$ 1,056

(1) Audit fees consist of fees billed for professional services by Ernst & Young LLP for audit and quarterly review of our consolidated financial statements and review of the registration statement on Form S-1 for our IPO, and related services that are normally provided in connection with statutory and regulatory filings or engagements.
(2) Tax fees consist of fees for professional services performed by Ernst & Young LLP with respect to tax compliance, tax advice and tax planning.

Pre-Approval Policies and Procedures

The audit committee of our board of directors has adopted policies and procedures for the pre-approval of audit and non-audit services for the purpose of maintaining the independence of our independent auditor. We may not engage our independent auditor to render any audit or non-audit service unless either the service is approved in advance by the audit committee, or the engagement to render the service is entered into pursuant to the audit committee's pre-approval policies and procedures. Notwithstanding the foregoing, pre-approval is not required with respect to the provision of services, other than audit, review or attest services, by the independent auditor if the aggregate amount of all such services is no more than 5% of the total amount paid by us to the independent auditor during the fiscal year in which the services are provided, such services were not recognized by us at the time of the engagement to be non-audit services and such services are promptly brought to the attention of the audit committee and approved prior to completion of the audit by the audit committee.

From time to time, our audit committee may pre-approve services that are expected to be provided to us by the independent auditor during the following 12 months. At the time such pre-approval is granted, the audit committee must identify the particular pre-approved services in a sufficient level of detail so that our management will not be called upon to make a judgment as to whether a proposed service fits within the pre-approved services and, at each regularly scheduled meeting of the audit committee following such approval, management or the independent auditor shall report to the audit committee regarding each service actually provided to us pursuant to such pre-approval.

The audit committee has delegated to its chairman the authority to grant pre-approvals of audit or non-audit services to be provided by the independent auditor. Any approval of services by the chairman of the audit committee is reported to the committee at its next regularly scheduled meeting.

PART IV

Item 15. Exhibit and Financial Statement Schedules.

(1) The financial statements listed below are filed as part of this Annual Report on Form 10-K.

(2) All financial statement schedules have been omitted because they are not applicable, not required, or the information required is shown in the consolidated financial statements or the notes thereto.

(3) The following is a list of exhibits filed as part of this Annual Report on Form 10-K

Exhibit Index

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on March 16, 2020)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K filed with the SEC on March 16, 2020)
4.1	Specimen stock certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
4.2	Amended and Restated Investors' Rights Agreement, dated as of March 15, 2019, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
4.3	Description of Securities of the Registrant*
10.1#	2016 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1/A, filed with the SEC on March 3, 2020)
10.2#	Form of Incentive Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.3#	Form of Nonstatutory Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.4#	2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A, filed with the SEC on March 3, 2020)
10.5#	Form of Stock Option Agreement under the 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.6#	2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1/A, filed with the SEC on March 3, 2020)
10.7†	Exclusive License Agreement, dated as of April 11, 2016, by and between H. Lundbeck A/S and the Registrant, as amended (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)

10.8#	Amended and Restated Letter Agreement, dated as of September 23, 2019, by and between the Registrant and Rahul D. Ballal, Ph.D. (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.9#	Amended and Restated Letter Agreement, dated as of September 23, 2019, by and between the Registrant and Willem H. Scheele, M.D. ((incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.10#	Amended and Restated Letter Agreement, dated as of September 23, 2019, by and between the Registrant and Michael P. Gray (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.11	Form of Indemnification Agreement with directors and executive officers (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.12	Office Lease Agreement, dated as of May 20, 2019, by and between Columbia REIT – 116 Huntington, LLC and the Registrant (incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.13#	Form of Restricted Stock Unit Agreement under the 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.14#	Separation and Release of Claims Agreement, dated as of May 1, 2020, by and between the Registrant and Willem H. Scheele, M.D. (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on August 14, 2020)
21.1	List of Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm
31.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

\# Indicates a management contract or any compensatory plan, contract or arrangement.

† Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the Registrant if disclosed.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

IMARA INC.

Date: March 5, 2021

By: /s/ Rahul D. Ballal

Rahul D. Ballal, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Rahul D. Ballal **Rahul D. Ballal, Ph.D.**	President and Chief Executive Officer, Director (Principal Executive Officer)	March 5, 2021
/s/ Michael P. Gray **Michael P. Gray**	Chief Financial Officer and Chief Operating Officer (Principal Financial and Accounting Officer)	March 5, 2021
/s/ David M. Mott **David M. Mott**	Chairman of the Board	March 5, 2021
/s/ Mette Kirstine Agger **Mette Kirstine Agger**	Director	March 5, 2021
/s/ David Bonita **David Bonita, M.D.**	Director	March 5, 2021
/s/ Mark Chin **Mark Chin**	Director	March 5, 2021
/s/ Edward Conner **Edward Conner**	Director	March 52021
/s/ Carl Goldfischer **Carl Goldfischer, M.D.**	Director	March 5, 2021
/s/ Barbara J. Dalton **Barbara J. Dalton, Ph.D.**	Director	March 5, 2021
/s/ Sara Nayeem **Sara Nayeem, M.D.**	Director	March 5, 2021

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of IMARA Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of IMARA Inc. (the Company) as of December 31, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.
Boston, Massachusetts
March 5, 2021

IMARA INC.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 47,698	$ 4,936
Short-term investments	40,524	23,971
Prepaid expenses and other current assets	2,183	1,717
Total current assets	90,405	30,624
Property and equipment, net	349	442
Other assets	88	2,232
Total assets	$ 90,842	$ 33,298
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	1,971	1,658
Accrued expenses and other current liabilities	4,276	2,540
Total current liabilities	6,247	4,198
Deferred rent	160	184
Total liabilities	$ 6,407	$ 4,382
Commitments and contingencies (Note 8)		
Series Seed convertible preferred stock, par value of $0.001 per share; no shares and 2,712,960 shares authorized, issued and outstanding as of December 31, 2020 and 2019, respectively; liquidation value of $0 December 31, 2020	—	1,460
Series A convertible preferred stock, par value of $0.001 per share; no shares and 31,499,040 shares authorized, issued and outstanding as of December 31, 2020 and 2019, respectively	—	30,729
Series B convertible preferred stock, par value of $0.001 per share; no shares, issued and outstanding as of December 31, 2020; 36,166,661 shares authorized and 26,321,313 shares issued and outstanding as of December 31, 2019	—	45,575
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value per share; 10,000,000 shares authorized; no shares issued or outstanding as of December 31, 2020; no shares authorized, issued or outstanding as of December 31, 2019	—	—
Common stock, par value of $0.001 per share; 200,000,000 and 100,000,000 shares authorized as of December 31, 2020 and 2019, respectively; 17,548,263 and 702,510 shares issued and outstanding as of December 31, 2020 and 2019, respectively	18	1
Additional paid-in capital	180,526	5,872
Accumulated other comprehensive income	4	32
Accumulated deficit	(96,113)	(54,753)
Total stockholders' equity (deficit)	84,435	(48,848)
Total liabilities, convertible preferred stock and stockholders’ equity (deficit)	$ 90,842	$ 33,298

The accompanying notes are an integral part of these consolidated financial statements.

IMARA INC.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Years ended December 31,	
	2020	**2019**
Operating expenses:		
Research and development	$ 32,154	$ 19,009
General and administrative	9,544	5,107
Total operating expenses	$ 41,698	$ 24,116
Loss from operations	(41,698)	(24,116)
Total other income:		
Interest income	483	578
Other income (expense)	(145)	75
Total other income, net	$ 338	$ 653
Net loss	$ (41,360)	$ (23,463)
Accretion of Series B convertible preferred stock	(7,858)	—
Net loss attributable to common stockholders—basic and diluted	$ (49,218)	$ (23,463)
Net loss per share applicable to common stockholders—basic and diluted	$ (3.53)	$ (33.40)
Weighted-average common shares outstanding—basic and diluted	$ 13,924,730	$ 702,455
Comprehensive loss:		
Net loss	(41,360)	(23,463)
Other comprehensive loss:		
Unrealized gain (loss) on investments, net	(28)	32
Comprehensive loss	$ (41,388)	$ (23,431)

The accompanying notes are an integral part of these consolidated financial statements.

IMARA INC.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share and per share data)

	CONVERTIBLE PREFERRED STOCK											
	SERIES SEED $0.001 PAR VALUE		SERIES A $0.001 PAR VALUE		SERIES B $0.001 PAR VALUE		COMMON STOCK $0.001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE INCOME	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY (DEFICIT)
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT				
Balance at December 31, 2018	2,712,960	$ 1,460	31,499,040	$ 30,729	—	$ —	702,510	$ 1	$ 4,973	$ —	$ (31,290)	$ (26,316)
Issuance of Series B convertible preferred stock, net of issuance costs of $274	—	—	—	—	26,321,313	45,575	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	899	—	—	899
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	32	—	32
Net loss	—	—	—	—	—	—	—	—	—	—	(23,463)	(23,463)
Balance at December 31, 2019	2,712,960	$ 1,460	31,499,040	$ 30,729	26,321,313	$ 45,575	702,510	$ 1	$ 5,872	$ 32	$ (54,753)	$ (48,848)
Issuance of Series B convertible preferred stock, net of issuance costs of $20 and beneficial conversion charge	—	—	—	—	9,845,348	9,271	—	—	7,858	—	—	7,858
Accretion of Series B converted preferred stock	—	—	—	—	—	7,858	—	—	(7,858)	—	—	(7,858)
Conversion of convertible preferred stock into common stock	(2,712,960)	(1,460)	(31,499,040)	(30,729)	(36,166,661)	(62,704)	11,172,955	11	94,882	—	—	94,893
Initial public offering, net of underwriting discounts, commissions and offering costs of $3,902	—	—	—	—	—	—	5,405,000	6	76,520	—	—	76,526
Exercise of stock options and issuance of stock under the Employee Stock Purchase Plan	—	—	—	—	—	—	267,798	—	1,021		—	1,021
Stock-based compensation expense	—	—	—	—	—	—	—	—	2,231	—	—	2,231
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	(28)	—	(28)
Net loss											(41,360)	(41,360)
Balance at December 31, 2020	—	—	—	—	—	—	17,548,263	$ 18	$ 180,526	$ 4	$ (96,113)	$ 84,435

The accompanying notes are an integral part of these consolidated financial statements.

IMARA Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (41,360)	$ (23,463)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	2,231	899
Depreciation expense	97	33
Amortization and accretion on investments	122	(19)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(465)	(1,394)
Other assets	(60)	(88)
Accounts payable	313	750
Accrued expenses and other current liabilities	1,748	1,305
Deferred rent	(24)	100
Net cash used in operating activities	(37,398)	(21,877)
Cash flows from investing activities:		
Proceeds from maturities and sales of short-term investments	47,500	—
Purchases of short-term investments	(64,203)	(23,920)
Purchases of property and equipment	(18)	(140)
Net cash used in investing activities	(16,721)	(24,060)
Cash flows from financing activities:		
Proceeds from initial public offering, net of underwriting discounts, commissions and offering costs	80,427	—
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	17,150	45,575
Proceeds from exercise of options	1,022	—
Payment of issuance costs	(1,718)	(1,996)
Net cash provided by financing activities	96,881	43,579
Net increase in cash, cash equivalents and restricted cash	42,762	(2,358)
Cash, cash equivalents and restricted cash, beginning of period	5,024	7,382
Cash, cash equivalents and restricted cash, end of period	$ 47,786	$ 5,024
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of convertible preferred stock into common stock	$ 94,893	$ —
Accretion of redeemable convertible preferred stock to redemption value	$ (7,858)	$ —
Reclassification of deferred offering costs from other assets to additional paid-in capital	$ (2,144)	$ —
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ 60
Property and equipment purchases included in accrued expenses	$ 12	$ 335
Unrealized loss on investments	$ (28)	$ —

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the dates shown below:

	December 31,	
	2020	2019
Cash and cash equivalents	$ 47,698	$ 4,936
Restricted cash (included in other assets)	88	88
Total cash, cash equivalents and restricted cash	$ 47,786	$ 5,024

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of the Business

IMARA Inc. ("IMARA" or the "Company") is a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat rare inherited genetic disorders of hemoglobin, known as hemoglobinopathies, which have significant unmet medical need. The Company was incorporated in January 2016 under the laws of the State of Delaware, and its principal offices are in Boston, Massachusetts.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, risks associated with completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. The Company's sole product candidate currently under development, IMR-687, as well as any other product candidates the Company may develop, will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

In February 2020, the Company effected a 1-for-6.299 reverse stock split of the Company's issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each of the Company's outstanding series of Series Seed convertible preferred stock ("Series Seed Preferred Stock"), Series A convertible preferred stock ("Series A Preferred Stock"), Series B convertible preferred stock ("Series B Preferred Stock"), collectively referred to as "Preferred Stock.". All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the change in par value of common stock to additional paid-in capital.

On February 25, 2020, the Company issued and sold 1,562,994 shares of Series B Preferred Stock at a price of $10.9722 per share, upon a waiver of specified milestone conditions from the holders of a majority of the shares then held by holders of Series B Preferred Stock, and raised approximately $17.1 million in net proceeds after deducting less than $0.1 million of issuance costs.

On March 16, 2020, the Company completed an initial public offering ("IPO") of its common stock and issued and sold 4,700,000 shares of common stock at a public offering price of $16.00 per share, resulting in gross proceeds of $75.2 million. On April 13, 2020, the Company issued and sold an additional 705,000 shares of common stock pursuant to the exercise of the underwriters' option to purchase additional shares for aggregate gross proceeds of $11.3 million. Inclusive of the exercise by the underwriters of their option to purchase additional shares, the Company received approximately $76.5 million in net proceeds from the IPO after deducting $10.0 million of underwriting discounts and commissions and offering expenses.

Upon the closing of the IPO, all 70,378,661 shares of outstanding Preferred Stock automatically converted into 11,172,955 shares of common stock. Upon conversion of the convertible Preferred Stock, the Company reclassified the carrying value of the convertible Preferred Stock to common stock and additional paid-in capital.

Liquidity

The Company has incurred recurring negative cash flows since inception and has funded its operations primarily from the sale of Preferred Stock. As of December 31, 2020, the Company had cash, cash equivalents, and investments of $88.2 million and an accumulated deficit of $96.1 million. The Company expects its operating losses and negative operating cash flows to continue into the foreseeable future as it continues to expand its research and development efforts.

The Company believes its cash, cash equivalents and investments will be sufficient to fund its operating expenses and capital expenditure requirements for at least twelve months from the date of filing this Annual Report on Form 10-K. The Company will need additional funding to support its planned operating activities. There can be no assurances, however, that

the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all. If the Company is unable to obtain sufficient funding, it could be required to delay its development efforts, limit activities and reduce research and development costs, which could adversely affect its business prospects.

2. Summary of Significant Accounting Policies

Basis of presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and as amended by Accounting Standards Updates of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The accompanying consolidated financial statements of the Company include the accounts of its wholly owned subsidiaries, IMARA Security Corporation and IMARA E.U. Limited. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, accrued research and development expenses, stock-based compensation expense, the fair value of the common stock and Preferred Stock and income taxes. Actual results could differ materially from those estimates.

Segments

Operating segments are defined as components of an enterprise for which separate and discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources. All of the Company's long-lived assets are held in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments that are readily convertible into cash with original maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds. Cash equivalents are stated at cost, which approximates market value.

Restricted Cash

Restricted cash of less than $0.1 million as of December 31, 2020 and December 31, 2019, represents a letter of credit held as collateral in support of the Company's facility lease. Restricted cash is included as a component of other assets on the Company's consolidated balance sheets.

Investments

The Company's investments are maintained by investment managers and consist of corporate debt securities and commercial paper with original maturities of over 90 days, all of which are considered available-for-sale securities. The Company classifies its available-for-sale securities as short-term investments on the consolidated balance sheets, even though the stated maturity date may be one year or more beyond the current balance sheet date, as the Company views those securities as available for use in current operations, if needed.

Available-for-sale securities are carried at fair value with their unrealized gains and losses included in accumulated other comprehensive income within stockholders' equity (deficit), until such gains and losses are realized in other income (expense) within the consolidated statements of operations and comprehensive loss or until an unrealized loss is considered other-than-temporary.

The Company evaluates its investments with unrealized losses for other-than-temporary impairment. When assessing investments for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions. If the Company determines from this analysis that it does not expect to receive cash flows sufficient to recover the entire amortized cost of the security, a credit loss exists, the impairment is considered other-than-temporary and is recognized in the consolidated statements of operations and comprehensive loss.

Deferred Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity issuances as deferred offering costs until such equity issuances are consummated. After consummation of the equity issuance, these costs are recorded as a reduction in the capitalized amount associated with the equity issuance. Should the equity issuance be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. On March 16, 2020, the Company completed its IPO; accordingly, the Company recognized the deferred offering costs of approximately $3.9 million as a reduction from gross proceeds associated with the IPO through additional paid-in capital in the accompanying consolidated balance sheet. Deferred offering costs classified in other assets on the accompanying consolidated balance sheet as of December 31, 2019 were $2.1 million. There were no deferred offering costs as of December 31, 2020.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and investments. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and have not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships. Such deposits have and will continue to exceed federally insured limits. The Company has not experienced any losses on its cash deposits. The Company's available-for-sale investments primarily consist of high-grade corporate debt and commercial paper, and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment and requires all investments held by the Company to be highly rated, thereby reducing credit risk exposure.

As of December 31, 2020 and 2019, the Company had no off-balance sheet risk such as foreign exchange contracts, option contracts, or other hedging arrangements.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity (deficit) that are excluded from net loss. For the years ended December 31, 2020 and 2019, as a result of the Company's investments in available-for-sale securities, the Company's comprehensive loss includes unrealized gains and losses on those available-for-sale securities.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings.

The carrying amounts reflected in the consolidated balance sheets for prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to their short-term nature of these assets and liabilities.

Property and Equipment, Net

Property and equipment is stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

	Estimated Useful Life
Computer equipment and software	3 years
Furniture and fixtures	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

Purchased assets that are not yet in service are recorded to construction-in-process and no depreciation expense is recorded. Once they are placed in service they are reclassified to the appropriate asset class. Upon the retirement or sale of an asset, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is recorded to other income (expense), net. Expenditures for maintenance and repairs are expensed as incurred.

Deferred Rent

Deferred rent consists of rent escalation payment terms, tenant improvement allowances and other incentives received from landlords related to the Company's operating leases. Rent escalation represents the difference between actual operating lease payments due and straight-line rent expense, which is recorded by the Company over the term of the lease. Tenant improvement allowances and other incentives are recorded as deferred rent and amortized as a reduction of periodic rent expense, over the term of the applicable lease.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside vendors engaged to conduct preclinical development activities and clinical trials as well as to manufacture research and development materials. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are expensed as the goods are delivered or the related services are performed or until it is no longer expected that the goods will be delivered, or the services rendered.

Costs incurred in obtaining technology licenses are recognized as research and development expense as incurred if the technology licensed has not reached technological feasibility and has no alternative future uses.

Accrued Research and Development Expenses

The Company has entered into various research and development related contracts with parties both inside and outside of the United States, including contracts with third-party contract research organizations and contract manufacturing organizations. These agreements are cancelable, and related payments are recognized as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes the progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. To date, the Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure and are classified as general and administrative expenses.

Stock-Based Compensation

The Company accounts for all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value. For stock-based awards issued to employees and members of the Company's board of directors (the "Board") for their services as a member of the Board, the Company measures the estimated fair value of the stock-based award on the date of grant.

Since the Company's initial public offering in March 2020, the fair value of the common stock has been determined based on the closing price of the Company's stock on the date of grant. Prior to the Company's initial public offering, the Company determined the fair value of the underlying common stock based on input from management and approved by the Board, which utilized the valuation of the Company's enterprise value determined utilizing various methods including the back-solve method, the option-pricing method ("OPM") or a hybrid of the probability-weighted expected return method ("PWERM") and the OPM. The total enterprise value was then allocated to the various outstanding equity instruments, including the underlying common stock, utilizing the option-pricing model.

For employee and non-employee awards, the Company recognizes compensation expense over the requisite service period, which is generally the vesting period of the respective award based on the grant date fair value of the award. For awards that include performance-based vesting conditions expense is recognized using the accelerated attribution method when the performance condition is deemed to be probable. The Company accounts for forfeitures as they occur. The Company determines the fair value of restricted stock awards in reference to the fair value of its common stock less any applicable purchase price.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option and the Company's expected dividend yield. The fair value of each restricted stock award is determined on the date of grant based on the fair value of the Company's common stock on that same date. Given the Company's limited trading history as a public company, the Company determines the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Under the simplified method, the expected term is presumed to be the midpoint between the vesting date and the end of the contractual term. The Company utilizes this method due to lack of historical exercise data and the plain nature of its stock-based awards. Prior to the Company's IPO, the expected term of stock options granted to non-employees also used the "simplified" method. Following the Company's IPO, the expected term of options granted to non-employees is determined by contractual term. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The Company has not paid, and does not anticipate paying, cash dividends on its common stock; therefore, the expected dividend yield is assumed to be zero.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's cash compensation costs are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or the Company's tax returns. Under this method, deferred tax assets and liabilities are determined based on the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Net loss per share attributable to common stockholders is calculated using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company's common shares and participating securities. The Company's Preferred Stock contained participation rights in any dividend paid by the Company and is deemed to be a participating security. Net loss attributable to common stockholders and participating preferred shares are allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities do not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the if-converted method. The Company allocates earnings first to preferred stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. The weighted-average number of common shares included in the computation of diluted net loss effect to all potentially dilutive common equivalent shares, including outstanding stock options and Preferred Stock. Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which, among other things, requires lessees to recognize an obligation to make lease payments arising from a lease, measured on a discounted basis, and a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Expenses are recognized in the consolidated statement of operations in a manner similar to current accounting guidance. The Company expects to make an accounting policy election to not recognize an asset and liability for leases with a term of twelve months or less. The standard is effective for fiscal years beginning after December 15, 2021. The Company will early adopt the accounting standard effective January 1, 2021 using a modified retrospective approach, which applies the provisions of the new guidance at the effective date without adjusting the comparative periods presented. The Company is finalizing its evaluation of the impacts that the adoption of this accounting guidance will have on the consolidated financial statements and estimates approximately $1 million of right-to-use assets and lease liabilities will be recognized in the balance sheet upon adoption.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which requires entities to estimate all expected credit losses for certain types of financial instruments, including trade receivables, held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. The updated guidance also expands the disclosure requirements to enable users of financial statements to understand the entity's assumptions, models and methods for estimating expected credit losses over the entire contractual term of the instrument from the date of initial recognition of that instrument. For public business entities that meet the definition of a United States Securities and Exchange Commission ("SEC") filer,

excluding entities eligible to be smaller reporting companies as defined by the SEC, the standard is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, the standard is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact of this new guidance on the Company's consolidated financial statements and related disclosures, but does not expect the adoption of ASU 2016-13 to be material.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11")**.** Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. The amendments in Part I of this update became effective for the Company for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted for all entities, including adoption in an interim period. The adoption had no material impact on the Company's financial position, results of operations or cash flows. The amendments in Part II of this update do not require any transition guidance because those amendments do not have an accounting effect.

On August 5, 2020, the FASB issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU-2020-06"), which simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. ASU 2020-06 eliminates the beneficial conversion and cash conversion accounting models in ASC 470-20 that require separate accounting for embedded conversion features from convertible instruments. As a result, after adopting the ASU's guidance, entities will not separately present in equity an embedded conversion feature in such debt. Additionally, the guidance simplifies the evaluation of whether a contract in the issuer's own equity can be classified in equity or an embedded feature qualifies for the derivative scope exception. Although the guidance is not effective until 2022, early adoption of ASU 2020-06 is permitted for all entities for fiscal years beginning after December 15, 2020. The Company is currently evaluating the impact of this new guidance on the Company's consolidated financial statements and related disclosures.

3. Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	December 31, 2020			
Description	**Total**	**Quoted Prices in Active Markets for Identical Assets (Level 1)**	**Significant Other Observable Inputs (Level 2)**	**Significant Other Observable Inputs (Level 3)**
Assets:				
Money market funds, included in cash and cash equivalents	$ 41,208	$ 41,208	$ —	$ —
Marketable securities:				
Corporate debt securities	14,807	—	14,807	—
Commercial paper	25,717	—	25,717	—
Total financial assets	$ 81,732	$ 41,208	$ 40,524	$ —

Description	December 31, 2019 Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets:				
Money market funds, included in cash and cash equivalents	$ 4,477	$ 4,477	$ —	$ —
Marketable securities:				
Corporate debt securities	5,772	—	5,772	—
Commercial paper	18,199	—	18,199	—
Total financial assets	$ 28,448	$ 4,477	$ 23,971	$ —

As of December 31, 2020 and 2019, the Company's cash equivalents consisted of money market funds, classified as Level 1 financial assets, as these assets are valued using quoted market prices in active markets without any valuation adjustment. The financial assets valued based on Level 2 inputs consist of corporate debt securities and commercial paper, which consist of investments in highly-rated investment-grade securities. The Company estimates the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by its third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

During the years ended December 31, 2020 and 2019, there were no transfers between fair value measurement levels.

4. Investments

As of December 31, 2020, the Company had short-term investments consisting of corporate debt securities and commercial paper, which are considered to be available-for-sale investments. These are included in short-term investments on the consolidated balance sheets, even though the stated maturity date may be one year or more beyond the current balance sheet date, as the Company views those securities as available for use in current operations, if needed. The following table summarizes the Company's investments as of December 31, 2020 and 2019 (in thousands):

	December 31, 2020 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Current:				
Commercial paper	$ 25,716	$ 1	$ —	$ 25,717
Corporate debt securities	14,804	3	—	14,807
Total	$ 40,520	$ 4	$ —	$ 40,524

	December 31, 2019 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Current:				
Commercial paper	$ 18,167	$ 32	$ —	$ 18,199
Corporate debt securities	5,772	—	—	5,772
Total	$ 23,939	$ 32	$ —	$ 23,971

As of December 31, 2020 and 2019, the Company had no available-for-sale securities in unrealized loss positions. The Company determined that there was no material change in the credit risk of its investments. As a result, the Company determined it did not hold any investments with an other-than-temporary impairment as of December 31, 2020 and 2019.

5. Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Property and equipment:		
Leasehold improvements	$ 336	$ 339
Furniture and fixtures	143	136
Property and equipment	$ 479	$ 475
Less: accumulated depreciation	(130)	(33)
Property and equipment, net	$ 349	$ 442

Depreciation expense was $0.1 million and less than $0.1 million for the years ended December 31, 2020 and 2019, respectively.

6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Accrued research and development expenses	$ 2,732	$ 1,106
Accrued compensation and benefits	1,090	802
Accrued professional services	355	330
Accrued other	99	302
Total accrued expenses	$ 4,276	$ 2,540

7. License Agreements

Agreement with Lundbeck

In April 2016, the Company entered into a license agreement with Lundbeck (the "Lundbeck Agreement") pursuant to which Lundbeck granted the Company the following licenses within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies: (1) an exclusive, royalty-bearing license to certain patent rights and certain know-how owned or otherwise controlled by Lundbeck ("Licensed Technology") to research, develop, make, use, sell, and commercialize products ("Licensed Products") from PDE9 inhibitors, which included IMR-687 ("Licensed Compounds"); (2) a non-exclusive license to the Licensed Technology to make, research, develop, and use such Licensed Technology to enable research and development, with certain restrictions; and (3) a sublicensing right that allows the Company to grant sublicenses to third parties to use the Licensed Technology subject to the certain terms detailed in the Lundbeck Agreement. Under the Lundbeck Agreement, the Company is subject to certain achievement dates for development milestones as defined in the agreement. The regulatory milestones due under the Lundbeck Agreement depend on the products being developed. Development milestones due under the Lundbeck Agreement with respect to the Licensed Compounds total up to $23.5 million, and, for any products that contain PDE9 inhibitors other than Licensed Compounds, total up to $11.8 million. The Company also agreed to pay tiered royalties based on net sales of all products licensed under the agreement in the low single-digit percentages.

To date, pursuant to the license agreement, the Company has made cash payments to Lundbeck of $1.8 million consisting of an upfront payment and ongoing milestone payments, which are recorded as research and development expense. No payments were made during the year ended December 31, 2020. As partial consideration for the license, the Company issued 167,523 shares of common stock to Lundbeck in 2016, which represented 8.0% of the Company's then outstanding equity pursuant to a restricted stock agreement. The shares were fully vested on the date of issuance.

The Lundbeck Agreement can be terminated by the Company at any time with 180 days' written notice. The Company or Lundbeck may terminate the agreement by written notice within a specified period of time in the event of a material breach.

8. Commitments and Contingencies

Lease Agreements

In 2016, the Company entered into an agreement for office space located in Cambridge, Massachusetts, which was a month-to-month lease, with a related party (see Note 14). The Company recorded rent expense of $0.2 million and $0.2 million during the years ended December 31, 2020 and 2019, respectively.

In May 2019, the Company entered into a new operating lease agreement for office space totaling 4,210 square feet, located in Boston, Massachusetts with a 62-month term. The lease includes a rent escalation clause which results in cash rental payments of approximately $0.3 million annually. Rent expense is being recognized on a straight-line basis over the lease term. In addition to the base rent, the Company is also responsible for its share of operating expenses, electricity and real estate taxes, in accordance with the terms of the Lease Agreement. The Company provided a security deposit of approximately $0.1 million during the year ended December 31, 2019, which is included as a component of other assets on the Company's consolidated balance sheets. The Company occupied the space in August 2019 and commenced recognition of rent expense.

The following table summarizes the future minimum lease payments due under the Company's operating leases as of December 31, 2020 exclusive of amounts prepaid by the Company (in thousands):

	December 31, 2020
2021	273
2022	278
2023	284
2024	229
	$ 1,064

Legal Proceedings

The Company may from time to time be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the years ended December 31, 2020 and 2019, and no material legal proceedings are currently pending or, to the best of its knowledge, threatened.

Indemnification Agreements

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to the indemnification agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third-party with respect to the Company's products. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

9. Convertible Preferred Stock

Prior to the sale of common stock in connection with its IPO, the Company had funded its operations primarily with proceeds from the sale of Preferred Stock.

In March 2019, the Company issued Series B Preferred Stock and, in connection with such issuance, restated its certificate of incorporation (the "Second Amended and Restated Certificate of Incorporation" or "Second A&R COI") such that as of December 31, 2019, the authorized capital stock of the Company included 70,378,661 shares of $0.001 par value Preferred Stock, of which 36,166,661 are designated as Series B Preferred Stock, 31,499,040 have been designated as Series A Preferred Stock, and 2,712,960 have been designated as Series Seed Preferred Stock.

In March 2019, the Company issued and sold 25,316,663 shares of Series B Preferred Stock, at a price of $1.7419 per share. The terms of the Series B Preferred Stock Purchase Agreement included the obligation of the investors to purchase, and the Company to sell, 10,849,998 additional shares of Series B Preferred Stock at a purchase price of $1.7419 per share, contingent upon the achievement of a specified pre-designated milestone event. The Company concluded that the tranche

feature is not a freestanding financial instrument as the right to purchase the future tranche is not legally detachable from the shares of Series B Preferred Stock. The pre-designated milestone event was not achieved and as such, the milestone tranche closing may take place within 18 months of the initial closing upon a waiver from the holders of a majority of the shares purchased at the initial closing. In addition, any Series B Preferred Stock investor has an option to purchase all or some of its milestone shares prior to any waiver of the milestone conditions. In May 2019, one of the investors exercised this option to purchase 1,004,650 of its milestone shares prior to the milestone closing, at a purchase price of $1.7419 per share. At initial issuance and subsequent closing, the Company concluded that no beneficial conversion features were present.

On February 25, 2020, the Company raised $17.1 million in net proceeds from the sale of 1,562,994 shares of Series B Preferred Stock, at a price of $10.9722 per share, upon a waiver of specified milestone conditions from the holders of a majority of the shares then held by the holders of Series B Preferred Stock. Upon issuance, each share of Series B Preferred Stock included an embedded beneficial conversion feature as the estimated fair value of the Company's common stock on the date of issuance of the Series B Preferred Stock was higher than the effective conversion price of the Series B Preferred Stock of $10.9722 per share. Given the proximity of the issuance to the Company's public offering, the Company utilized the $16.00 public offing price of its common stock to determine the intrinsic value of the beneficial conversion feature. As a result, the Company recorded the intrinsic value of the beneficial conversion feature of $7.9 million as a discount on the Series B Preferred Stock at issuance. Because the Series B Preferred Stock was immediately convertible upon issuance and did not include mandatory redemption provisions, the discount on the Series B Preferred Stock was immediately accreted.

Upon the completion of the IPO on March 16, 2020, all 70,378,661 shares of outstanding Preferred Stock automatically converted into 11,172,955 shares of common stock.

As of December 31, 2019, convertible preferred stock consisted of the following (in thousands, except share data):

	December 31, 2019				
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Value	Common stock Issuable Upon Conversion
Series Seed Preferred Stock	2,712,960	2,712,960	$ 1,460	$ 2,713	430,693
Series A Preferred Stock	31,499,040	31,499,040	30,729	31,499	5,000,623
Series B Preferred Stock	36,166,661	26,321,313	45,575	45,849	4,178,645
	70,378,661	60,533,313	$ 77,764	$ 80,061	9,609,961

Liquidation Rights

In the event of any voluntary or involuntary liquidation event, dissolution, winding up of the Company or upon the occurrence of certain other deemed liquidation events described in the Company's charter, each holder of the then outstanding Series B Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of Series A Preferred Stock, Series Seed Preferred Stock and common stock, an amount equal to $1.7419 per share (adjusted in the event of any stock dividend, stock split, combination or other similar recapitalization) plus any declared but unpaid dividends thereon.

After the payment of all preferential amounts to the holders of Series B Preferred Stock, each holder of the then outstanding Series A Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of Series Seed Preferred Stock and common stock, an amount equal to $1.00 per share (adjusted in the event of any stock dividend, stock split, combination or other similar recapitalization) plus any declared but unpaid dividends thereon.

After the payment of all preferential amounts to the holders of Series A Preferred Stock, each holder of the then outstanding Series Seed Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of common stock, an amount equal to $1.00 per share (adjusted in the event of any stock dividend, stock split, combination or other similar recapitalization) plus any declared but unpaid dividends thereon.

After payments were made in full to the holders of the Preferred Stock, then, to the extent available, the remaining amounts would have been distributed among the holders of the shares of common stock, Series A Preferred Stock and Series B Preferred Stock, pro rata based on the number of shares held by each holder (determined on an as-converted basis).

Conversion

Pursuant to the Second A&R COI, each share of Preferred Stock is convertible into common stock, at any time, at the option of the holder, and without the payment of additional consideration, at the applicable conversion ratio then in effect for each series of Preferred Stock. In addition, each share of Preferred Stock will be automatically converted into common stock at the applicable conversion ratio then in effect for each series of Preferred Stock upon either (i) the closing of a firm commitment underwritten public offering of its common stock at a price per share of at least $2.6129 per share (subject to adjustment for any stock split, combination or similar recapitalization) resulting in $60.0 million or more of gross offering proceeds to the Company, or (ii) the date and time, or the occurrence of an event, specified by vote or written consent of the requisite holders of Preferred Stock.

Redemption

Upon certain change in control events that are outside of the Company's control, including liquidation, sale or transfer of control of the Company, holders of the Preferred Stock could have caused redemption of the Preferred Stock. Shares of Preferred Stock must be redeemed by the Company in an amount equal to the liquidation preference for each series of Preferred Stock.

10. Stockholders' Equity (Deficit)

On August 13, 2019, the Company's board of directors, and on February 26, 2020, the Company's stockholders, approved the Company's restated certificate of incorporation, which became effective upon closing of the IPO on March 16, 2020, to authorize 10,000,000 shares of undesignated preferred stock, $0.001 per share par value, and to increase the number of authorized shares of common stock from 100,000,000 to 200,000,000 shares, $0.001 per share par value.

Common stockholders are entitled to receive dividends, as may be declared by the Board, if any, subject to the preferential dividend rights of any preferred stock then outstanding. Through December 31, 2020, no cash dividends have been declared or paid.

As of December 31, 2020, 10,000,000 shares of preferred stock were authorized and no shares of preferred stock were issued or outstanding.

As of December 31, 2020 and December 31, 2019, the Company has reserved for future issuance the following shares of common stock:

	December 31, 2020	December 31, 2019
Conversion of outstanding preferred stock	—	9,609,961
Shares reserved for future issuance under the 2016 Stock Incentive Plan	—	228,852
Shares reserved for future issuance under the 2020 Equity Incentive Plan	1,110,675	—
Shares reserved for future issuance under the 2020 Employee Stock Purchase Plan	191,363	—
	1,302,038	9,838,813

11. Stock-Based Compensation

2016 Stock Incentive Plan

The Company's 2016 Stock Incentive Plan, (the "2016 Plan") provided for the grant of restricted stock, restricted stock units, stock appreciation rights, incentive stock options, non-statutory stock options and other stock-based awards to employees, officers, members of the Board, consultants and advisors of the Company.

As of December 31, 2019, the number of shares of common stock authorized to be issued under the 2016 Plan was 2,091,969, of which 228,852 shares remained available for future grants as of December 31, 2019. As of the effective date of the 2020 Equity Incentive Plan, no shares remained available for future issuance under the 2016 Plan. Any options or awards outstanding under the 2016 Plan remain outstanding and effective.

2020 Equity Incentive Plan

On October 1, 2019, the Company's board of directors adopted, and on February 26, 2020 the Company's stockholders approved, the 2020 Equity Incentive Plan (the "2020 Plan"), which became effective on March 11, 2020. The 2020 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares reserved for issuance under the 2020 Plan is the sum of: (1) 1,220,283 shares of the Company's common stock; plus (2) the number of shares (up to a maximum of 2,091,969 shares) equal to the sum of (x) 228,852 shares, which represents the Company's common stock reserved for issuance under the 2016 Plan that remained available for grant under the 2016 Plan as of March 11, 2020 and (y) the number of shares of the Company's common stock subject to outstanding awards granted under the 2016 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right. The number of shares reserved shall be annually increased on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing until, and including, the fiscal year ending December 31, 2030, equal to the lesser of (i) 4% of the number of shares of the Company's common stock outstanding on the first day of such fiscal year and (ii) an amount determined by the Company's board of directors. No more than 8,541,982 shares of common stock may be issued as incentive stock options under the 2020 Plan. The shares of common stock underlying any awards that expire, terminate, or are otherwise surrendered, cancelled, forfeited or repurchased by the Company under the 2016 Plan or the 2020 Plan will be added back to the shares of common stock available for issuance under the 2020 Plan.

As of December 31, 2020, there were 1,110,675 shares available for future issuance under the 2020 Plan.

For financial reporting purposes, the Company performed common stock valuations with the assistance of a third-party specialist through October 23, 2019 to determine stock-based compensation expense for stock options. Upon completion of the IPO, the fair value of the common stock on the grant date was based on the closing price of the stock on the Nasdaq Global Select Market on the date of grant.

The following table summarizes the Company's stock option activity:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2019	1,863,117	$ 4.60	8.90	$ 15,151
Granted	759,139	19.80		
Exercised	(265,945)	4.34		
Forfeited	(420,679)	8.02		
Outstanding as of December 31, 2020	1,935,632	$ 9.85	8.14	$ 24,260
Options vested and exercisable as of December 31, 2020	602,986	$ 4.34	6.42	$ 10,678

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the common stock as of the end of the period.

The weighted-average grant date fair value of the Company's stock options granted during the years ended December 31, 2020 and 2019 was $12.95 and $3.46, respectively.

The assumptions that the Company used to determine the grant date fair value of stock options granted to employees, non-employees and members of the Board during the years ended December 31, 2020 and 2019 were as follows, presented on a weighted-average basis:

	Year Ended December 31,	
	2020	2019
Expected term (in years)	6.17	6.11
Expected volatility	74.7%	69.3%
Expected dividend yield	0.00%	0.00%
Risk-free interest rate	0.52%	2.18%

Performance-based awards

The Company granted stock options to purchase an aggregate of 220,928 shares of common stock to certain employees, officers and consultants and advisors of the Company on May 16, 2019, June 5, 2019 and June 21, 2019, which contain performance-based vesting criteria. Vesting of these options was contingent on the closing of the second tranche of Series B Preferred Stock financing. Stock-based compensation expense associated with performance-based stock options is recognized if the performance conditions are considered probable of being achieved, using management's best estimates. As a result of the performance condition being met on February 25, 2020, these options will vest as to 25% of the shares underlying each option on February 25, 2021 and as to the remainder of the shares in equal quarterly installments for three years thereafter. The Company recognized stock-based compensation expense of $0.3 million for these options during the year ended December 31, 2020.

Stock-Based Compensation

Stock-based compensation expense included in the Company's consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Year Ended December 31,	
	2020	**2019**
Research and development	$ 1,490	$ 301
General and administrative	741	598
Total stock-based compensation expense	$ 2,231	$ 899

As of December 31, 2020, total unrecognized compensation cost related to the unvested stock-based awards was $9.5 million, to be recognized over a weighted-average period of 3.22 years.

2020 Employee Stock Purchase Plan

On October 1, 2019, the Company's board of directors adopted, and on February 26, 2020, the Company's stockholders approved the 2020 Employee Stock Purchase Plan (the "2020 ESPP"), which became effective on March 11, 2020. The 2020 ESPP permits eligible employees who elect to participate, in six-month offering periods, to purchase shares of common stock through payroll deductions at a price equal to 85% of the fair market value of the common stock on the first or last business day of each applicable six-month offering period, whichever is lower. Purchase dates under the ESPP occur on or about June 14 and December 14 each year.

The 2020 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 193,216 shares of the Company's common stock. The number of shares of the Company's common stock reserved for issuance under the 2020 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2021 and continuing until, and including, the fiscal year commencing on January 1, 2031, in an amount equal to the lowest of (i) 386,432 shares of the Company's common stock, (ii) 1% of the number of shares of the Company's common stock outstanding on the first day of such fiscal year and (iii) an amount determined by the Company's board of directors.

During the year ended December 31, 2020, less than $0.1 million was withheld from employees, on an after-tax basis, in order to purchase 1,853 shares of the Company's common stock. The Company recorded stock-based compensation expense related to the 2020 ESPP of less than $0.1 million. As of December 31, 2020, 191,363 shares of the Company's common stock remained available for issuance under the 2020 ESPP.

As of December 31, 2020, there was less than $0.1 million of total unrecognized stock-based compensation expense related to the ESPP. The expense is expected to be recognized over a period of 5.5 months.

12. Income Taxes

For the years ended December 31, 2020 and 2019, the Company did not record a current or deferred income tax expense or benefit due to current and historical losses incurred by the Company. The Company's losses before income taxes consist solely of losses from domestic operations.

On March 27, 2020, the United States enacted the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"). The Cares Act includes provisions relating to refundable payroll tax credits, deferment of the employer portion of certain payroll taxes, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations and technical corrections to tax depreciation methods for qualified improvement property. The CARES Act also established a Paycheck Protection Program whereby certain small businesses are eligible for a loan to fund payroll expenses, rent, and related costs.

The Company considered the provisions under the CARES Act and elected not to take advantage of the provisions of CARES Act as the effect of such provisions was not expected to have a material impact on the Company's results of operations, cash flows and consolidated financial statements.

A reconciliation of income tax expense (benefit) computed at the statutory federal income tax rate to income taxes as reflected in the consolidated financial statements is as follows:

	2020	2019
Income taxes at U.S. statutory rate	21%	21%
State income taxes	6	6
Tax Credit	7	3
Other	2	(1)
Change in valuation allowance	(36)	(29)
Total provision for income taxes	0%	0%

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets and liabilities as of December 31, 2020 and 2019 are comprised of the following (in thousands):

	Year Ended December 31,	
	2020	2019
Deferred tax assets		
Net operating loss carryforwards	$ 24,657	$ 13,284
Tax credits carryforwards	3,948	1,020
Stock-based compensation	686	246
Amortization	545	611
Accruals	272	200
Lease incentive liability	17	21
Other	42	31
Total deferred tax assets	30,167	15,413
Valuation allowance	(30,149)	(15,385)
Net deferred tax assets	18	28
Deferred tax liabilities		
Tenant improvement allowance	(17)	(21)
Unrealized gains/losses on investments	(1)	(7)
Total deferred tax liabilities	(18)	(28)
Net deferred taxes	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets, which are comprised primarily of net operating loss carryforwards and tax credits. Management has considered the Company's history of cumulative net losses in the United States, estimated future taxable income and prudent and feasible tax planning strategies and has concluded that it is more likely than not that the Company will not realize the benefits of its U.S. federal and state deferred tax assets. Accordingly, a full valuation allowance has been established against these net

deferred tax assets as of December 31, 2020 and 2019, respectively. The Company reevaluates the positive and negative evidence at each reporting period. The Company's valuation allowance increased during 2020 by approximately $14.8 million primarily due to the generation of net operating loss and tax credit carryforwards.

As of December 31, 2020 and 2019, the Company had U.S. federal net operating loss carryforwards of $91.7 million and $48.6 million, respectively, which may be available to offset future income tax liabilities. The 2017 Tax Cuts and Jobs Act ("TCJA") will generally allow losses incurred after 2017 to be carried over indefinitely but will generally limit the net operating loss deduction to the lesser of the net operating loss carryover or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended). Also, there will be no carryback for losses incurred after 2017. Losses incurred prior to 2018 will generally be deductible to the extent of the lesser of a corporation's net operating loss carryover or 100% of a corporation's taxable income and be available for twenty years from the period the loss was generated. The Company has federal net operating losses generated following 2017 of $74.5 million, which do not expire. The federal net operating losses generated prior to 2018 of $17.2 million will expire at various dates through 2037. The CARES Act temporarily allows the Company to carryback net operating losses arising in 2018, 2019 and 2020 to the five prior tax years. In addition, net operating losses generated in these years could fully offset prior year taxable income without the 80% taxable income limitation under the TCJA. The Company has been generating losses since its inception. As such, the net operating loss carryback provision under the CARES Act is not applicable to the Company.

As of December 31, 2020 and 2019, the Company also had U.S. state net operating loss carryforwards of $85.5 million and $48.9 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2040.

As of December 31, 2020 and 2019, the Company had federal tax credit carryforwards of approximately $3.6 million and $0.9 million, respectively, available to reduce future tax liabilities which expire at various dates through 2040. As of December 31, 2020 and 2019, the Company had state research and development tax credit carryforwards of approximately $0.4 million and $0.1 million, respectively, available to reduce future tax liabilities which expire at various dates through 2035.

Utilization of the U.S. federal and state net operating loss and research and development and orphan drug credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax liabilities, respectively. The Company has not completed a study to assess whether a change of ownership has occurred, or whether there have been multiple ownership changes since its formation, due to the significant cost and complexity associated with such a study. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development and orphan drug credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has not, as of yet, conducted a study of research and development and orphan drug credit carryforwards. Such a study, once undertaken by the Company, may result in an adjustment to the Company's research and development and orphan drug credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development and orphan drug credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheet or statement of operations if an adjustment is required.

The Company files tax returns in the United States and Massachusetts. The Company is subject to U.S. federal and state tax examinations by tax authorities for years 2017 through present. As of December 31, 2020 and 2019, the Company has recorded no liability for unrecognized tax benefits, interest, or penalties related to federal and state income tax matters and there currently no pending tax examinations. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense.

13. Net Loss Per Share

The following table sets forth the computation of the Company's basic and diluted net loss per share for the years ended December 31, 2020 and 2019 (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2020	2019
Numerator:		
Net loss attributable to common stockholders—basic and diluted	$ (49,218)	$ (23,463)
Denominator:		
Weighted-average number of common shares used in net loss per share—basic and diluted	13,924,730	702,455
Net loss per share—basic and diluted	$ (3.53)	$ (33.40)

As of December 31, 2020 and 2019, the Company's potentially dilutive securities were Preferred Stock, shares reserved for issuance under the ESPP and stock options, which have been excluded from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2020 and 2019, as the effect would be to reduce the net loss per share. All the Company's restricted stock was vested as of December 31, 2019. Net loss applicable to common stockholders for the year ended December 31, 2020 did not equal net loss due to the accretion of the beneficial conversion feature of Series B Preferred Stock in the amount of $7.9 million. The beneficial conversion feature was initially recorded as a discount on the Series B Preferred Stock with a corresponding amount recorded to Additional Paid-in Capital. The discount on the Series B Preferred Stock was then immediately written off as a deemed dividend as the Series B Preferred Stock does not have a stated redemption date and is immediately convertible at the option of the holder. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including convertible preferred stock and options to purchase common stock during the period determined using the if-converted method, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share have been the same.

The Company excluded the following potential common shares from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2020 and 2019 because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2020	2019
Series Seed Preferred Stock	—	430,693
Series A Preferred Stock	—	5,000,623
Series B Preferred Stock	—	4,178,645
Options to purchase common stock	1,935,632	1,863,117
Shares reserved for future issuance under the ESPP	191,363	—

14. Related Party Transactions

Lundbeck

Lundbeckfond Invest A/S is one of the Company's stockholders and participated in all tranches of the Series A preferred stock financing and both tranches of the Series B preferred stock financing. Prior to the conversion of the Company's preferred stock, Lundbeckfond Invest A/S owned 5,470,492 shares of Series A Preferred Stock as of December 31, 2019, and 478,749 shares of Series Seed Preferred Stock as of December 31, 2019. Lundbeckfond Invest A/S owned 1,326,111 shares of Series B Preferred Stock as of December 31, 2019. All shares of Preferred Stock converted into shares of common stock upon closing of the IPO. Lundbeckfond Invest A/S also purchased 187,500 shares of common stock in the IPO. This reflects a 7.4% and a 9.3% ownership interest on a fully diluted basis as of December 31, 2020 and 2019, respectively. Mette Kirstine Agger, a member of the Company's board of directors, is a Managing Partner at Lundbeckfonden Ventures, which is an affiliate of Lundbeckfond Invest A/S.

Lundbeck, an affiliate of Lundbeckfond Invest A/S, is also one of the Company's stockholders and participated in the fourth tranche of the Company's Series A Preferred Stock financing. Prior to the conversion of the Company's Preferred Stock, Lundbeck owned 499,069 shares of Series A Preferred Stock as of December 31, 2019, as well as 443,271 shares of

common stock issued in conjunction with the Lundbeck Agreement (See Note 7). All shares of Preferred Stock converted into shares of common stock upon closing of the IPO. This reflects a 2.7% and a 4.2% ownership interest on a fully diluted basis as of December 31, 2020 and 2019, respectively. Lundbeck did not participate in the Series B Preferred Stock financing.

To date, pursuant to the Lundbeck Agreement, the Company has made cash payments to Lundbeck of $1.8 million consisting of an upfront payment and ongoing milestone payments which are recorded as research and development expense.

Cydan Development, Inc.

In January 2016, the Company entered into a Business Services Agreement with Cydan Development, Inc., or Cydan, pursuant to which Cydan provided office space, personnel assistance, and other business services to the Company on an as-needed basis. At the time the agreement was signed, Cydan was considered a related party because Cydan was a holder of more than 5% of the Company's capital stock and Dr. James McArthur was the Company's founder, President and Chief Executive Officer, a member of the Company's board of directors and a holder of more than 5% of the Company's capital stock and the Chief Scientific Officer of Cydan. As of June 30, 2020, Cydan was no longer considered a related party. The Company paid Cydan less than $0.3 million during the year ended December 31, 2019 related to the Business Services Agreement, all of which was recorded as research and development expense. The Company agreed with Cydan to terminate the Business Services Agreement and all related services rendered by Cydan to the Company effective as of August 17, 2019. Accordingly, there were no amounts due to Cydan as of December 31, 2020 and 2019, respectively.

15. Benefit Plans

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code effective as of January 2019. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the plan may be made at the discretion of the Board. The Company contributed a match of $0.1 million to the 401(k) plan during the year ended December 31, 2020. The Company did not make any contributions to the plan in 2019.

Exhibit 4.3

DESCRIPTION OF SECURITIES REGISTERED UNDER SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

The following description of the securities of IMARA Inc. ("us," "our," "we" or the "Company") registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is intended as a summary only and therefore is not a complete description. This description is based upon, and is qualified by reference to, our restated certificate of incorporation, our amended and restated bylaws and applicable provisions of the Delaware General Corporation Law (the "DGCL"). You should read our restated certificate of incorporation and amended and restated bylaws, which are incorporated by reference as Exhibit 3.1 and Exhibit 3.2, respectively, to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, for the provisions that are important to you.

Authorized Capital Stock

Our authorized capital stock consists of 200,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share, all of which preferred stock is undesignated. Our common stock is registered under Section 12(b) of the Exchange Act.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Any matters other than the election of directors to be voted upon by the stockholders at a meeting are decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter, except when a different vote is required by law, our restated certificate of incorporation or our amended and restated bylaws.

Dividends. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend or other rights of any outstanding preferred stock.

Liquidation, Dissolution and Winding Up. In the event of our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to any preferential or other rights of any outstanding preferred stock.

Other Rights. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized to issue up to 10,000,000 shares of "blank check" preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. The issuance of preferred stock could impede the completion of a merger, tender offer or other takeover attempt.

Provisions of Our Restated Certificate of Incorporation and Amended and Restated Bylaws and the DGCL That May Have Anti-Takeover Effects

Board of Directors; Removal of Directors. Our restated certificate of incorporation and our amended and restated bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our restated certificate of incorporation and our amended and restated bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of at least 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our restated certificate of incorporation and amended and restated bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our restated certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our restated certificate of incorporation and our amended and restated bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our restated certificate of incorporation and our amended and restated bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our board of directors. In addition, our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock because even if the third party acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting. The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our amended and restated bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our restated certificate of incorporation described above.

Delaware Business Combination Statute. We are subject to Section 203 of the DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Exclusive Forum Selection. Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for the following types of proceedings: (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware or as to which the General Corporation Law of the State of Delaware confers jurisdiction on the Court of Chancery of the State of Delaware, or (4) any action asserting a claim arising pursuant to any provision of our restated certificate of incorporation or amended and restated bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction. Although our restated certificate of incorporation contains the choice of forum provisions described above, it is possible that a court could rule that such provisions are inapplicable for a particular claim or action or that such provisions are unenforceable.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-237117) pertaining to the IMARA Inc. 2016 Stock Incentive Plan, the IMARA Inc. 2020 Equity Incentive Plan, and the IMARA Inc. 2020 Employee Stock Purchase Plan of our report dated March 5, 2021, with respect to the consolidated financial statements of IMARA Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 5, 2021

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Rahul D. Ballal, certify that:

1. I have reviewed this Annual Report on Form 10-K of IMARA Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 5, 2021

By: /s/ Rahul D. Ballal

Rahul D. Ballal, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael P. Gray, certify that:

1. I have reviewed this Annual Report on Form 10-K of IMARA Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 5, 2021

By: /s/ Michael P. Gray

Michael Gray
Chief Financial Officer and Chief Operating Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of IMARA Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 5, 2021

By: /s/ Rahul D. Ballal

Rahul D. Ballal, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of IMARA Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 5, 2021

By: /s/ Michael P. Gray

Michael Gray
Chief Financial Officer and Chief Operating Officer
(Principal Financial Officer)