Company Presentation

September 2024

Disclaimer

This presentation contains forward-looking statements that involve substantial risks and uncertainties of Enliven Therapeutics, Inc. ("Enliven" or the "Company"). All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, potential market opportunities for, and expectations regarding Enliven's product candidates and programs, including ELVN-001 and ELVN-002; expectations regarding the positioning of ELVN-001 with respect to other therapies; Enliven's ability to advance additional programs; the expected milestones and timing of such milestones including for ELVN-001, ELVN-002 and its discovery programs (including the timing of presentation of updated Phase 1a clinical data, dosing of patients in Phase 1a/b, presentation of Phase 1b data, and initial regulatory interactions, for ELVN-001, and the timing of Phase 1 monotherapy data and initial proof of concept combination data in HER2+ cancers for ELVN-002); and statements regarding Enliven's financial position, including its liquidity, cash runway and the sufficiency of its cash resources. In some cases, you can identify forward-looking statements by terminology such as "estimate," "intend," "may," "plan," "potentially" "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the limited operating history of Enliven; the ability to advance product candidates through preclinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, product candidates; the outcome of preclinical testing and early clinical trials for product candidates and the potential that the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials; Enliven's limited resources; the risk of failing to demonstrate safety and efficacy of product candidates; Enliven's limited experience as a company in designing and conducting clinical trials; the potential for interim, topline and preliminary data from Enliven's preclinical studies and clinical trials to materially change from the final data; potential delays or difficulties in the enrollment or maintenance of patients in clinical trials; developments relating to Enliven's competitors and its industry, including competing product candidates and therapies; the potential market opportunity for any of Enliven's programs; the decision to develop or seek strategic collaborations to develop Enliven's current or future product candidates in combination with other therapies and the cost of combination therapies; the ability to attract, hire, and retain highly skilled executive officers and employees; the ability of Enliven to protect its intellectual property and proprietary technologies; the scope of any patent protection Enliven obtains or the loss of any of Enliven's patent protection; reliance on third parties, including contract manufacturing organizations, contract research organizations and strategic partners; general market or macroeconomic conditions; and Enliven's ability to obtain additional capital to fund Enliven's general corporate activities and to fund Enliven's research and development. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in documents that Enliven files from time to time with the Securities and Exchange Commission. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

The Enliven Story: a Clinical-Stage Precision Oncology Company

Discovery process rooted in **validated biology**, **differentiated chemistry**, and **disciplined trial design**

+

Capital-efficient approach on **high potential programs** aiming to develop **first-in-class** or **best-in-class** candidates

+

ELVN-001 and ELVN-002 supported by **preclinical evidence** of an **improved therapeutic index**

+

Multiple **near-term milestones** in lead programs targeting **large** and **attractive markets**

+

Experienced team with a track record of inventing and developing **multiple FDA-approved cancer therapies**

Strong balance sheet expected to provide cash runway into late 2026

Highly Distinguished & Industry-Leading Team

Leadership Team

Sam Kintz, MBA
Co-founder and CEO
abbvie
Genentech
A Member of the Roche Group

Joe Lyssikatos, PhD
Co-founder and CSO
ARRAY BIOPHARMA
Genentech
A Member of the Roche Group

Anish Patel, PharmD
Co-founder and COO
abbvie
pharmacyclics
An AbbVie Company

Helen Collins, MD
CMO
FivePrime
GILEAD

Ben Hohl
CFO, Head of
Corporate Development
Goldman Sachs

Galya Blachman, PhD, Esq
Chief Legal Officer,
Head of BD
5AM VENTURES
abbvie

Stefan Gross, PhD
VP, Biology
blueprint MEDICINES
ARRAY BIOPHARMA

Wei Deng, PhD
VP, Biometrics
FivePrime
GILEAD

Andy Ren, PhD
VP, Chemistry
ARRAY BIOPHARMA

Frank Silanos
VP, Finance &
Accounting
AVIDITY BIOSCIENCES

Anne Thomas
VP, Clinical Operations
FivePrime
GILEAD

Isagani "Izzy" Cornelio
VP, Clinical Operations
Day One BIOPHARMACEUTICALS
MERCK

Ian Scott, PhD
VP, CMC & Supply Chain
zentalis
ARRAY BIOPHARMA

Qi Wang, PhD
VP, Clinical
Pharmacology
Bristol Myers Squibb
Jazz Pharmaceuticals

Damiette Smit, MD
VP, Clinical Development
janssen
AMGEN

Board of Directors

Rich A. Heyman, PhD, Chairman
Aragon Pharmaceuticals,
Seragon Pharmaceuticals

Sam Kintz, MBA
Enliven Therapeutics

Rishi Gupta, JD
OrbiMed

Andy Phillips, PhD
Nexo Therapeutics,
Alexia Therapeutics, Broad Institute

Mika Derynck, MD
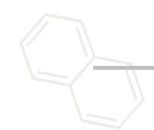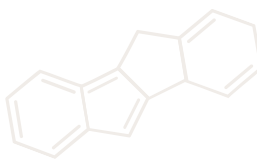Amunix, Genentech

Jake Bauer, MBA
Myokardia

Rahul Ballal, PhD
Imara Therapeutics,
Mediar Therapeutics

Lori Kunkel, MD
Loxo Oncology, Pharmacyclics

Scientific Advisors

Brian Druker, MD
Oregon Health &
Science University

Kevin Koch, PhD
Array Biopharma,
Edgewise Therapeutics

Leadership Team with Broad Range of Experience and Success

World-Renowned Chemists

- Inventor or co-inventor of over **20 product candidates** that have advanced to clinical trials

Precision Oncology and Kinase Inhibitor Experts

- Led or been involved with the discovery, development, or commercialization of over **60 kinase inhibitor programs**

Leaders with a Track Record of Success

- Significant experience building and/or leading research, development, and commercial operations
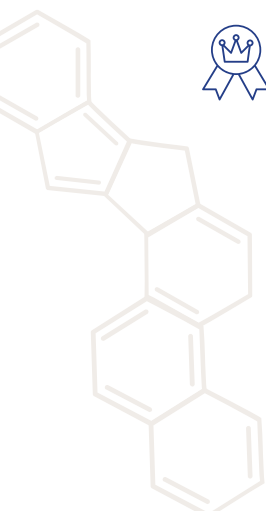
FDA-Approved Drugs Co-Invented by Enliven Chemists

MEKTOVI®
(binimetinib) 15 mg tablets

Koselugo™
(selumetinib)
10 mg & 25 mg capsules

TUKYSA®
tucatinib
50 mg | 150 mg tablets

Retevmo™
selpercatinib capsules
40 mg · 80 mg

Pipeline & Discovery Programs Address New and Emerging Unmet Needs

Parallel lead product candidates:

Program	Target	Differentiation	Disease	Regimen	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Next Milestone	Milestone Expected
ELVN-001	BCR-ABL	Highly selective active site inhibitor w/activity against asciminib emergent mutations	CML	Monotherapy	monotherapy					Phase 1 Safety/Efficacy	2025
ELVN-002	HER2 & HER2 mutants	Irreversible, highly selective, CNS penetrant	NSCLC, other solid tumors	Monotherapy	monotherapy					Phase 1 Safety/Efficacy	2025
			HER2+ MBC and CRC	Combination	+ trastuzumab +/- chemotherapy					Phase 1a Safety/Efficacy	

Multiple discovery stage efforts ongoing at various stages

BCR-ABL = breakpoint cluster region-Abelson leukemia virus. CML = Chronic myeloid leukemia. CNS = Central nervous system. CRC = colorectal cancer. HER2 = human epidermal growth factor receptor 2. IND = Investigational new drug. MBC = metastatic breast cancer. NSCLC = Non-small cell lung cancer.

Parallel Lead Programs Supported by Clinical Data

ELVN-001

- Highly selective, active site, active form BCR-ABL inhibitor for the treatment of CML

- Designed to drive deeper responses and improve tolerability, safety and convenience compared to 1st, 2nd and 3rd Generation agents

- Significant market opportunity that has historically generated ~$6 billion of combined BCR-ABL TKI annual sales, despite generic options

- Clear need for better agents, demonstrated by successful launch of asciminib (Scemblix®), a recently approved 4th Generation TKI

- ELVN-001 has a MoA that is complementary to asciminib, and it has activity against known asciminib-resistant mutations

Clinical Data Reported at ESH-iCMLf in September 2024

- Achieved **cumulative MMR rate of 44%** (8/18) by 24 weeks in response-evaluable late line patients, which compares favorably to historical Phase 1 cumulative MMR rates from other TKIs

- Among **TKI-resistant patients,** ELVN-001 achieved a **cumulative MMR rate of 42%** (5/12) by 24 weeks

- **Well-tolerated** with no ≥ Grade 3 treatment-related non-hematologic toxicities reported and **no dose reductions**

ELVN-002

- CNS penetrant, highly selective and irreversible HER2+ and HER2 mutant inhibitor

- Designed to maximize HER2 inhibition as well as enable rational combination therapies, particularly for HER2+ cancers

- Significant potential opportunity as Enhertu® disrupts the current treatment paradigm across HER2-altered tumors leading to a new unmet need in patients who progress on, or are intolerant to, this new treatment option

- Clinical data with tucatinib (Tukysa®), a selective reversible HER2 TKI, suggest that dual HER2 targeting can produce clinically meaningful improvements in patients with HER2+ MBC and CRC

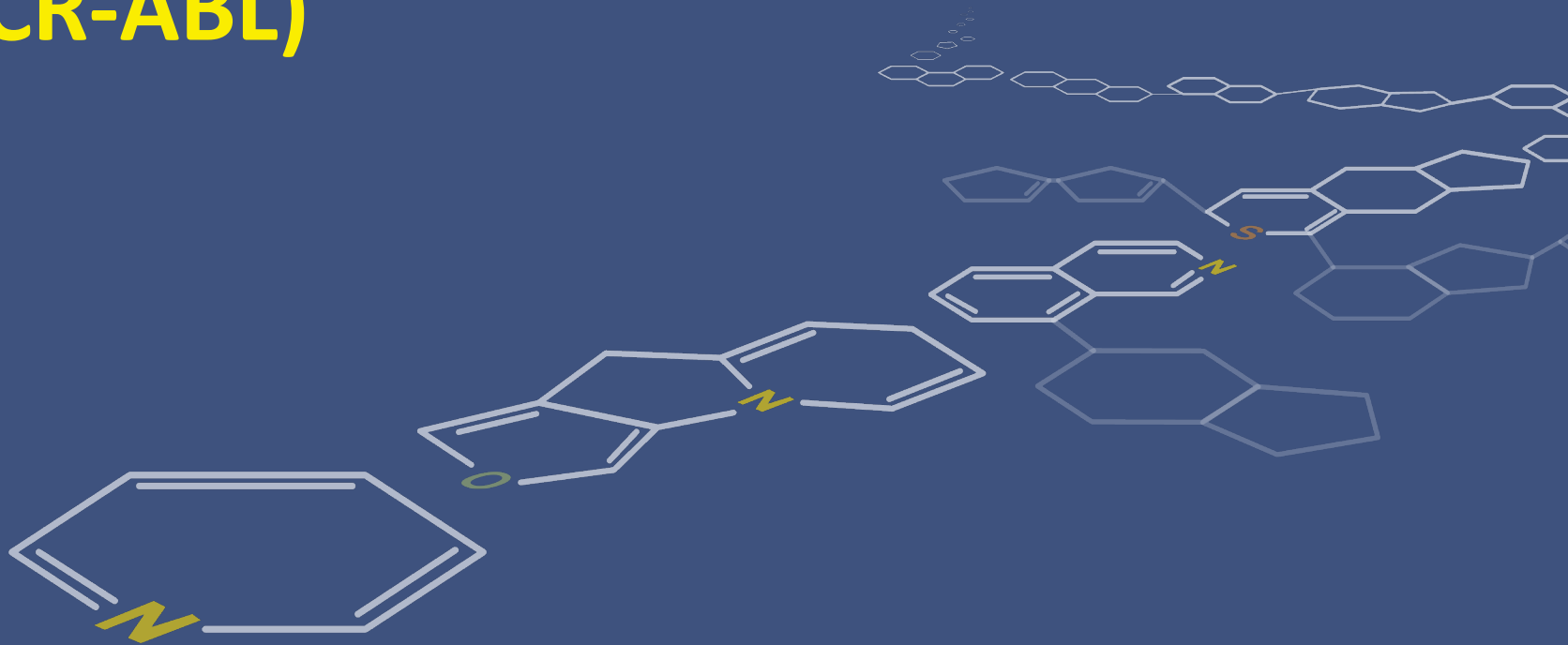**Clinical Data Reported in March 2024**

- Investigator reported **responses** (including unconfirmed) in patients with both **HER2+ and HER2 mutant tumors**, including in patients who **progressed on Enhertu** and in patients **with brain metastases**, at doses that were well-tolerated

- **>10x better target coverage** at the clinically predicted monotherapy dose based on PK in patients and preclinical HER2+ efficacy, compared to tucatinib
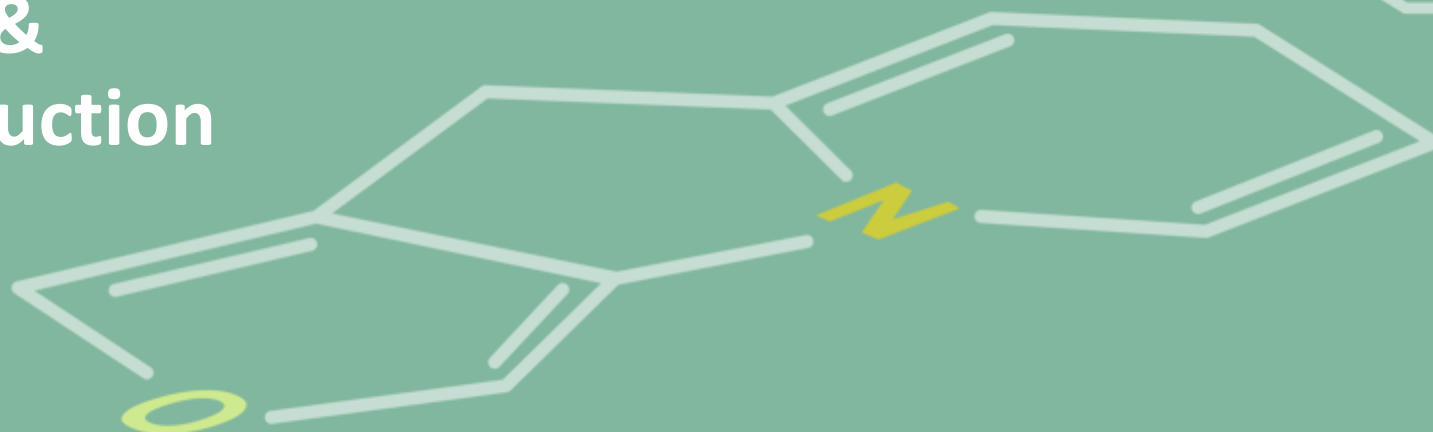
ELVN-001 (BCR-ABL)
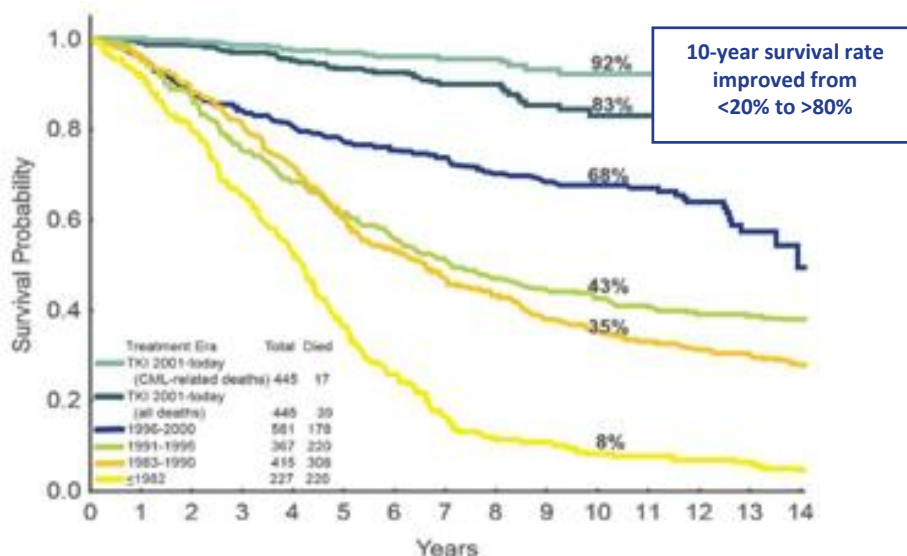
CML Landscape &
ELVN-001 Introduction

CML is Now a Long-Term Condition

As patients live longer on treatment, **quality of life** and **tolerability** have become important treatment goals
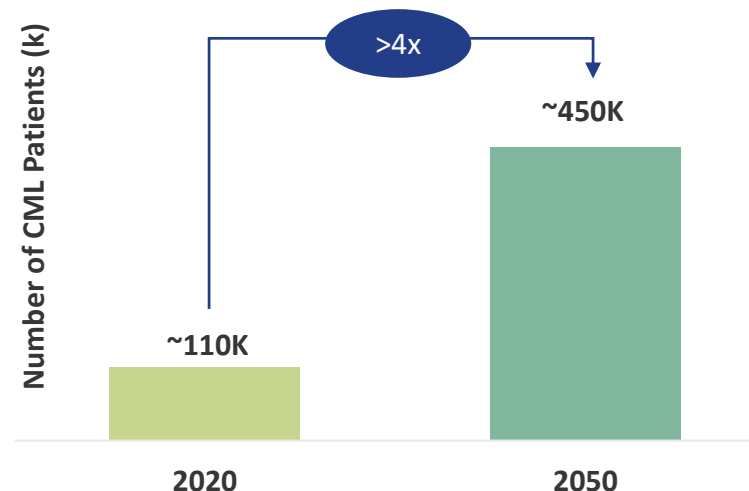
CML 10-Year Survival Rate Over Time

Prior to imatinib, the annual CML survival rate was

<20%

10-year survival rate improved from <20% to >80%

92%
83%
68%
43%
35%
8%

Treatment Era	Total	Died
TKI 2001–today (CML-related deaths)	445	17
TKI 2001–today (all deaths)	445	39
1996–2000	561	178
1991–1996	367	220
1983–1990	415	308
≤1982	227	220

Estimated Prevalence of CML in the US Over Time

Number of CML Patients (k)

>4x

~110K (2020)

~450K (2050)

- Prevalence is increasing globally with expected overall survival approaching age-matched controls
- CML has become a chronic disease that can require life-long TKI-treatment

Top Treatment Goals for Physicians and Patients*

1st Maintain or improve quality of life

2nd Manageable side effects

CML = Chronic myeloid leukemia. FIH = First-in-human. k = thousands. TKI = Tyrosine kinase inhibitors.
References: Huang X et al. Cancer. 2012;118:3213-3127; Kantarjian et al. Chronic Myeloid Leukemia, In: Harrison's Principles of Internal Medicine. 2014.; Lang et al, EHA 2023. American Journal of Hematology: Chronic myeloid leukemia: 2025 update on diagnosis, therapy, and monitoring
*For patients who have received two prior therapies.

Significant Need Remains for Better Treatment Options for CML

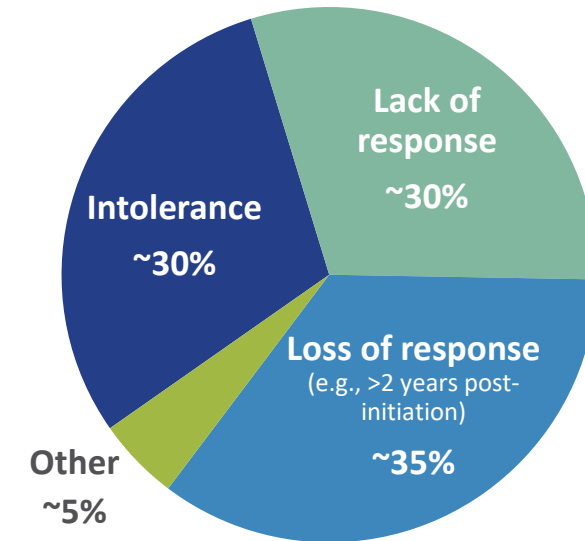## Challenges with Current Standard of Care

- **Growing 3L+** patient population (>25% of CP-CML) with **limited treatment options**

- Except for asciminib, approved TKIs have **poor kinase selectivity,** resulting in tolerability issues that can impact efficacy

- **Long-term use of 2nd generation TKIs is associated with adverse events** such as pleural effusions, GI and cardiovascular events

- Adverse events, comorbidities, restrictions with concomitant medications, and specific administration requirements may **impede long-term patient adherence**

- **Fewer than 10%** of patients successfully achieve sustained treatment-free remission (TFR)

- 77% of HCPs indicated **need for more effective, safe, and tolerable agents** for CML

~25% of 1L patients switch therapy within the first year | **~30% of 2L patients switch within the first year of 2nd treatment**

Switching Dynamics Demonstrate Unmet Need

Rationale for Switching Treatment

Pie chart:
- Lack of response ~30%
- Loss of response (e.g., >2 years post-initiation) ~35%
- Other ~5%
- Intolerance ~30%

In the US and EU3, majority of treatment switches across lines of therapy and TKIs are driven by intolerance or initial lack of molecular response (~60% combined)

Poor Selectivity Limits Tolerability & Efficacy of 1st, 2nd & 3rd Gen Agents

	Compound	Company	T315I Coverage	Off Target(s) & Treatment-Emergent, Non-Hematologic Adverse Events (All Gr / Gr 3+)		1L Efficacy	Drug & Administration Requirements	Annualized Sales (USD)‡
1st Gen	**Imatinib (Gleevec®)**	Novartis	X	c-KIT, CSFR-1, PDGFR	Peripheral Edema (20% / 0%) Nausea (41% / 2%)	28% MMR 3% MR4.5	Avoid strong CYP3A inhibitors or inducers	**$500M**
2nd Gen	**Dasatinib (Spyrcel®)**	BMS	X	SRC family, c-KIT, PDGFR-αβ	Fluid Retention (38% / 5%) Pleural Effusions (28% / 3%) Diarrhea (22% / 1%)	46% MMR 5% MR4.5	Avoid strong CYP3A inhibitors or inducers, PPIs, antacids, and H2 blockers	**$1.7B**
	Nilotinib (Tasigna®)	Novartis	X	c-KIT, PDGFR, CSFR-1, DDR-1 (hERG Channel)	Rash (38% / <1%) Headache (32% / 3%) Nausea (22% / 2%); Diarrhea (19% / 1%) **Black Box:** QT Prolongation/Sudden Deaths	44% MMR 11% MR4.5	Avoid strong CYP3A inhibitors or inducers and PPIs; avoid food 2 hours before and 1 hour after each dose	**$1.8B**
	Bosutinib (Bosulif®)	Pfizer	X	SRC family	Hepatic dysfunction (45% / 27%) Diarrhea (75% / 9%) Abdominal Pain (39% / 2%)	41% MMR 7.5% MR4.5	Avoid strong CYP3A inhibitors or inducers, PPIs, antacids, and H2 blockers	**$670M**
3rd Gen	**Ponatinib (Iclusig®)**	Takeda	✓	KDR, FGFR, c-KIT, RET, FLT3, PDGFR	**Black Box:** Arterial Occlusive Events, Heart Failure, VTE, Hepatoxicity	N/A	Avoid strong CYP3A inhibitors or inducers	**$650M**
STAMP	**Asciminib (Scemblix®)**	Novartis	✓ **(US, high dose only)**	N/A	Hypersensitivity (32% / 2%) Hypertension (19% / 9%) Cardiovascular (13% / 3.4%)	68% MMR 17% MR4.5	Avoid CYP2C9 substrates and certain statins; avoid food 2 hours before and 1 hour after each dose	**$660M**

A selective BCR-ABL inhibitor could yield enhanced target coverage, leading to greater efficacy and better long-term tolerability

Review of Asciminib ASCEMBL Study and Initial 3rd Line Launch

Observations

- Asciminib's **strong launch** demonstrates the **large market** size and **need for better agents**

- However, unmet needs still exist. In ASCEMBL, only **1.2% of patients discontinued due to PD/death, but due to lack of efficacy/AE:**
  - ~30% of patients discontinue by week 48
  - **~50% of patients discontinue** by week 96

- Asciminib has limitations:
  - **Resistance mutations** in both the allosteric binding site and the ATP pocket result in loss of activity
  - **Drug-drug interactions** require avoiding drugs that are CYP2C9 substrates (up to 20% of commonly prescribed medications)
  - **Requires fasting** 2 hours before and 1 hour after each dose
  - **Substrate for efflux transporters** (P-gP & BCRP), which may contribute to **lack of efficacy**
  - Treatment of **T315I mutations requires 5x dose** resulting in more dose reductions (23%), increased pancreatic & liver enzyme elevation

Scemblix's Robust Launch Continues to Demonstrate Patient Need for More Effective and Tolerable Agents

US 3L+ Approval	Q4 2021
EU 3L+ Approval	Q3 2022
US 1L Approval	**Est. H2 2024**

$164M
2Q24 Sales

$656M of annualized sales

Current U.S. 3L+ Market Dynamics

44%
share of new to brand prescriptions

26%
share of U.S. 3L+ market

~$1.6B
implied market size in the **U.S. 3L+ alone**

Asciminib has the Potential to Disrupt Early Line Standard of Care

CML Patient Population

1L — ON 1L
NEWLY DIAGNOSED ANNUALLY

15k | (49k)

2L — ON 2L
SWITCH ANNUALLY (1L to 2L)

10k | (22.4k)

3L — ON 3L+
SWITCH ANNUALLY (2L to 3L)

6k | (11.5k)

PREVALENCE
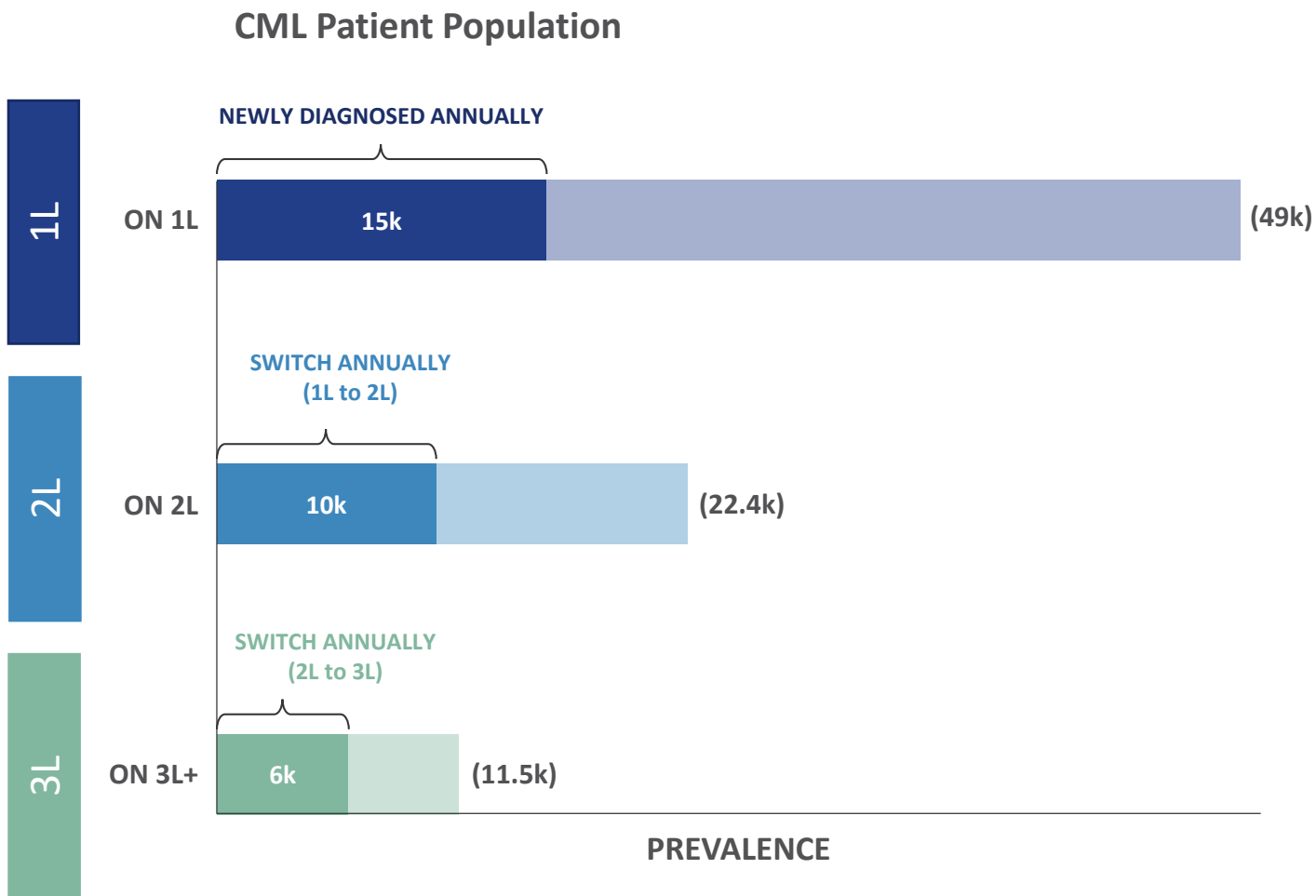
CML Treatment Landscape

1L
~50% of patients are treated with imatinib, and the other ~50% with 2nd Gen TKIs

Pie: 46%, 20%, 28%, 4%, 1%

2L
>80% of patients receive 2nd Gen TKIs (mainly nilotinib or dasatinib)

Pie: 9%, 30%, 33%, 20%, 5%, 2%

3L+
>50% of patients receive 2nd Gen TKIs

Pie: 15%, 20%, 13%, 19%, 14%, 19%

Legend:
- Asciminib
- Ponatinib
- Imatinib
- 2nd Generation TKIs { Nilotinib, Dasatinib, Bosutinib }

1L = First line. 2L = Second line. 3L+ = Third line or later. CML = Chronic myeloid leukemia. Gen= Generation. TKI = Tyrosine kinase inhibitor.
References: November 2023 Novartis R&D Investor Event. HCP Qualitative & Quantitative Interviews (ClearView).

Review of Asciminib ASC4FIRST Front Line Study Results

Key Results

Discontinuation Rate

Asciminib 14%, Imatinib 37%, 2G TKI 24%

Median follow-up was 16.3 and 15.7 mo. for ASC and IS TKI, respectively

Time to MMR (Weeks)

Asciminib 24, Imatinib 49 | Asciminib 24, 2G TKIs 36 | Asciminib 24, All IS-TKIs 36

MMR @ 48 wk*					
69%	40%	66%	58%	68%	49%

Safety / Tolerability

Grade ≥ 3 AEs

Asciminib 38%, Imatinib 44%, 2G TKIs 55%

AEs Leading to Dose Adjustment/Interruption

Asciminib 30%, Imatinib 39%, 2G TKIs 53%

Observations

- *Real-world switching rates continue to increase*:
    - *~25%* of 1L patients switch treatments in the *first year*
    - *~30%* of patients switch within the *first year of their second therapy*
- *Rate of resistance to asciminib* (4%) was 2x higher than imatinib (2%) and the 2G TKIs (2%) and will likely *continue to grow* as duration of therapy increases

- Significant and clinically meaningful reduced *time to MMR is an advantage in 1L setting compared to 2G TKIs* and was consistent with ASCEMBL (24-week MMR endpoint)
- *Largest treatment difference at 48 weeks vs. 2G TKIs observed in patients with intermediate-risk (+21%) and high-risk (+14%) ELTS scores* (NCCN Guidelines currently recommend 2G TKIs for these patients)
- Study was not designed or powered to show a 12 mo. MMR rate difference compared to 2G TKIs

- Most importantly, asciminib had *significantly favorable safety/tolerability profile compared to all TKIs, including imatinib*
- Notably, *reduced rates and severity of GI toxicity* (diarrhea, nausea), *rash, swelling* (edema, effusion) typically associated with off-target kinase activity
- Consistent with real-world use, *ASC4FIRST enrolled fewer older patients with comorbidities on 2G TKI arm,* making it hard to compare to precedent Ph3 studies**

1L = First line. 2G = Second Generation. AE = Adverse event. ASC = Scemblix = asciminib. ELTS = EUTOS long-term survival. GI = Gastrointestinal. IS = Investigator selected. MMR = Major molecular response. Mo = months. NCCN = National Comprehensive Cancer Network. Ph3 = Phase 3. TKI = Tyrosine kinase inhibitor. Wk = week. ASCEMBL: A phase 3, open-label, randomized study 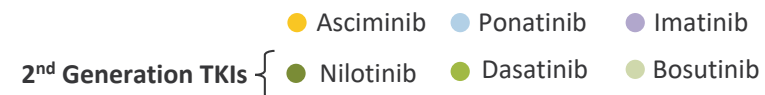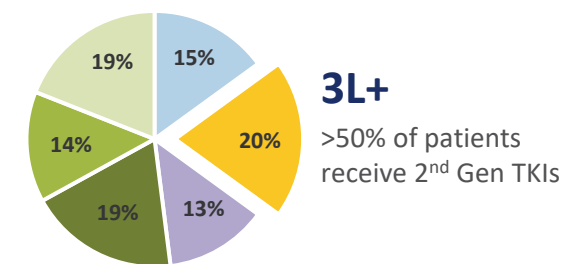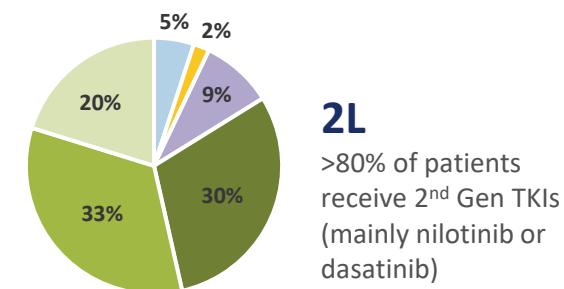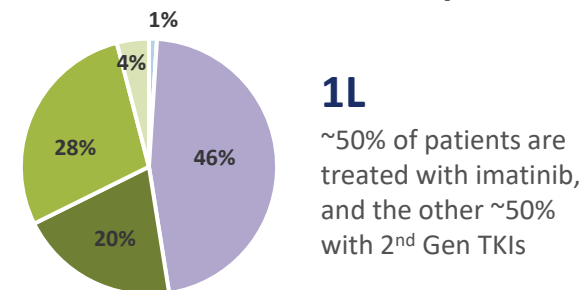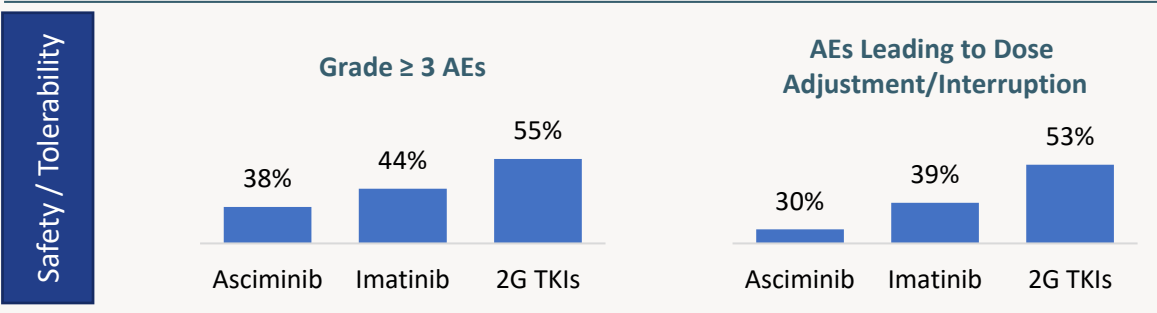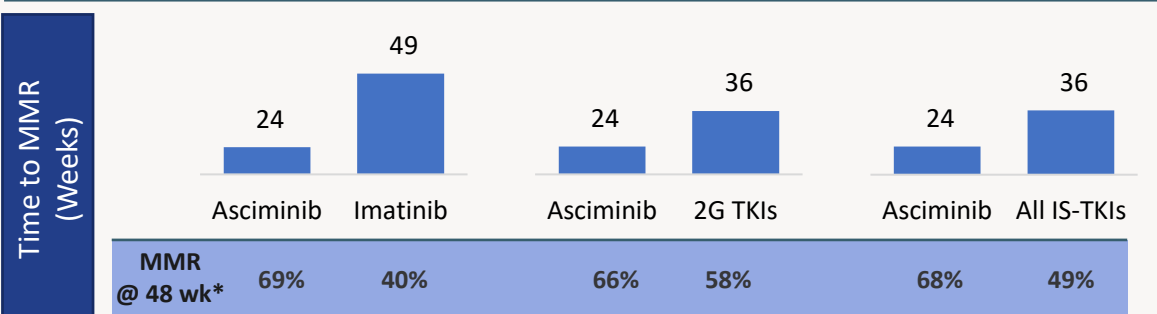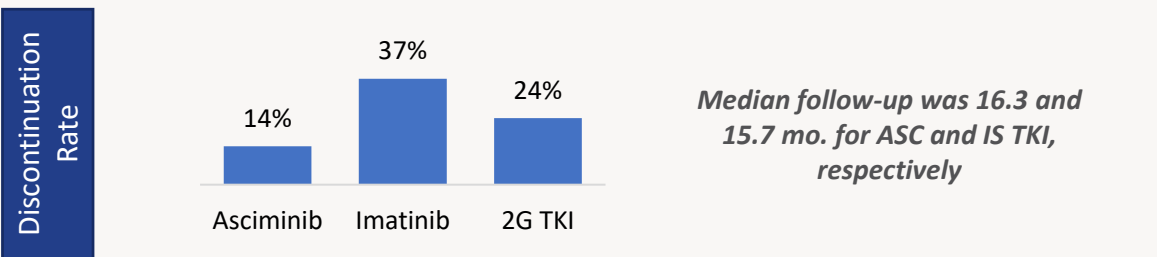of asciminib vs bosutinib in CML after 2 or more prior TKIs. *Endpoint for accelerated approval. **In a real-world study, dose reductions were required in 66% of elderly patients on 2G TKIs.

References: Hughes et al. N ENGL J MED 2024; Rea D et al., Blood. 2021; ASCO 2024 Novartis R&D Investor Event; 2024 NCCN Guidelines Version 2.2024; Seo HY et al. Clin Lymphoma Myeloma Leuk. 2019.

ELVN-001 is Well Positioned to Follow Asciminib in Future CML Treatment Paradigm

Limitations of Current Treatment Paradigm

(if data supports)

- Efficacy (vertical axis): LOW to HIGH
- Safety / Tolerability (horizontal axis): LOW to HIGH
- 2nd Gen TKIs
- **Selective TKIs** — **ELVN-001 Asciminib** — **Potential for Improved Efficacy & Safety/Tolerability**
- Imatinib

Future Treatment Paradigm

(if data supports)

1L	**1st Gen TKI** Imatinib	**4th Gen TKI** Asciminib
2L	**4th Gen TKI** Asciminib	ELVN-001
3L+	ELVN-001	

Market Insights & Assumptions

Asciminib could capture significant 1L market share given potentially superior efficacy compared to imatinib & **improved tolerability compared to 2nd Gen TKIs**

ELVN-001 is well positioned to follow asciminib given its **unique binding mode and complementary MoA** (ATP-site/active form vs. allosteric/inactive form)

With more early line use of asciminib, there may be a significant **need for treatment options with improved efficacy & tolerability** in later lines

- **Initial opportunity to address the ~16k patients** who switch therapies annually in 2L+ CML
- Additionally, an **opportunity may exist to compete directly with asciminib across lines of therapy** based on differentiated efficacy, tolerability or administration requirements

1L = First line. 2L = Second line. 2L+ = Second line or later. 3L+ = Third or later line. Gen = Generation. 2nd Gen TKIs = Nilotinib, Dasatinib, Bosutinib. ATP = Adenosine triphosphate. CML = Chronic myeloid leukemia. MoA = Mechanism of action. TKI = Tyrosine kinase inhibitor.
Note: Illustrative current and future treatment paradigm.
References: HCP Qualitative & Quantitative Interviews (ClearView).

ELVN-001 is a Selective Active Site, Active Form Inhibitor of BCR::ABL1

ATP-BINDING SITE

DRUG	BINDING CONFORMATION
ELVN-001	Active
BOSUTINIB	Active
DASATINIB	Active
IMATINIB	Inactive
NILOTINIB	Inactive
PONATINIB	Inactive

MYRISTOYL POCKET

DRUG	BINDING CONFORMATION
ASCIMINIB	Inactive

BCR

ABL

SH3

SH2

Kinase domain
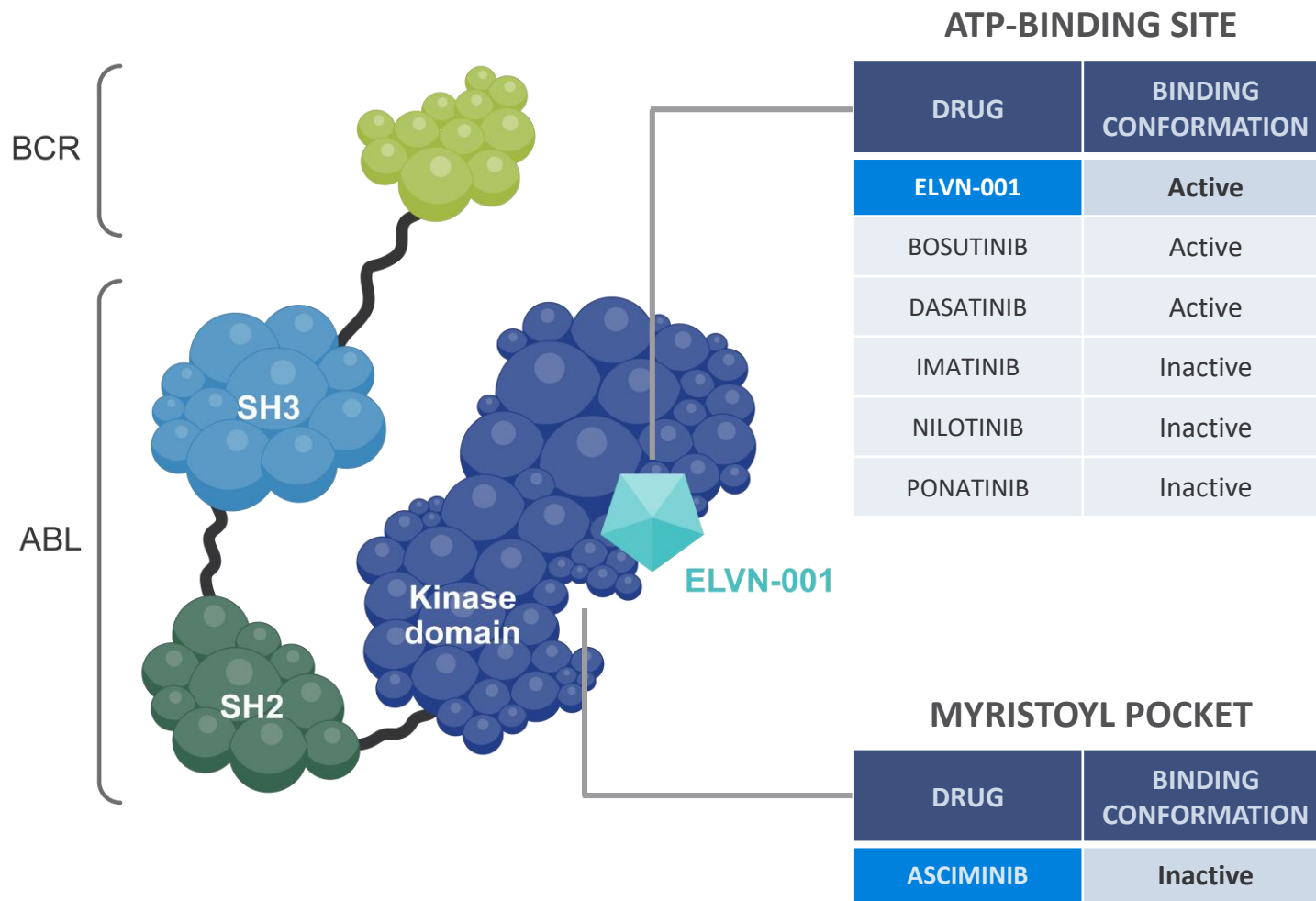
ELVN-001

Key Attributes of ELVN-001:

- Type 1 small molecule inhibitor of BCR::ABL1 targeting the ATP-binding site of the ABL1 kinase domain that binds to a unique P-loop "folded-in" active conformation of ABL1 creating a narrow selectivity tunnel

- Unique binding mode confers exquisite selectivity against the broader kinome

- Broad activity against multiple clinically important BCR::ABL1 mutations, including T315I, and those that confer resistance to asciminib

- Unlike all the approved TKIs, ELVN-001 is not a substrate for the common drug efflux transporters, P-gp and BCRP, which may play a role in resistance to TKIs in CML

ELVN-001 is Highly Selective and Active Against Asciminib Emergent Mutations

ELVN-001 selectively inhibits ABL with low off-target activity against other kinases

Cellular Phosphorylation IC$_{50}$ (nM)

	cKIT	FLT3wt	PDGFRb	VEGFR2	cSRC
ELVN-001	>10,000	>10,000	>10,000	>10,000	>10,000
Ponatinib	30	3.8	89	4.8	630
Nilotinib	200	>10,000	720	2,900	>10,000
Dasatinib	0.6	>1,000	7.1	>1,000	10
Bosutinib	1,000	4,700	7,900	>10,000	16
Imatinib	82	>10,000	230	9,600	>10,000
Asciminib	>10,000	>10,000	>10,000	>10,000	>10,000

Off-target kinase inhibition (IC50) by ELVN-001 vs. approved ABL TKIs in cell-based assays

ELVN-001 maintains activity against T315I and other BCR::ABL1 mutations known to confer resistance to asciminib

Fold-Shift from Native BCR::ABL1

	T315I	M244V	A337T	E355G	F359C	F359V	P465S
Asciminib	96	611	173	>2380	>2380	>2380	>2380
ELVN-001	4	2	1	4	3	2	2
Dasatinib	2935	2	1	3	4	2	2
Bosutinib	113	3	1	4	5	5	4
Ponatinib	3	2	1	3	5	5	2
Imatinib	>20	3	1	8	18	10	4
Nilotinib	>341	2	1	5	33	21	3
Vodobatinib	445	2	1	3	10	7	2
Olverembatinib	5	2	1	3	6	6	2

Antiproliferative activity of ELVN-001 vs. approved ABL TKIs in Ba/F3 cells harboring various BCR::ABL1 mutations

A337T and M244V were the most frequent emergent mutations to asciminib and F359C/V were the most frequent mutations at baseline in patients resistant to asciminib in ASCEMBL

ASCEMBL = phase 3 study of asciminib vs bosutinib in CML after 2 or more prior TKIs. BCR::ABL1 = breakpoint cluster region-Abelson leukemia virus 1. IC$_{50}$ = half-maximal inhibitory concentration. nM = nanomolar. TKI = tyrosine kinase inhibitor. WT = wildtype.
Cell viability measured with Cell titer glo luminescent assay. Values expressed as fold-shift in IC$_{50}$ from BCR::ABL1^{WT}.
References: Enliven data on file; Réa D and Hughes TP. Development of asciminib, a novel allosteric inhibitor of BCR-ABL1. Crit Rev Oncol Hematol. 2022;171:103580.; Qiang W et al. Mechanisms of Resistance to the BCR-ABL1 Allosteric inhibitor Asciminib. Leukemia. 2017;31(12):2844-2847.; Réa D et al. A phase 3, open-label, randomized study of asciminib, a STAMP inhibitor, vs bosutinib in CML after 2 or more prior TKIs. Blood. 2021;138:2031-2041.

ELVN-001 Clinical Focus and Target Product Profile

Our Opportunity

Drive Deeper Responses	Improve Tolerability	Enhance Safety & Convenience

Target Product Profile

- Activity against native BCR::ABL1, T315I, and known asciminib-resistant mutations

- **Highly selective:** No/minimal clinically relevant off-target toxicity

- **Efficacy**: MMR greater than approved TKIs driven by an enhanced therapeutic window

- **Tolerability**: Fewer dose reductions & discontinuations

- **Safety**: No black box warnings; no edema, effusions, reduced GI toxicity

- **No restrictions** with concomitant medications

Phase 1a/b: Dose Escalation in Late Line

- Patients with CML who have exhausted all available treatment options
- Seek to demonstrate improved therapeutic window & efficacy (BCR::ABL1 transcript level reductions) in highly resistant/intolerant disease

H2H vs Physician's Choice

- Superiority based on 6mo and/or 12mo MMR in CP-CML
- Better overall tolerability, fewer dose reductions & discontinuations vs. approved agents

Optionality: Post-asciminib and T315I mutation

- Single-arm study; precedent for approval in late line based on CCyR/MR2 (ponatinib, OPTIC trial)
- Asciminib-resistant/intolerant and/or T315I mutant CML

BCR::ABL1 = breakpoint cluster region-Abelson leukemia virus 1. CCyR = Complete cytogenetic response. CML = Chronic myeloid leukemia. CP-CML = Chronic phase CML. GI = Gastronintestinal. H2H = Head-to-head. mo = Month. MMR = Major molecular response.
MR2 = BCR::ABL1 ≤ 1%. TKI = Tyrosine kinase inhibitor.
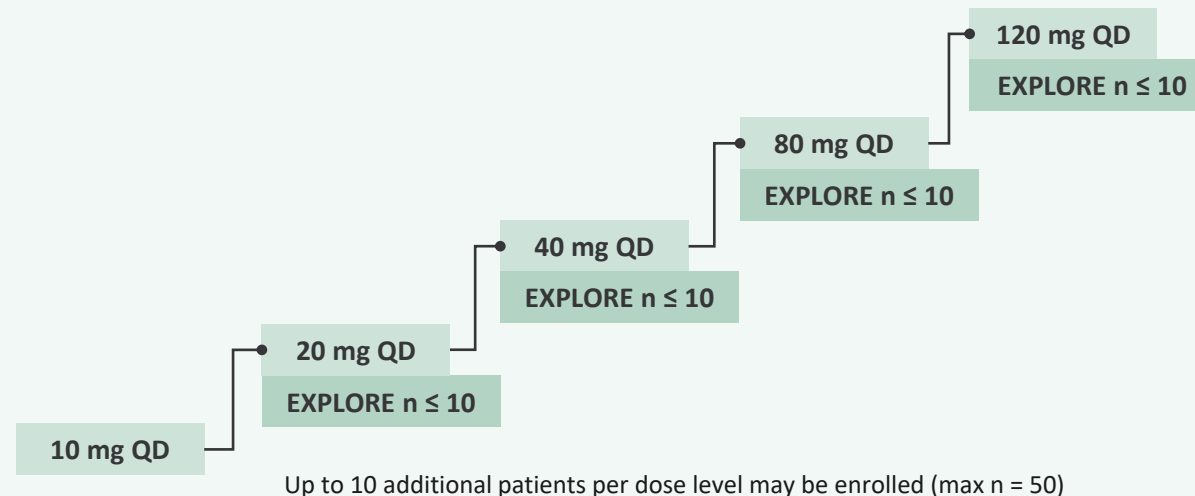
ELVN-001 Phase 1 Clinical Data

ENABLE (ELVN-001 Phase 1) Trial Design

ENABLE

Key eligibility criteria:

- Chronic Phase CML (CP-CML)
- Failed, intolerant to, or not a candidate for, available therapies known to be active for treatment of their CML[a]

Phase 1a: Dose Escalation[b]

120 mg QD
EXPLORE n ≤ 10

80 mg QD
EXPLORE n ≤ 10

40 mg QD
EXPLORE n ≤ 10

20 mg QD
EXPLORE n ≤ 10

10 mg QD

Up to 10 additional patients per dose level may be enrolled (max n = 50)

Phase 1b: Dose Expansion

Dose level 1	Dose level 2	T315I
Phase 1b expansion in CP-CML no T315I mutations; n=20	Phase 1b expansion in CP-CML no T315I mutations; n=20	Phase 1b expansion in CP-CML with T315I mutations; n=20

Additional expansion cohorts may be opened for patients based on emerging data

Primary endpoints:

- Incidence of dose limiting toxicities, adverse events, clinically significant laboratory abnormalities and ECG abnormalities

Secondary endpoints (Phase 1a[d]):

- Pharmacokinetics parameters[c]
- Molecular response (MR) by central qPCR using the International System (measured every 4 weeks x 6, then every 12 weeks)

ELVN-001 Phase 1 Continues to Enroll a Heavily Pre-treated Patient Population

Patient Demographics and Baseline Characteristics

Parameter	All Patients (N = 39)	Parameter	All Patients (N = 39)
Age, years, median (range)	60 (29–76)	Median number of prior TKIs, n (range)	3 (0–6)[d]
Male / female, n (%)	26/13 (66.7%/33.3%)	2 prior TKIs, n (%)	10 (25.6%)
Race		3 prior TKIs, n (%)	11 (28.2%)
White	26 (66.7%)	4 prior TKIs, n (%)	6 (15.4%)
Asian	9 (23.1%)	≥ 5 prior TKIs, n (%)	10 (25.6%)
Black or African American	1 (2.6%)	Prior TKI, n (%)	
Other or not reported	3 (7.7%)	Dasatinib	30 (76.9%)
ECOG performance status, n (%)		Imatinib	28 (71.8%)
0	32 (82.1%)	Asciminib	21 (53.8%)
1	7 (17.9%)	Ponatinib	20 (51.3%)
Median time since diagnosis, months (range)	72.7 (5.2–240.6)	Nilotinib	19 (48.7%)
Typical *BCR::ABL1* transcript	36 (92.3%)[a]	Bosutinib	10 (25.6%)
BCR::ABL1 mutation at baseline (central)[b]		Reason for discontinuation of last TKI, n (%) [e]	
T315I mutation, n (%)	4 (10.3%)[c]	Lack of efficacy	27 (69.2%)
E255V, n (%)	1 (2.6%)	Lack of tolerability	11 (28.2%)

[a] e13a2 and e14a2.
[b] Only available for patients with typical transcripts. Notable local testing in 1 patient with transcript level below the threshold for central mutational testing: A337T/V506M.
[c] Includes one re-enrolled patient, hence 3 individual patients with T315I.

[d] Number reflects individual TKIs. Median lines of prior TKIs is 4 (range 0-9). Range includes recently enrolled patient whose prior history had not been entered yet and one patient with 1 prior TKI who discontinued ELVN-001 after 1 dose due to protocol violation.
[e] One patient had no prior history entered.

Data cutoff date: 25 June 2024.
BCR::ABL1 = breakpoint cluster region-Abelson leukemia virus 1. ECOG = Eastern Cooperative Oncology Group. TKI= tyrosine kinase inhibitor.
Note: Patients who had gone through intra-patient dose escalation as per protocol were counted under their initial treatment group only. 2 patients who were re-enrolled were counted under their initial treatment group and their re-enrolled treatment group.

Median Time on ELVN-001 at Cutoff was 20 Weeks

Time on Study (weeks)

Legend:
- 10 mg
- 20 mg
- 40 mg
- 80 mg
- 120 mg
- T315I
- Atypical
- ◆ Evaluable for MMR
- ★ Re-enrolled
- ✖ Discontinued
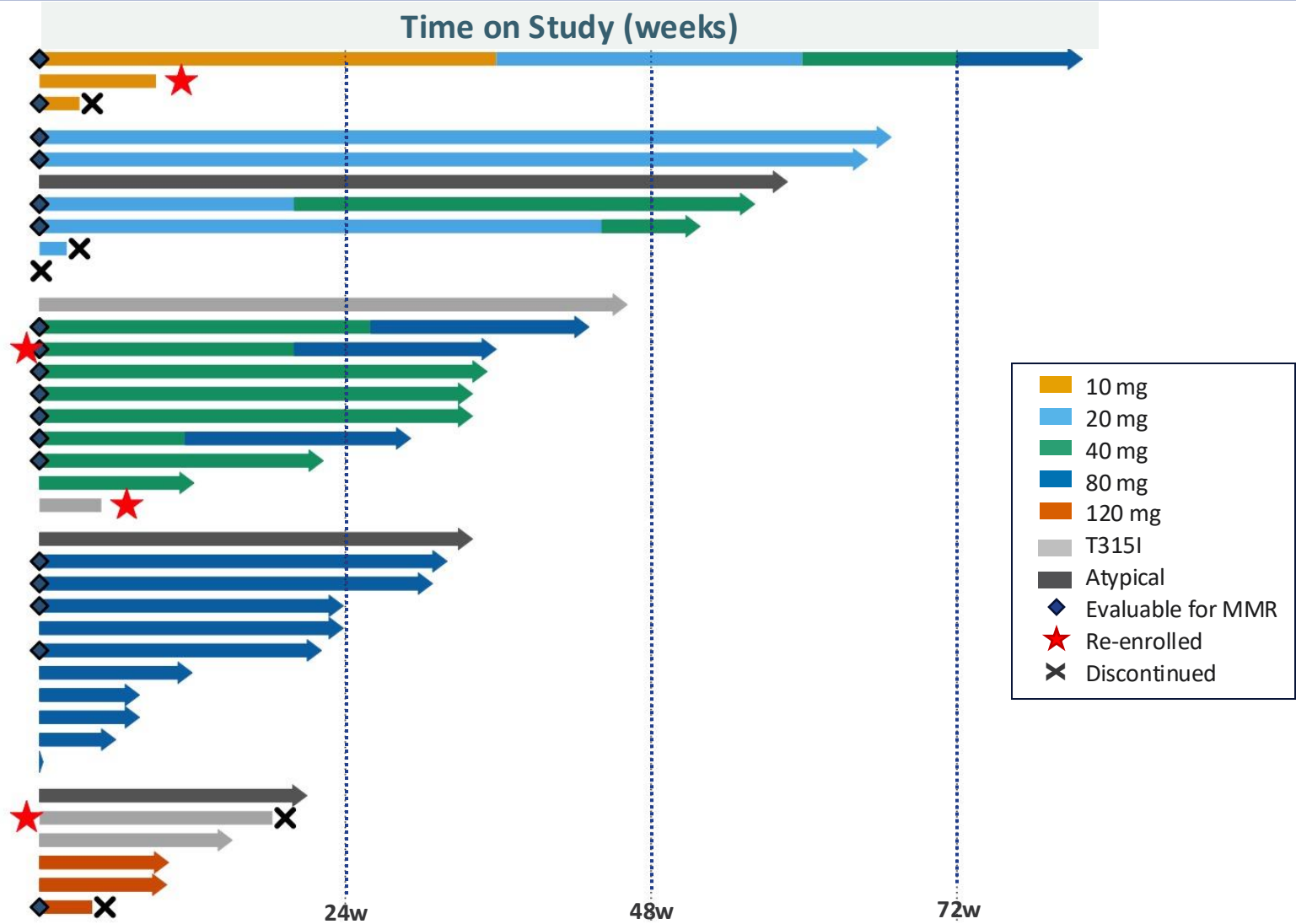
- At cutoff, the **vast majority** of patients enrolled **remained on study** with a median time on ELVN-001 of 20 weeks

- **44% (8/18) cumulative MMR** by 24 weeks

- All of the patients enrolled with T315I mutated CML had prior ponatinib and asciminib

24w   48w   72w

Data cutoff date: 25 June 2024.
CML = chronic myeloid leukemia. MMR = major molecular response. qPCR = quantitative reverse transcriptase polymerase chain reaction.
The protocol allows re-enrollment and intra-subject dose escalation. MMR is defined as BCR::ABL1 ≤ 0.1%. Evaluable patients had baseline typical BCR::ABL1 transcript without T315I mutation and postbaseline assessment of BCR::ABL1 transcript at 24 weeks or achieved MMR within 24 weeks or discontinued treatment before 24 weeks without achieving MMR. For patients with MMR at baseline, only postbaseline assessments beyond 70 days were included in the analysis. The swimmer plot does not include 2 patients that received their first ELVN-001 dose in June (these patients were included in the safety analysis as it was confirmed they received at least one dose of ELVN-001, but daily dosing information had yet to be provided at cutoff date).

ELVN-001 Data Compares Favorably to Precedent Phase 1 Trials

		Asciminib Phase 1 (2019)	Bosutinib Phase 1 (2012)	ELVN-001 Phase 1a[1]	
Demographics (Prior TKIs)	2	30 (27%)	115 (97%)	10 (26%)	More heavily pre-treated patients
	3	41 (36%)	3 (3%)[2]	11 (28%)	
	4	32 (28%)		6 (15%)	
	≥ 5	9 (8%)		10 (26%)	
Efficacy (Non-T315I)	Cumulative MMR	37/99 (37%)	16/105 (15%)	8/18 (44%)	ELVN-001 in post-asciminib patients: 4/10 MMR by 24 wk.
	TKI-resistant[3]	3/32 (11%)	3/54 (6%)	5/12 (42%)	
	Response Achieved	19/80 (24%)		3/13 (23%)	
	Response Maintained	18/19 (95%)		5/5 (100%)	
	Time Frame	by 24 weeks	median follow-up 28.5 mo.	by 24 weeks	

ELVN-001's cumulative MMR rate compares favorably despite a more heavily pre-treated patient population

CML = Chronic myeloid leukemia. f/up = Follow-up. MMR = Major molecular response. Mo. = month. TKI = Tyrosine kinase inhibitor. Wk. = Weeks.
1. Data cutoff date: 25 June 2024; MMR is defined as BCR::ABL1 ≤ 0.1%. MMR rates includes all patients treated who had typical BCR::ABL1 transcripts without T315I mutation 2. Refers to ≥ 3 prior TKIs. 3. For asciminib, this does not include ponatinib-resistant patients (MMR by 6 mo. = 0%, n=4); for bosutinib, this includes patients that were resistant to nilotinib (n=27) or dasatinib (n=37).
These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, conclusions from cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.
References: Hughes et al., NEJM 2019; Khoury HJ et al. Blood. 2012.

Change in BCR::ABL Transcript in Patients with CML by 24 Weeks

Change in BCR::ABL1 Transcript in CML Patients without T315I Mutation by 24 Weeks

Legend:
- Improvement in MR Category (dark green)
- Stable (light green)
- Lack of Efficacy (yellow)

BCR::ABL1 transcript by 24-weeks	Baseline *BCR::ABL1* transcript						
	MR5 ≤ 0.001 (n = 0)	MR4.5 > 0.001 to 0.0032 (n = 0)	MR4 > 0.0032 to 0.01 (n = 1)	MR3 > 0.01 to 0.1 (n = 4)	> 0.1 to 1 (n = 6)	> 1 to 10 (n = 2)	> 10 (n = 5)
MR5 ≤ 0.001			1	1[a]			
MR4.5 > 0.001 to 0.0032							
MR4 > 0.0032 to 0.01					1		
MR3 > 0.01 to 0.1				3	1	1	
> 0.1 to 1					4		1
> 1 to 10							1
> 10						1[b]	3

Within 24 weeks of treatment:

7 patients with improved MR category
- 2 improved by 1 category
- 4 improved by 2 categories
- 1 improved by 3 categories

- Among the 16 patients previously evaluated for efficacy by 12 weeks, all 16 had stable or deepening responses between weeks 12 and 24

- To date, no emerging mutations identified

[a] Deep response (MR3 → MR5) in patient with lack of efficacy to prior asciminib and A337T mutation by local lab (below the threshold for central mutation testing).

[b] Worsening of transcript level from 6.3% at baseline to 13% after 4 weeks in patient with E255V mutation who previously discontinued asciminib and ponatinib due to lack of efficacy.

Data cutoff date: 25 June 2024. BCR::ABL1 = breakpoint cluster region-Abelson leukemia virus 1. CML = Chronic myeloid leukemia. MR = molecular response. Stable = transcript levels remain within listed category.
NOTE: MR5 category assigned based on transcript level; < limit of quantitation. Evaluable patients had baseline typical BCR::ABL1 transcript without T315I mutation and postbaseline assessment of BCR::ABL1 transcript at 24 weeks or achieved MMR within 24 weeks or discontinued treatment before 24 weeks without achieving MMR. For patients with MMR at baseline, only postbaseline assessments beyond 70 days were included in the analysis.

BCR::ABL1 (atypical, e19a2), T315I (post-Ponatinib): Deep Response

Achieved Deep Response in T315I 80mg → 120 mg QD ELVN-001
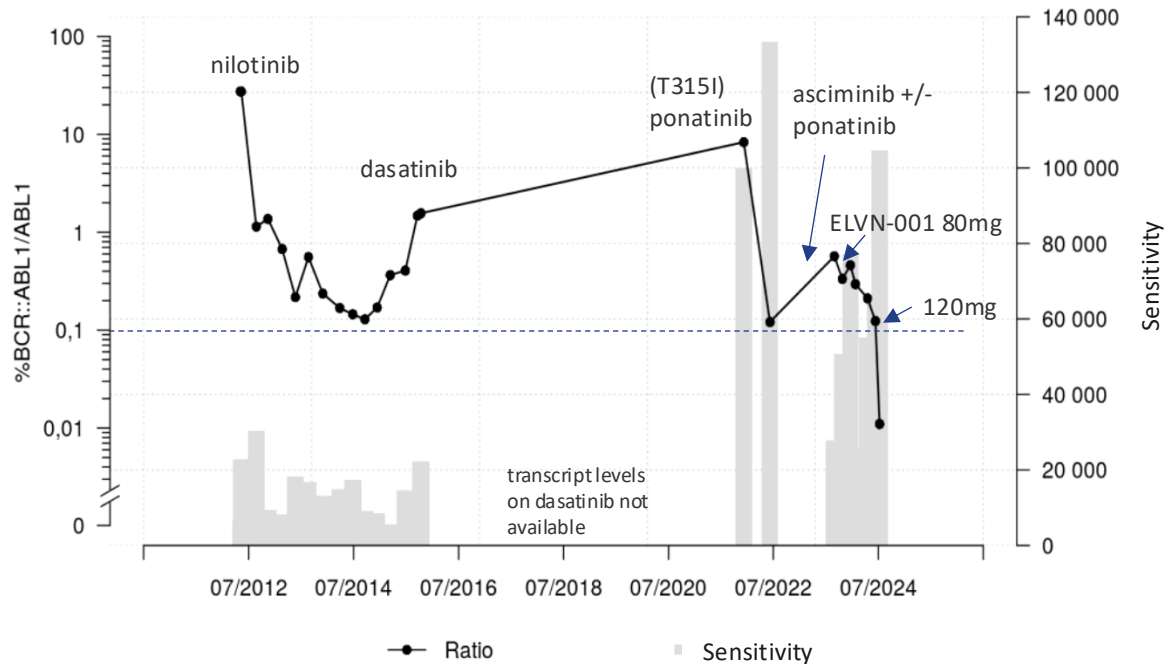
Patient Background

Prior therapy (reason for switch)	nilotinib (LOE), dasatinib (LOE), ponatinib (LOE), asciminib (LOE) and ponatinib + asciminib combination (LOE)
Mutations	T315I
Safety	G1 dry skin
Efficacy	>1-log decrease

Resistant to 4 prior TKIs, deep response on ELVN-001

Safety and Tolerability of ELVN-001

- Well-tolerated to date
  - Maximum tolerated dose has not been reached
  - No dose reductions
  - No ≥ Grade 3 non-hematologic treatment-related AEs; no Grade 1/2 TRAEs >11%
  - No exposure-toxicity relationship identified to date

- Only 5.1% (2/39) of patients discontinued due to AEs
  - The 2 patients that discontinued due to AEs did so within the first 30 days of treatment
  - No discontinuations at doses ≥ 40mg QD

ELVN-001's safety profile remains consistent with its high selectivity, even with longer duration and more patients enrolled at higher dose levels

Data cutoff date: 25 June 2024.
AE = adverse event. BCR-ABL = breakpoint cluster region-Abelson leukemia virus 1. TRAE = treatment related adverse event.

Hematologic Treatment Emergent Adverse Events

Hematologic TEAEs

Preferred term n (%)	ELVN-001 Dose Group										Total (N = 37)	
	10 mg QD (n = 3)		20 mg QD (n = 7)		40 mg QD (n = 11)		80 mg QD (n = 11)		120 mg QD (n = 7)			
	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4
Neutropenia[a]	2 (66.7%)	2 (66.7%)	2 (28.6%)	2 (28.6%)	0	0	0	0	0	0	4 (10.8%)	4 (10.8%)
Thrombocytopenia[b]	0	0	2 (28.6%)	2 (28.6%)	0	0	2 (18.2%)	0	0	0	4 (10.8%)	2 (5.4%)
Leukopenia[c]	0	0	0	0	0	0	1 (9.1%)	0	0	0	1 (2.7%)	0
Pancytopenia	0	0	1 (14.3%)	1 (14.3%)	0	0	0	0	0	0	1 (2.7%)	1 (2.7%)
Anemia	1 (33.3%)	0	1 (14.3)	0	0	0	0	0	0	0	2 (5.4%)	0

[a] Grouped term for neutropenia includes neutrophil count decreased; [b] Grouped term for thrombocytopenia includes platelet count decreased; [c] Grouped term for leukopenia includes white blood cell count decreased

- Most Grade 3/4 TEAEs were hematologic, all occurring within the first 8 weeks

- No dose reductions due to cytopenias

- One patient discontinued ELVN-001 in the setting of Gr 3/4 cytopenias (at 20 mg QD; DLT)

- No exposure-toxicity relationship identified to date

Data cutoff date: 25 June 2024.
DLT = dose-limiting toxicity. Gr = Grade. QD = once daily. SAE = serious adverse event. TEAE = treatment-emergent adverse event. TKI = Tyrosine Kinase Inhibitor.
NOTE: Severity grades were defined by CTCAE (Common Terminology Criteria for Adverse Events) Version 5.0. Patients who had gone through intra-patient dose escalation as per protocol were counted under their initial treatment group only. 2 patients who were re-enrolled were counted under their initial treatment group and their re-enrolled treatment group but counted as one patient in the total column.

Low Incidence of Non-Hematologic Adverse Events Consistent with Selective Kinase Profile

Non-Hematologic TRAEs in ≥ 5% of Patients

Preferred term n (%)	ELVN-001 Dose Group											Total (N = 37)	
	10 mg QD (n = 3)		20 mg QD (n = 7)		40 mg QD (n = 11)		80 mg QD (n = 11)		120 mg QD (n = 7)				
	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4		Any Gr	Gr 3/4
Lipase elevation	1 (33.3%)		1 (14.3%)		1 (9.1%)		1 (9.1%)					4 (10.8%)	
Rash			1 (14.3%)		2 (18.2%)							3 (8.1%)	
Arthralgia									2 (28.6%)			2 (5.4%)	
Headache			1 (14.3%)				1 (9.1%)					2 (5.4%)	
Muscle Spasms					1 (9.1%)				1 (14.3%)			2 (5.4%)	
Myalgia			1 (14.3%)						1 (14.3%)			2 (5.4%)	
Nausea			1 (14.3%)						1 (14.3%)			2 (5.4%)	

- No Grade 3 or higher non-hematologic TRAEs

- No dose reductions due to non-hematologic TRAEs

- One patient discontinued ELVN-001 due to SAE of Gr 2 pancreatitis (at 10 mg QD); no additional TEAEs of pancreatitis reported
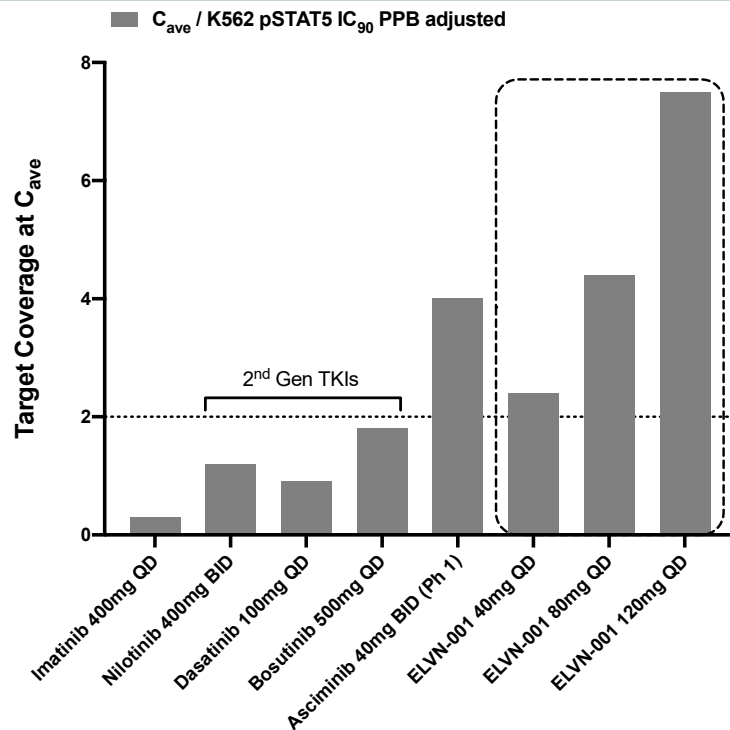
Data cutoff date: 25 June 2024.
CTCAE = Common Terminology Criteria for Adverse Events. Gr = Grade. QD = once daily. SAE = Serious Adverse Event. TEAE = Treatment Emergent Adverse Event. TRAE = Treatment Related Adverse Event.
NOTE: Severity grades were defined by CTCAE Version 5.0. Patients who had gone through intra-patient dose escalation as per protocol were counted under their initial treatment group only. 2 patients who were re-enrolled were counted under their initial treatment group and their re-enrolled treatment group but counted as one patient in the total column.

ELVN-001 Achieved Superior Target Coverage Compared to 2nd Gen TKIs and Similar Target Coverage Compared to Asciminib

C_{ave} Target Coverage vs. All TKIs (Late Line)

Legend: C_{ave} / K562 pSTAT5 IC_{90} PPB adjusted

Y-axis: Target Coverage at C_{ave} (0 to 8)

Categories: Imatinib 400mg QD, Nilotinib 400mg BID, Dasatinib 100mg QD, Bosutinib 500mg QD, Asciminib 40mg BID (Ph 1), ELVN-001 40mg QD, ELVN-001 80mg QD, ELVN-001 120mg QD

2nd Gen TKIs

C_{ave} Target Coverage vs. Asciminib (Phase 1)

Legend:
- C_{ave} / K562 GI_{50} PPB adjusted
- C_{ave} / K562 pSTAT5 IC_{90} PPB adjusted

Y-axis: Target Coverage at C_{ave} (0 to 6)

Categories: Asciminib 40mg BID Phase 1, ELVN-001 80mg QD

- ELVN-001 had better target coverage based on plasma protein binding adjusted pSTAT5 IC_{90} at ≥ 40mg QD compared to 2nd Gen TKIs, and similar target coverage as asciminib at 80mg QD
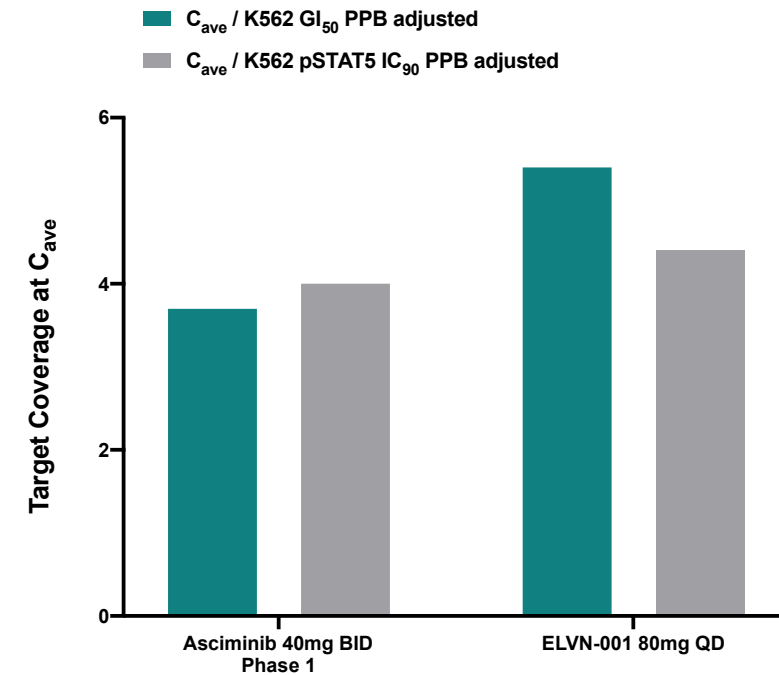
- Novartis referenced preclinical 90% inhibitory concentration for phosphorylated STAT5 or pSTAT5 IC_{90} and anti-proliferation GI_{50} as the key target coverage metrics supporting an optimal asciminib dose of 40mg BID or 80mg QD for CML patients without T315I mutations

Summary

CML Opportunity

- CML is a chronic condition, often requiring decades of daily therapy

- Despite generics, the commercial market supports ~$6B in sales from six approved BCR::ABL1 TKIs, which are used interchangeably across lines of therapy

- Clear need for better agents, demonstrated by the recent asciminib (Scemblix) launch that is already generating >$650M in annualized sales with only ~26% penetration into US 3L+

- Based on recently announced positive 1L Phase 3 data, asciminib is potentially poised to penetrate early lines of therapy

- We believe an opportunity exists to become the preferred active site TKI option post-asciminib, as well as to compete directly with asciminib based on differentiated efficacy, tolerability and/or administration requirements across lines of therapy

ELVN-001 Updated Proof of Concept Data

- As a highly selective, active site, active form inhibitor of BCR::ABL1, ELVN-001 represents a complimentary MoA compared to asciminib

- Based on updated Phase 1 data, ELVN-001:

  - Achieved cumulative MMR rate in heavily pre-treated patients, including post-asciminib patients, that is favorable when compared to historical Phase 1 cumulative MMR rates from other TKIs

  - Remains well-tolerated with no ≥ Grade 3 treatment related non-hematologic toxicities and no dose reductions

  - Only 5.1% (2/39) of patients discontinued due to AEs, and no discontinuations at doses ≥ 40mg QD due to AEs

  - Achieved target coverage superior to 2nd Gen TKIs and similar to asciminib at well-tolerated doses

  - Has a PK profile that supports once daily dosing with flexible administration requirements, including the ability to take with or without food

1L = First line. 3L+ = Third line or later. 2nd Gen TKIs = nilotinib, dasatinib, bosutinib. BCR::ABL1 = breakpoint cluster region-Abelson leukemia virus 1. CML = Chronic myeloid leukemia. MMR = Major molecular response. MoA = Mechanism of action.
PK = Pharmacokinetic. TKI = Tyrosine kinase inhibitor. Results from a head-to-head comparison may differ from those set forth herein.
References: public company filings and announcements.

Next Steps for ELVN-001

Today

Presentation of updated Phase 1a clinical data and continued dosing of patients in Phase 1a/b

2025

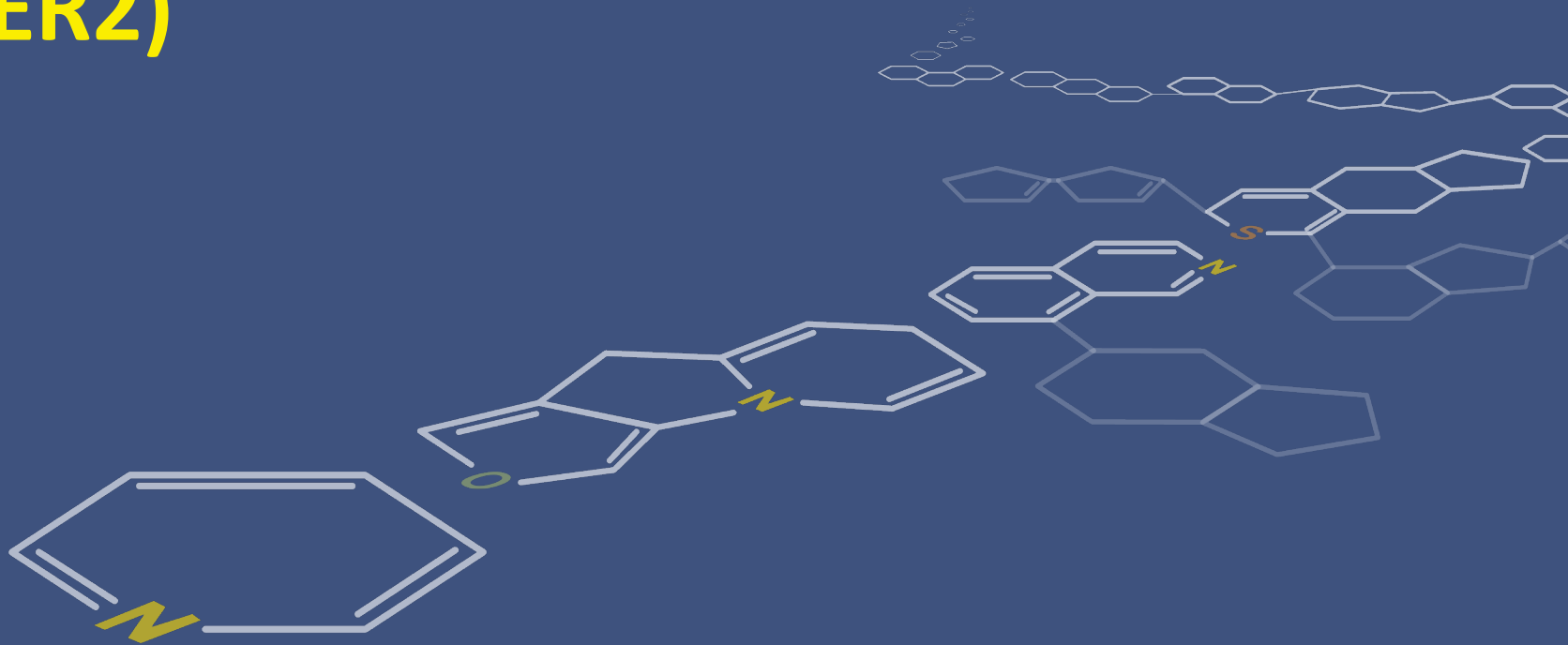Phase 1 data with ~60-100 patients across various lines of therapy with significant follow-up

2025 Year End

Initial regulatory interactions with the aim of achieving regulatory path clarity regarding the first head-to-head pivotal trial
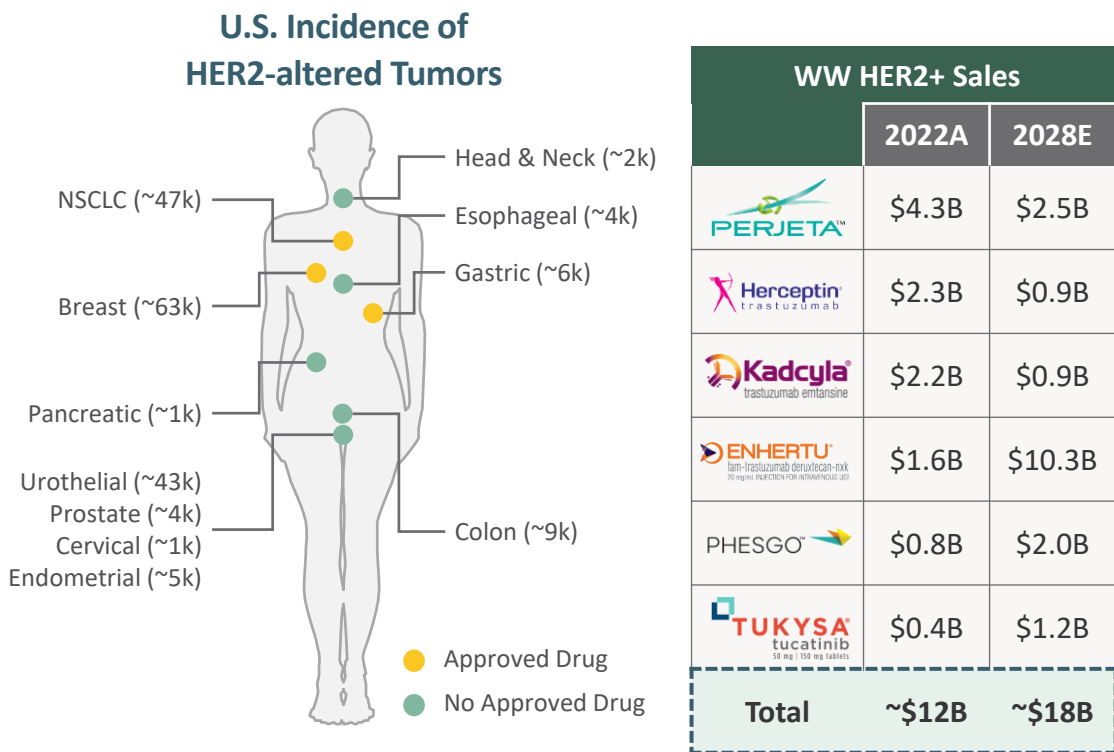
ELVN-002 (HER2)

Substantial Opportunity in HER2-altered Patient Populations

Reshuffling of Treatment Paradigm Could Create a Significant Post-Enhertu® Opportunity Across HER2-altered Cancers

U.S. Incidence of HER2-altered Tumors

- Head & Neck (~2k)
- Esophageal (~4k)
- NSCLC (~47k)
- Gastric (~6k)
- Breast (~63k)
- Pancreatic (~1k)
- Urothelial (~43k)
- Prostate (~4k)
- Colon (~9k)
- Cervical (~1k)
- Endometrial (~5k)

- 🟡 Approved Drug
- 🟢 No Approved Drug

WW HER2+ Sales	2022A	2028E
PERJETA	$4.3B	$2.5B
Herceptin trastuzumab	$2.3B	$0.9B
Kadcyla trastuzumab emtansine	$2.2B	$0.9B
ENHERTU fam-trastuzumab deruxtecan-nxki	$1.6B	$10.3B
PHESGO	$0.8B	$2.0B
TUKYSA tucatinib	$0.4B	$1.2B
Total	**~$12B**	**~$18B**

Multi-billion-dollar market opportunity post-Enhertu® with ~25% of patients receiving Enhertu® progressing within 12-months and up to 50% of patients developing brain metastases

Multiple Early-Line Settings Without Entrenched Drugs

- Lack of approved drugs for key tumors harboring HER2 mutations (e.g., 1L NSCLC) and HER2 amplified or overexpressing tumors (e.g., NSCLC and CRC)
- Trial timing opens the window for multiple fast-follower and follow-on opportunities

Key HER2 1L Trials

MBC			
Compound	**Company**	**Stage**	**Timing**
ENHERTU fam-trastuzumab deruxtecan-nxki	Daiichi-Sankyo	Phase III Ongoing	Initiated in Apr '21

HER2 Mutant NSCLC			
Compound	**Company**	**Stage**	**Timing**
ENHERTU fam-trastuzumab deruxtecan-nxki	Daiichi-Sankyo	Phase III Ongoing	Initiated in Dec '21
Zongertinib	Boehringer Ingelheim	Phase III Ready	Initiating in 2024

CRC			
Compound	**Company**	**Stage**	**Timing**
TUKYSA tucatinib	Seagen	Phase III Ongoing	Initiated in Oct '22

1L = First line. CRC = Colorectal cancer. HER2 = human epidermal growth factor receptor 2. HER2-altered = HER2 amplification/overexpression and HER2 mutant. MBC = Metastatic breast cancer. NSCLC = Non-small cell lung cancer.
References: EvaluatePharma. Cancer Metastasis Rev (2015) 34:157–164. Oncologist. 2019 Dec; 24(12): e1303–e1314. Seer, National Cancer Institute.

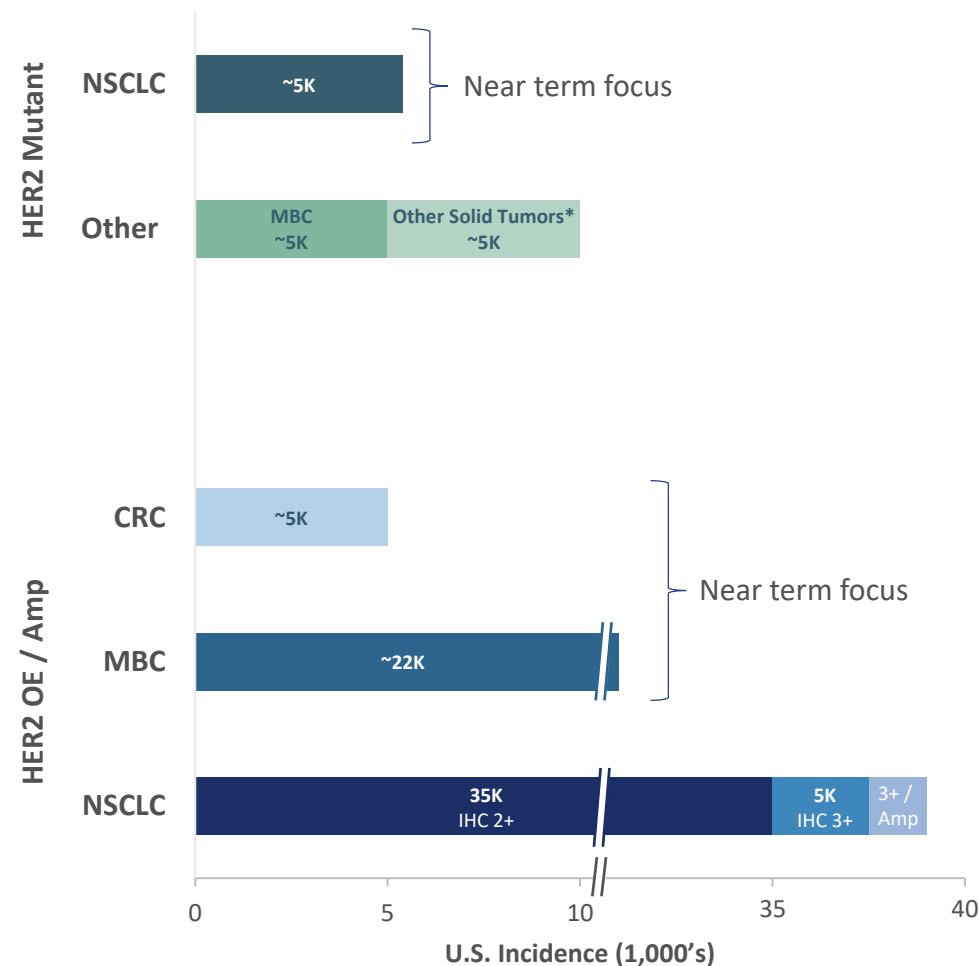# Significant Opportunities for ELVN-002 in a Rapidly Evolving Landscape

HER2 Mutant NSCLC and Other HER2 Mutant Cancers

- Approximately 3% of NSCLC patients harbor HER2 mutations, for which there are **no approved TKIs**

- Currently there is a **high unmet need** in this indication, but the landscape is evolving as ADCs and multiple investigational TKIs emerge

- Other HER2 mutant cancers represent a **larger market** with **limited treatment options**

HER2 Amplified or Overexpressing Cancers

- Largest potential market opportunity, with **nearly 70K addressable patients**

- As Enhertu® disrupts earlier lines of therapy in a broad set of indications, a **follow-on TKI combination** opportunity exists

- **Tukysa® (tucatinib) is generating >$475M annualized revenue** with a 2L+ HER2+ MBC label in combination with trastuzumab + chemotherapy (capecitabine)

- Recent tucatinib data shows **dual HER2 targeting without the need for chemotherapy** has clinical benefit in HER2+ CRC

- Additionally, recent tucatinib + Kadcyla® data in HER2+ MBC **supports a larger opportunity in MBC** and the **rationale for ADC + TKI combinations more broadly**

- Currently, **no targeted therapies are approved for HER2+ NSCLC**

U.S. Market Size Estimates (approximate)

Bar chart — U.S. Incidence (1,000's), x-axis 0, 5, 10, 35, 40

HER2 Mutant:
- NSCLC: ~5K — Near term focus
- Other: MBC ~5K | Other Solid Tumors* ~5K

HER2 OE / Amp:
- CRC: ~5K
- MBC: ~22K — Near term focus
- NSCLC: 35K IHC 2+ | 5K IHC 3+ | 3+ / Amp

*Other cancers include prostate, endometrial, gastric, stomach, hepatobiliary, etc.
2L+ = Second line or later. ADC = Antibody drug conjugate. CRC = Colorectal cancer. HER2 = human epidermal growth factor receptor 2. IHC = Immunohistochemistry. TKI = Tyrosine kinase inhibitors. NSCLC = Non-small cell lung cancer. MBC = Metastatic breast cancer. OE = Overexpressing. Amp = Amplified.
Reference: National Cancer Institute. SEER*Stat software. Bethesda, MD: National Cancer Institute, Surveillance Research Program; Robichaux et al. Cancer Cell. 2019;36(4):444-457.e7.
Note: Tukysa® annualized revenue calculated based on $121 million of revenue in Q2 2024

ELVN-002: Opportunity for a CNS Penetrant, Selective and Irreversible Pan-Mutant HER2 TKI

Current HER2 TKI Landscape & Limitations

- The **high degree of structural homology** between EGFR and HER2 makes it difficult to design HER2-selective inhibitors

- Tucatinib is the **only approved HER2-selective TKI,** but is a **reversible inhibitor and only achieves IC_{90} coverage in ~40% of patients**

- Tucatinib also **lacks potency against key mutations** in NSCLC and breast cancer

- Most approved and investigational **irreversible TKIs** are **dual EGFR/HER2 inhibitors** and are **dose-limited by EGFR-driven toxicity**

- Current HER2 TKIs potentially **leave room for further improvement in addressing brain metastases**

Our HER2 Candidate: ELVN-002

- Designed to **irreversibly inhibit HER2 and multiple key HER2 mutations** in NSCLC and breast cancer, including HER2 YVMA and L755, and

- Selectively inhibit HER2 while **sparing EGFR** to prevent EGFR-related toxicities, with the potential for **improved efficacy** across HER2-driven cancers

- Deliberately **designed to enable rational combination therapies**, particularly for HER2+ cancers

- Demonstrated **superior pre-clinical activity** in HER2-amplified **subcutaneous and intracranial models**, and an **improved safety margin** in NHPs compared to tucatinib

ELVN-002 was designed to achieve an improved therapeutic index compared to current approved and investigational TKIs in the broad HER2 population, including HER2 mutant and amplified / overexpressed tumors.

ELVN-002 Clinical Focus and Target Product Profile

Our Opportunity

Drive Durable Responses	Well-Tolerated	CNS activity

Target Product Profile

- **Activity against:**
  - HER2 mutant NSCLC (e.g., Exon 20 IM) and breast cancer (e.g., L755x)
  - HER2 amplified and/or overexpressed tumors (breast, CRC, NSCLC, etc.)
  - Brain metastases
- **Selective:** does not inhibit wild-type EGFR
- **Safety/tolerability**: minimal GI and skin toxicity (avoid EGFR-toxicity)
- **Combinable** with SOC including ADCs across HER2-driven tumors

Phase 1a Dose Escalation in solid tumors with HER2 alterations

- Monotherapy in HER2-altered solid tumors
- Evaluate the combination with ADCs in HER2+ breast cancer and HER2 NSCLC

Phase 1b in HER2 mutant NSCLC

- Complete Phase 1b, establish monotherapy dose
- Consider 2L+ single-arm study with potential to support accelerated approval

Phase 1 in HER2 Overexpressed/Amplified MBC & CRC

- Initiation of additional Phase 1 trial in combination with trastuzumab +/- chemotherapy
- FPI for Phase 1a in 2Q 2024

Multiple Indication Opportunities

- Driving proof of concept for mono/combo therapy in multiple tumors (mutant NSCLC, HER2+ breast and CRC)
- With additional indications to explore (HER2+ NSCLC and other HER2-driven solid tumors)

ADC = Antibody drug conjugate. CRC = Colorectal cancer. CNS = Central nervous system. EGFR = epidermal growth factor receptor. FPI = First patient in. GI = Gastrointestinal. HER2 = human epidermal growth factor receptor 2. IM = insertion mutations. MBC = Metastatic breast cancer. NSCLC = non-small cell lung cancer. SOC = Standard of care. TKI = Tyrosine kinase inhibitors.

ELVN-002 Potently Inhibited HER2 & HER2 Mutants While Sparing EGFR

IC_{50} values (nM)	Pyrotinib	Tucatinib	Compound (I) WO2023066296*	Zongertinib	ELVN-002	
BT474 HER2^{WT} pHER2 IC_{50} (10% FBS)	13	12	19	30	8.5	
Beas2b HER2^{S310F} pHER2 IC_{50} (10% FBS)	1.4	9.6	6.4	2	1.8	
Beas2b HER2^{L755S} pHER2 IC_{50} (10% FBS)	4.5	47	12	5.4	3.5	
Beas2b HER2^{YVMA} pHER2 IC_{50} (10% FBS)	4.5	74	20	1.5	3.4	
BT474 HER2^{WT} pHER2 IC_{50} (50% human serum)	**40**	**37**	**134**	**164**	**18**	ELVN-002 has differentiated potency in human serum, particularly vs. HER2^{WT}
Beas2b HER2^{S310F} pHER2 IC_{50} (100% human serum)	**51**	**304**	**903**	**433**	**17**	
Beas2b HER2^{YVMA} pHER2 IC_{50} (100% human serum)	**220**	**1,650**	**273**	**145**	**28**	
BT474 (HER2^{wt}) cytotox IC_{50}	2.3	23	58	7.8	3.9	
NCI-N87 (HER2^{wt}) cytotox IC_{50}	2.6	37	65	3.8	3.3	
Ba/F3 HER2^{L755S} cytotox IC_{50}	3.7	245	323	11	4.8	ELVN-002 maintains potency vs. major single-point and E20IM mutations
Ba/F3 HER2^{YVMA} cytotox IC_{50}	3.5	107	229	6.5	5.9	
H2073 (EGFR^{wt}) pEGFR IC_{50}	6.4	>10,000	218	2,030	2,160	
A431 (EGFR^{wt}) pEGFR IC_{50}	10	>7,690	980	2,200	1,700	
A431 (EGFR^{wt}) cytotox IC_{50}	75	>10,000	8,360	9,360	*3,530*	
Human Hepatocyte stability, extraction ratio (%)	74	76	83	42	22	ELVN-002 has exceptional drug-like properties and PK profile**
Kinetic Solubility pH 7.4 (µM)	< 0.1	9.3	108	< 0.07	260	

EGFR = epidermal growth factor receptor. E20IM = Exon 20 insertion mutations. FBS = fetal bovine serum. HER2 = human epidermal growth factor receptor 2. IC_{50} = half-maximal inhibitory concentration. PK = Pharmacokinetic. WT = wild type

*This compound, which is disclosed in WO2023066296, may be the same, or similar to, ZN-1041, which was sold to Roche by Zion Pharma in 2023 and is being developed for the treatment of HER2+ cancers, including breast cancer.

**Based on non-clinical results/data.

Note: IC values represent an average derived from multiple runs internally with a minimum of two independent experiments. ADMET data were generated internally.

ELVN-002 Had Favorable Mutant Coverage Compared to Tucatinib

Ba/F3 HER2 Mutation	Proliferation IC50 [nM]		Proliferation IC$_{50}$ Fold over	
	Tucatinib	ELVN-002	Tucatinib	ELVN-002
wild-type	29	6	1	1
P95	33	11	1	2
A775-G776-ins-C	24	2	1	0.2
A775-G776-ins-YVMA	225	11	8	2
A775-G776-ins-YVMS	510	15	18	2
A775-G776-ins-SVMA	157	6	5	1
A775-G776-ins-VVMA	294	12	10	2
A775-G776-ins-MMAY	287	7	10	1
A775-G776-ins-YVMA-R678Q	642	14	22	2
G776VC	499	17	17	3
G776-del-ins-IC	1104	41	38	7
G776-del-ins-LC	88	13	3	2
G776-del-ins-VV	1239	34	43	5
G776-V777-del-ins-CVC	209	13	7	2
G776-Del-ins-AVGC	438	14	15	2
V777-G778-ins-GC	20	5	1	1
P780-Y781-ins-GSP	29	3	1	1
S310F	11	3	0.4	0.5
S310Y	12	3	0.4	0.5
R678Q	29	5	1	1
L755S	418	8	14	1
L755P	1284	21	44	3
D769N	7	2	0.3	0.3
V773M	64	4	2	1
V777L	11	3	0.4	1
T798M	3412	194	118	32
L869R	148	2	5	0.4
L869R/T798I	2524	43	87	7
V842I	21	4	1	1
BaF3 parental cell line	>10000	>10000	>10000	>10000
EGFR	>10000	>10000	>10000	>10000

HER2 Exon20 Insertion Mutations

Common HER2 Point Mutations

YVMA: 71% E20IM NSCLC

VC: 11% E20IM NSCLC

22% HER2^{mut} MBC

E20IM = Exon 20 insertion mutations. HER2 = human epidermal growth factor receptor 2. IC$_{50}$ = half-maximal inhibitory concentration. MBC = Metastatic breast cancer. NSCLC = Non-small cell lung cancer.
Note: IC values represent an average derived from multiple runs internally with a minimum of two independent experiments.
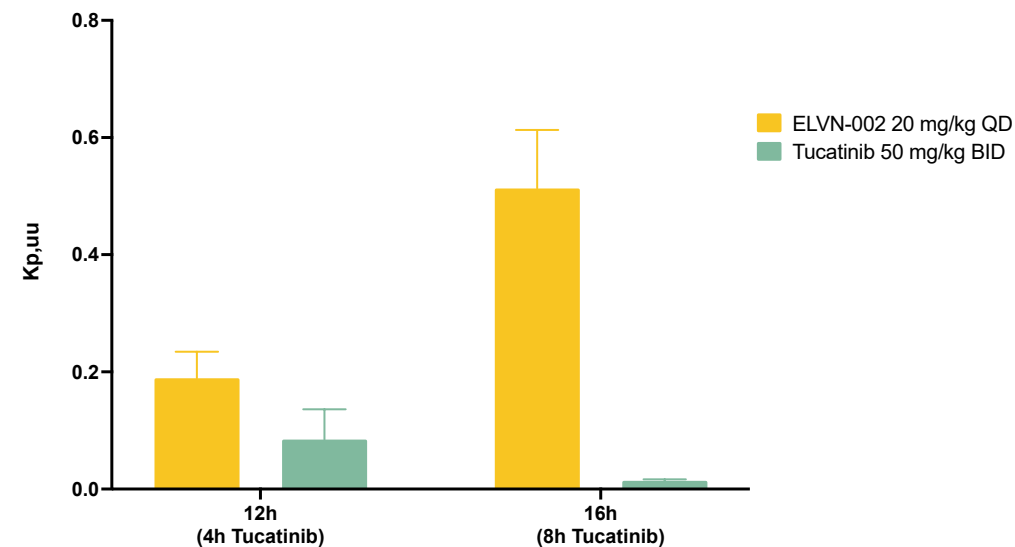
ELVN-002 Demonstrated Robust CNS Anti-Tumor Activity in NCI-N87 HER2^{WT} Intracranial Model at Well-Tolerated Doses

NCI-N87 HER2^{wt} Intracranial (CNS) Model
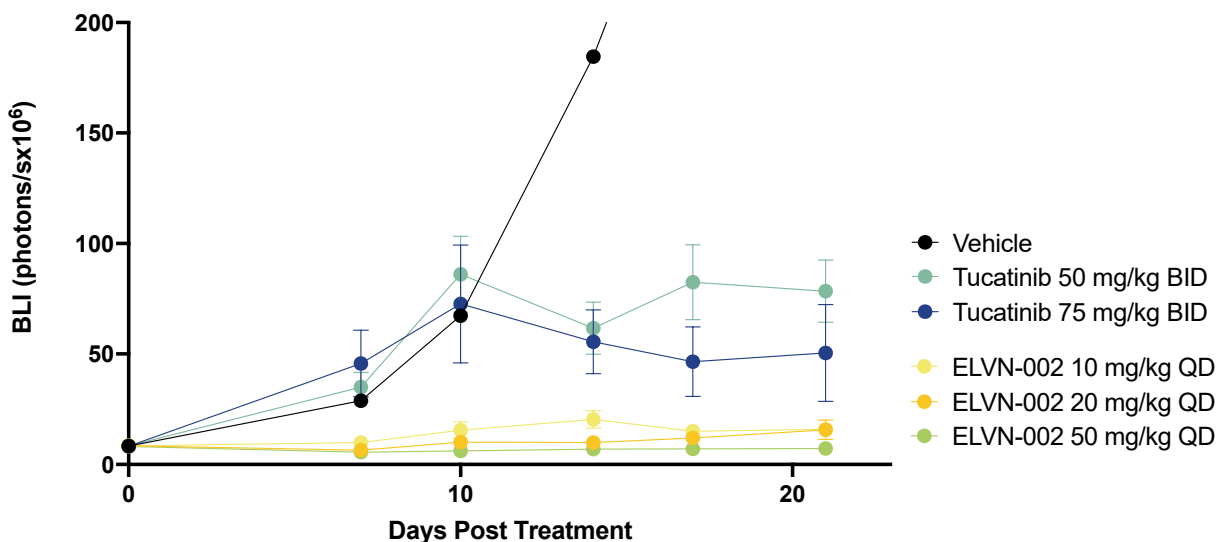
Tucatinib vs. ELVN-002 Brain Exposure

- **ELVN-002 yielded sustained tumor regressions** in the NCI-N87 intracranial model, and all doses were well-tolerated

- **Tucatinib's exposure in patients at its approved dose is ~4.5x and ~12x lower than** in mice treated with 50 mg/kg and 75 mg/kg BID, respectively

- ELVN-002 exhibited **superior CNS anti-tumor activity at up to ~100x lower exposures** compared to tucatinib in this model

- **ELVN-002 achieved significant free-drug exposure** in mouse brain across a plasma concentration range that we estimate will be clinically relevant

BID = Twice a day. BLI = bioluminescent imaging. QD = Once a day. CNS = Central nervous system. WT = wild type

Mouse brain exposures: Steady state Kp,uu for ELVN-002 and tucatinib in non–tumor-bearing BALB/c nude mice (n=3). Measurements were taken after 5 days of dosing at timepoints corresponding to estimated clinically relevant plasma concentrations. Tucatinib was dosed BID and measurements were made at 12h and 16h; however, Kp,uu levels were even lower than at 4h and 8h, respectively. Kp,uu = Free brain concentration (total brain concentration adjusted for brain tissue binding)/Free plasma concentration (total plasma concentration adjusted for protein binding).

ELVN-002 Achieved a Wide Safety Margin in Preclinical Species

ELVN-002 28-day GLP Tox NHP TK

Concentration (ng/mL) vs hours

- pEGFR IC_{50} (A431, 50% human serum)
- HER2 YVMA GI_{90} (Ba/F3, protien adj.)
- pHER2 YVMA IC_{50} (Beas2B, 100% human serum)

Legend:
- 15 mg/kg
- 10 mg/kg
- 5 mg/kg
- 5 mg/kg NOD-SCID mouse (highly efficacious dose)
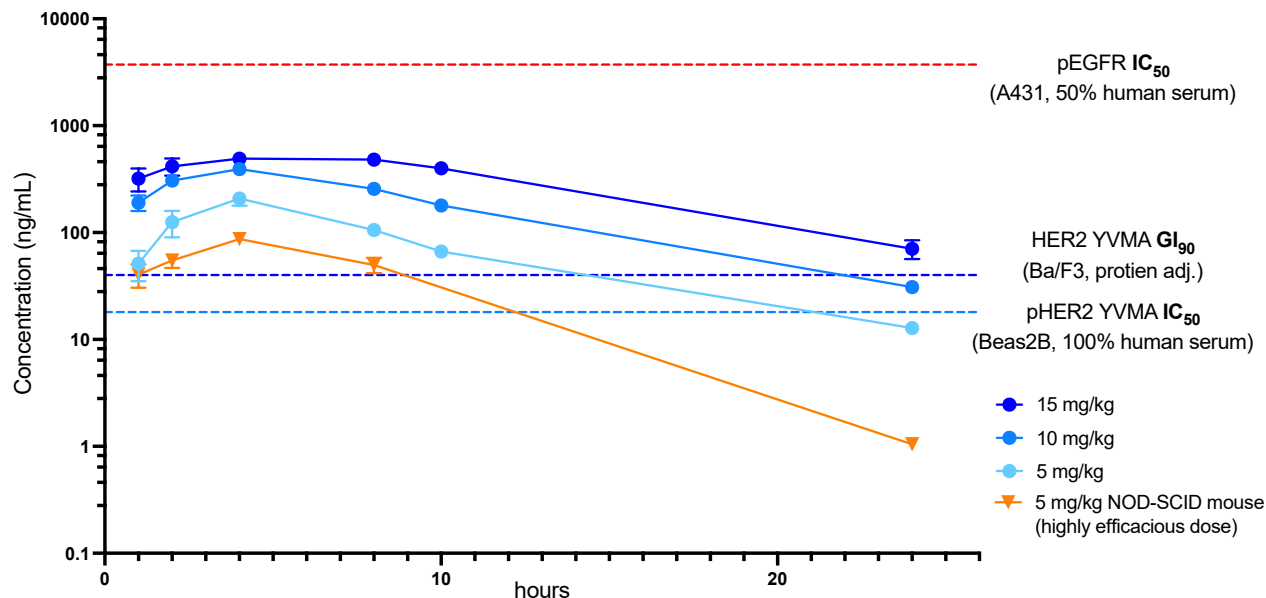
ELVN-002 Safety Margin at NHP NOAEL

Dose (mg/kg)	Fold vs. Highly Efficacious Exposure	Fold vs. Tucatinib TGI-matched exposure
5	2	5
10	5	12
15	**8**	**22**

NHP NOAEL

Based on preclinical exposures (AUC), ELVN-002 had a >10x larger safety margin compared to tucatinib in NHPs (HER2 amp setting)

- At its 28-day NOAEL, **ELVN-002 had a wide safety margin** in non-human primates (NHPs) and even wider safety margin in rats

- At its approved dose, **tucatinib only achieves IC_{90} all day (over 24 hours) in ~40% of patients**

- Due to its larger safety margin, irreversible inhibition and improved PK profile, we believe **ELVN-002 has the potential to achieve better target inhibition and improved efficacy compared to tucatinib**

Amp = amplification. AUC = area under the curve. GLP = Good lab practices. HER2 = human epidermal growth factor receptor 2. IC90 = 90% inhibitory concentration. NHP = Non-human primate. NOAEL = No observed adverse event level. TGI = Tumor growth inhibition. TK = toxicokinetics or PK from tox study. PK = Pharmacokinetics.
Highly Efficacious Exposure equals the total AUC of ELVN-002 at 5 mg/kg in NOD-SCID mouse, which yielded robust tumor regression in a HER YVMA xenograft
To determine Fold vs. Tucatinib TGI-matched exposure, we use the AUC of ELVN-002 at 2.5 mg/kg in Nude mouse, a dose that roughly matches the TGI of Tucatinib at 20 mg/kg BID measured in an NCI-N87 xenograft model. Protein adj. = GI90 value divided by the fraction unbound in serum.
ELVN-002 NHP data shown are measured averages from Day 1 TK male animals in a 28-day GLP tox study
References: Tucatinib NDA; Moulder SL et al. Data from a Completed Phase 1 Study to Assess the Safety, Tolerability and PK of ARRY-380 - an Oral Inhibitor of HER2. SABCS, December 8-12, 2010, San Antonio, TX.

ELVN-002 Clinical Development Strategy

Phase 1a

- HER2 mutant (e.g., Exon 20 IM)
- HER2 amplified or overexpressed

GOALS

- Demonstrate potential for efficacy at well-tolerated dose(s)
- Identify dose(s) for Phase 1b and beyond

Phase 1b / 2

- Late line HER2 mutant NSCLC
- Explore combinations (e.g., ADCs, chemotherapy, trastuzumab) in HER2+ CRC and MBC

GOALS

- Establish PoC for HER2-mutant NSCLC and evaluate intracranial activity
- Explore potential beyond NSCLC in other HER2-altered solid tumors (e.g., MBC, CRC, etc.)
- Demonstrate the potential for best-in-class efficacy and tolerability for combination therapies

Registrational / Phase 3

- Initial registrational studies as mono or combination therapy in NSCLC, CRC and MBC

GOALS

- Consider registrational options for HER2 mutant NSCLC
- Initiate registrational studies in combination therapies in HER2+ MBC and CRC

ADC = Antibody drug conjugate. CRC = Colorectal cancer. HER2 = human epidermal growth factor receptor 2. IM = Insertion mutation. MBC = Metastatic breast cancer. NSCLC = Non-small cell lung cancer. PoC = Proof of concept.

ELVN-002 || Current Status

Monotherapy Dose Escalation

- Investigator reported responses (including unconfirmed) in patients with both HER2+ and HER2 mutant tumors, including in patients who progressed on Enhertu and in patients with brain metastases, at doses that were well-tolerated
- At the clinically predicted optimal monotherapy dose (n=30), based on current Phase 1a data:
  - The most common reported (>10%) treatment-related AEs, were headache (37%), nausea (33%), vomiting (27%) and diarrhea (27%)
    - No ≥ Grade 4; Grade 3: headache (10%), nausea (7%), vomiting (3%), diarrhea (0%)
    - Of note, only Grade 1/2: AST/ALT (3%/0%), rash (3%)
  - Compared to tucatinib, ELVN-002 had >10x better target coverage based on pharmacokinetics in cancer patients and preclinical HER2+ efficacy of ELVN-002

Combination in HER2+ MBC and CRC

Rationale

- Preclinical and clinical data suggest that dual HER2 targeting results in clinically meaningful improvements in patients with HER2+ MBC and CRC
- Tucatinib + trastuzumab + capecitabine demonstrated a survival advantage in HER2+ MBC
- Tucatinib + trastuzumab produced durable responses in HER2+ CRC (DOR ~12.4 months)

Status

- Initiated Phase 1a/b trial of ELVN-002 in combination with trastuzumab +/- chemotherapy in patients with HER2+ cancer
- Initiated Phase 1a cohort evaluating ELVN-002 in combination with ado-trastuzumab emtansine (Kadcyla®) in MBC
- Both studies designed to evaluate safety, tolerability, PK, and preliminary efficacy in patients with advanced stage HER2+ tumors

Phase 1 monotherapy data and initial proof of concept combination data in HER2+ cancers expected in 2025

Target coverage is defined by the mean total drug exposure (area under the curve, AUC) achieved in cancer patients at the indicated dose divided by the mean AUC at the dose in head-to-head preclinical efficacy models that elicits ~100% tumor growth inhibition. Drug exposure of tucatinib in cancer patients was obtained from its NDA and was not obtained from head-to-head clinical trials in cancer patients.
AE = Adverse event. ALT = Alanine transaminase. AST = Aspartate aminotransferase. CRC = colorectal cancer. DOR = duration of response. FPI = First patient in. HER2 = human epidermal growth factor receptor 2. MBC = metastatic breast cancer. NDA = New drug application. PK = Pharmacokinetic.
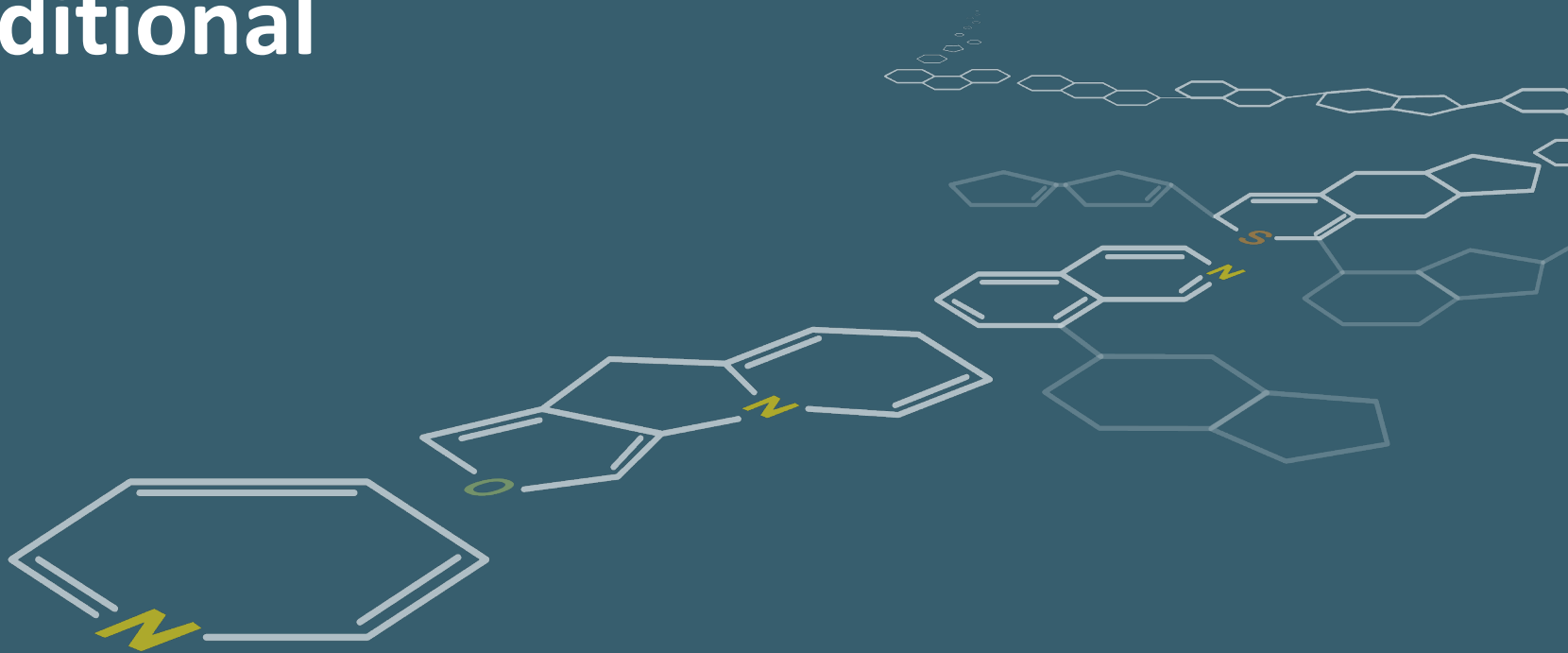
References: 1. Oh, DY et al., Nat Rev Clin Oncol 2020. 2. Cocco E. et al. Pharmacol Ther. 2019; 2. SEER 2022; 4. Dai WF et al., JAMA New Open 2022; 5. Murthy RK et al., NEJM 2020; 6. Tukysa® (tucatinib) USPI.

Appendix
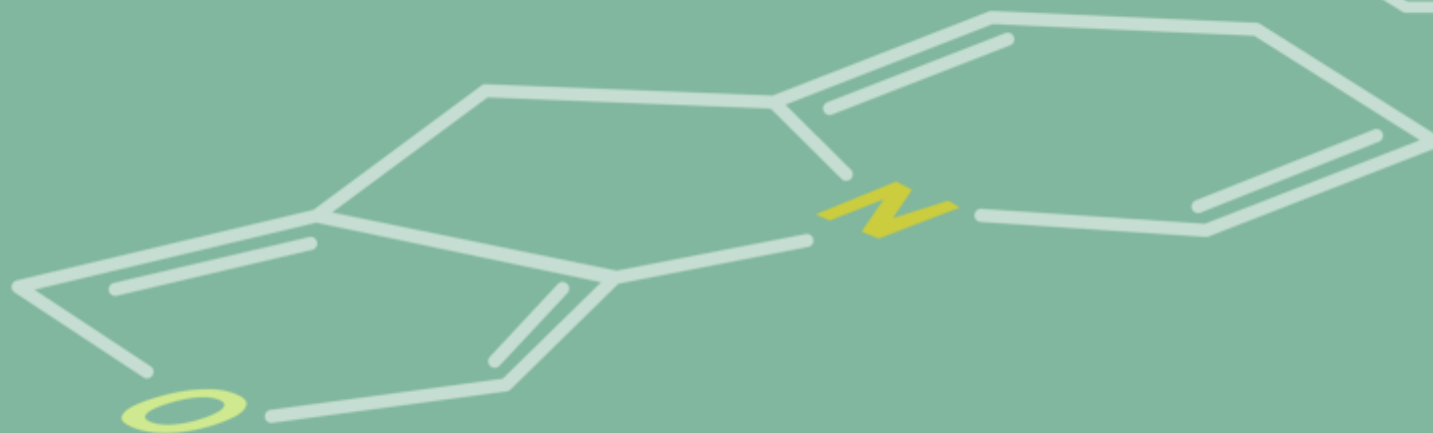
ELVN-001 Additional Information

Patient Disposition

	ELVN-001 Dose Group					Total[a] (N = 39)
	10 mg QD (n = 3)	20 mg QD (n = 7)	40 mg QD (n = 11)	80 mg QD (n = 11)	120 mg QD (n = 7)	
Median Duration of Exposure, weeks (range)	10 (4–80)	53 (0.1–64)	31 (0.3–45)	20 (0.3–32)	8 (0.3–20)	20 (0.1–80)
Ongoing, n (%)	1 (33.3%)[a]	5 (71.4%)	10 (90.9%)[a]	11 (100%)	5 (71.4%)	32 (82.1%)
Discontinued, n (%)	2 (66.7%)	2 (28.6%)	1 (9.1%)		2 (28.6%)	7 (17.9%)[b]
Due to AE	1 (33.3%)	1 (14.3%)				2 (5.1%)
Due to lack of efficacy	1 (33.3%)[c]		1 (9.1%)[c]		2 (28.6%)[d]	4 (10.3%)
Due to protocol violation		1 (14.3%)				1 (2.6%)

[a] Includes 2 re-enrolled patients (number of individuals enrolled was 37); [b] Includes 2 re-enrolled patients who discontinued at initial enrolled dose level. [c] Both patients who discontinued due to lack of efficacy at 10 mg and 40 mg were re-enrolled at higher dose levels (40 mg and 120 mg, respectively). [d] The 2 patients who discontinued at 120mg QD both discontinued prior asciminib and ponatinib for lack of efficacy; one had CML with T315I mutation and was the same patient who discontinued 40 mg, the other had CML with E255V mutation.

Data cutoff: 25 June 2024.
AE = adverse event. QD = once daily.
NOTE: Patients who had gone through intra-patient dose escalation as per protocol were counted under their initial treatment group only. 2 patients who were re-enrolled were counted under their initial treatment group and their re-enrolled treatment group.

46

Low Incidence of Non-Hematologic Adverse Events Consistent with Selective Kinase Profile

Non-Hematologic TEAEs in ≥ 10% of Patients

Preferred term n (%)	ELVN-001 Dose Group											Total (N = 37)	
	10 mg QD (n = 3)		20 mg QD (n = 7)		40 mg QD (n = 11)		80 mg QD (n = 11)		120 mg QD (n = 7)					
	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4	Any Gr	Gr 3/4
Headache	2 (66.7%)	0	2 (28.6%)	0	0	0	1 (9.1%)	0	0	0	5 (13.5%)	0
Lipase increased	1 (33.3%)	0	1 (14.3%)	0	1 (9.1%)	0	2 (18.2%)	0	0	0	5 (13.5%)	0
Arthralgia	0	0	1 (14.3%)	0	0	0	1 (9.1%)	0	2 (28.6%)	0	4 (10.8%)	0
Diarrhea	1 (33.3%)	0	1 (14.3%)	0	0	0	2 (18.2%)	0	0	0	4 (10.8%)	0
Nausea	0	0	1 (14.3%)	0	0	0	2 (18.2%)	0	1 (14.3%)	0	4 (10.8%)	0

- Almost all non-hematologic TEAEs were low grade; two patients had Gr 3 TEAEs* (one with Gr 3 hypertriglyceridemia; one with Gr 3 proctitis and Gr 3 appendicitis)

- No dose reductions due to non-hematologic TEAEs

- One patient discontinued ELVN-001 due to SAE of Gr 2 pancreatitis (at 10 mg QD); no additional TEAEs of pancreatitis reported

- No exposure-toxicity relationship identified to date

Data cutoff date: 25 June 2024.
G = Grade. QD = once daily. SAE = serious adverse event. TEAE = treatment-emergent adverse event; *assessed as not related by investigator
NOTE: Severity grades were defined by CTCAE (Common Terminology Criteria for Adverse Events) Version 5.0. Patients who had gone through intra-patient dose escalation as per protocol were counted under their initial treatment group only. 2 patients who were re-enrolled were counted under their initial treatment group and their re-enrolled treatment group but counted as one patient in the total column.

5 Patients that Maintained MMR by 24 Weeks

ELVN-001 Dose	# Prior TKIs	Reason for Discontinuation			Resistant to other prior TKIs	Baseline MR Status	By 24 Weeks
		Ponatinib	Asciminib	Last Prior TKI			
20mg	6	Intolerant	LOE	Intolerant (P)	I, D, B	MR4	MR5
40mg	2	LOE	LOE	LOE (P)		MR3	MR5
40mg	2			Intolerant (I)	D	MR3	MR3
80mg	3		LOE (A+D)	LOE (A+D)	N, D	MR3	MR3
80mg	3		LOE	LOE (A)	N, D	MR3	MR3

2/5 patients improved MR category by 24 weeks

- 4/5 patients were resistant to ponatinib and/or asciminib
- 3/5 patients were resistant to last prior TKI

A = Asciminib, B = bosutinib, D = dasatinib, I = imatinib, N = Nilotinib, P = ponatinib. A+D = asciminib + dasatinib combination. LOE = Lack or loss of efficacy. MR = Molecular response. MMR = Major molecular response = MR3, MR4, MR5. MR1 ≤ 10%. MR2 ≤ 1%. MR3 ≤ 0.1%. MR4 ≤ 0.01%. MR5 ≤ 0.001%.

ELVN-001's PK Profile Supports Once Daily Dosing with Flexible Administration Requirements

- Linear PK observed in healthy volunteers (HV) and patients
  - No time-dependent PK observed in either HVs or cancer patients
  - Both C_{max} and AUC increased dose-proportionally
  - High concordance between HV and patient PK based on current data

- Fast and complete absorption with no significant food effect

- Mean terminal $t_{1/2}$ is ~12 hours in healthy volunteers
  - Similar effective $t_{1/2}$ observed in patients (10-20 hours)
  - Suitable for QD regimen

- Minimal risk of drug-drug interactions (DDIs)
  - Not an inhibitor (competitive or time-dependent) or inducer of major CYP enzymes, or of UGT1A1
  - Not a substrate for major CYP enzymes
  - Not a substrate of BCRP or P-gp

- No correlation between AEs and PK parameters in patients

120 mg ELVN-001 (single dose)
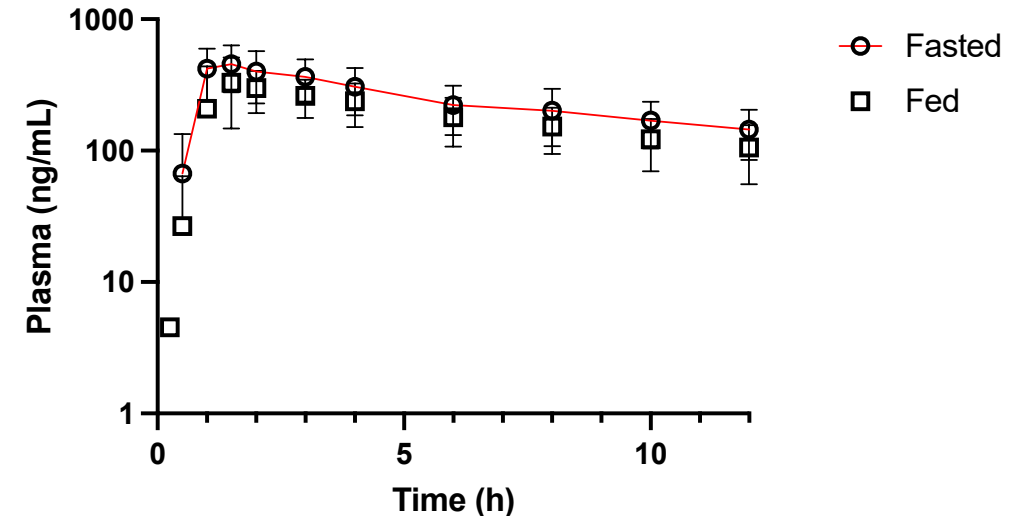
- Food effect study at 120mg single dose in HVs showed that:
  - AUC_{inf} under fasting conditions were similar to that under fed conditions, with a fed/fasted AUC ratio of 1.2.
  - C_{max} under fasting conditions were similar to that under fed conditions, with a fed/fasted C_{max} ratio of 0.8.

AEs = Adverse events. AUC = Area under the curve. AUC_{inf} = AUC extrapolated to infinity. BCRP = Breast cancer resistance protein. C_{max} = Maximum serum concentration. CYP = Cytochromes P450. DDI = drug-drug interactions. HV = Healthy volunteers. P-gp = P-glycoprotein. PK = Pharmacokinetics. QD = Once daily. UGT1A1 = UDP Glucuronosyltransferase Family 1 Member A1.

ELVN-001 Achieved Superior Target Coverage Compared to 2nd Gen TKIs

C_{ave} Target Coverage vs. 1L MMR at 12 mo.
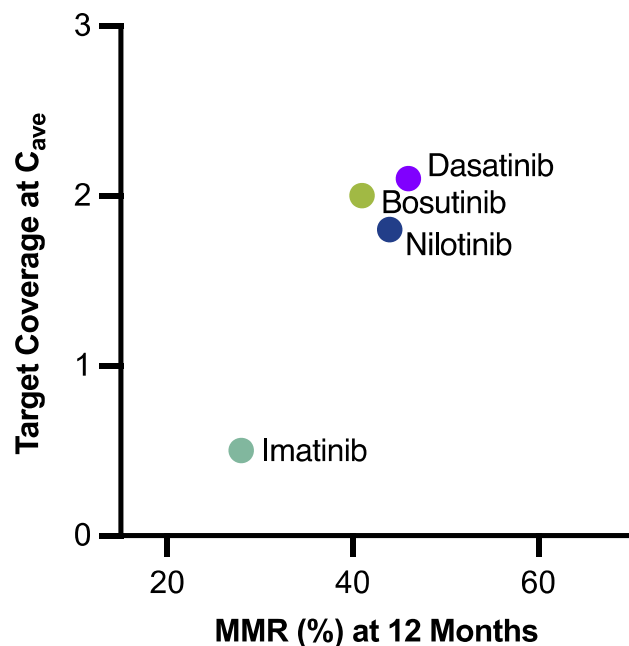
C_{ave} Target Coverage vs. Active Site TKIs (1L)
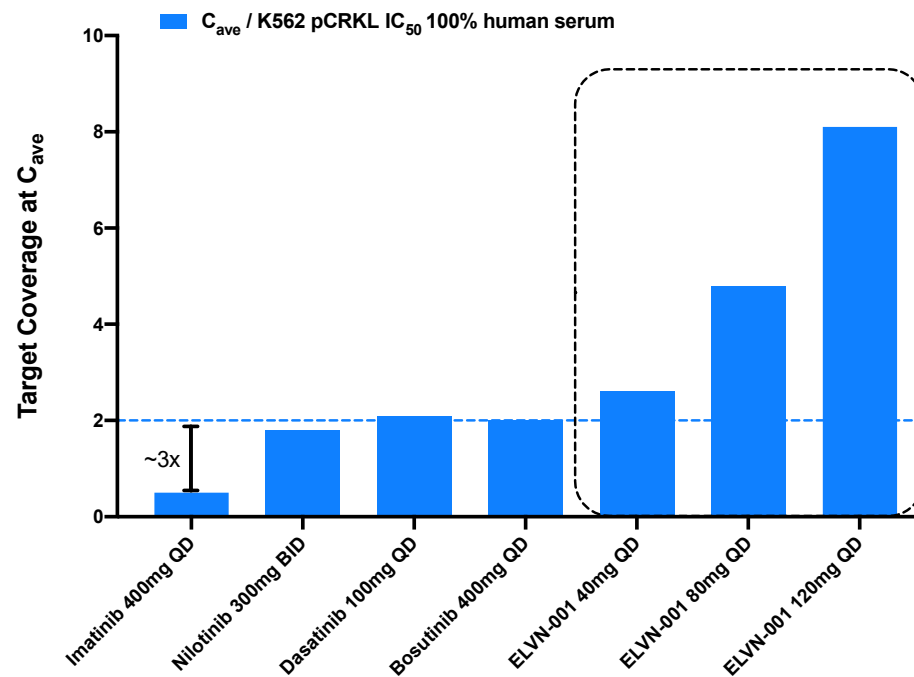
At doses ≥ 40mg QD, **ELVN-001 achieved better target coverage** compared to 2nd Generation TKIs

ELVN-001 is Highly Selective for ABL1

- ELVN-001 has a **very selective kinase profile**
  - Clean against key off-target kinases in cells compared to 2nd and 3rd Gen TKIs
  - 372 kinases screened at 1 μM compound (100 μM ATP)
  - Kinases with >50% inhibition selected for IC$_{50}$ determination
  - >100x window vs. all but 2 kinases profiled
- ELVN-001 is also very clean (>10 μM) in an *in vitro* safety panel of >130 receptors

ELVN-001 (100 μM ATP)

Kinase	IC$_{50}$ (nM)
ABL1	1
ABL2/ARG	31
TRKC	41
TNIK	110
LOK/STK10	183
LRRK2	486
FGR	550
ACK1	698
FYN	725
HGK/MAP4K4	973
LCK	>1,000

Large window for ABL2/ARG may result in a favorable safety profile

Cellular Phosphorylation IC$_{50}$ (nM)

	cKIT	FLT3wt	PDGFRb	VEGFR2	cSRC
ELVN-001	>10,000	>10,000	>10,000	>10,000	>10,000
Ponatinib	30	3.8	89	4.8	630
Nilotinib	200	>10,000	720	2,900	>10,000
Dasatinib	0.6	>1,000	7.1	>1,000	10
Bosutinib	1,000	4,700	7,900	>10,000	16

2nd Gen = Nilotinib, Dasatinib, Bosutinib. 3rd Gen = Ponatinib. ATP = Adenosine triphosphate. IC$_{50}$ = half-maximal inhibitory concentration. TKI = Tyrosine kinase inhibitors. WT = Wild type.
Note: IC values used to calculate fold shift represent an average derived from multiple runs internally with a minimum of two independent experiments.
Reference: Abl kinases are required for vascular function, Tie2, and angiopoietin-1-mediated survival. Pendergast et al. *PNAS*. 2013;110(30):12432-7.

In contrast to Ponatinib, ELVN-001 Does Not Affect Platelet Activation or Function

- Ponatinib, which has multiple black box warnings for cardiovascular toxicity, inhibits multiple platelet functions, including platelet activation, consistent with VEGFR inhibition
- ELVN-001 and asciminib have no effect on platelet function *in vitro*

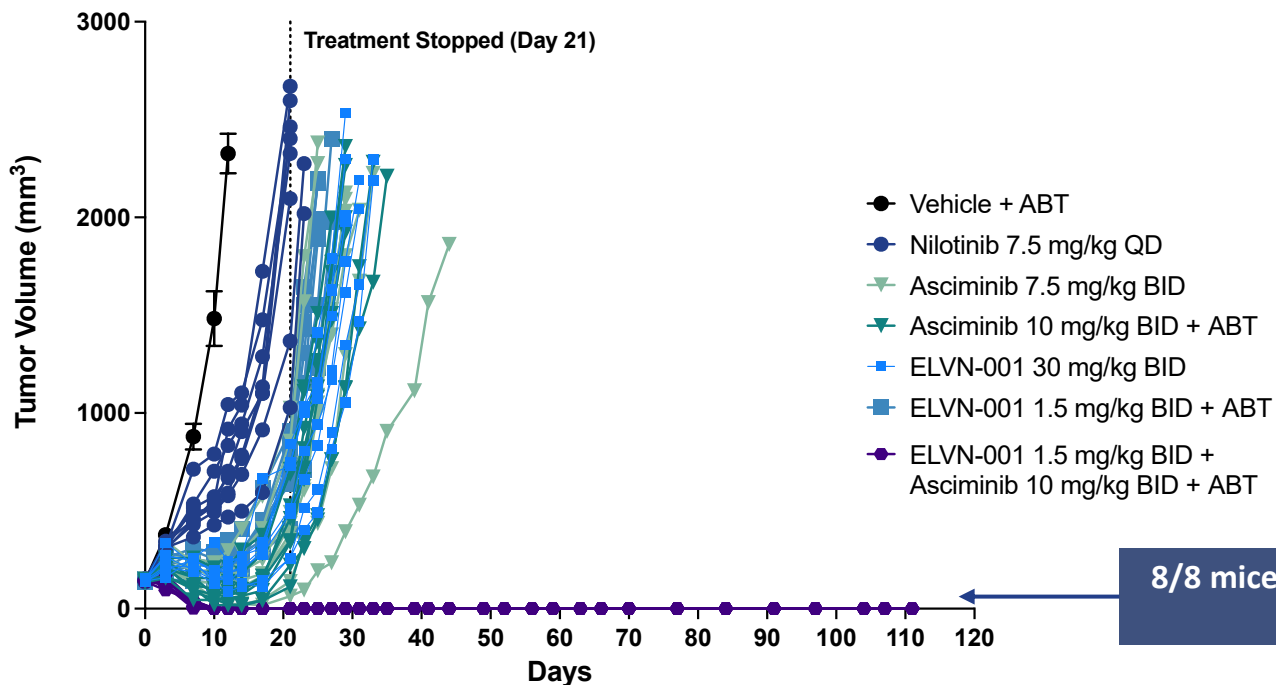| Inhibitor [1 μM]	Platelet Spreading	Platelet Aggregation	GPIIbIIIa Activation	α-granule secretion	PS Exposure	Fibrin Formation	Platelet Signaling
ELVN-001	No effect	No effect	No effect	No effect	No effect	No effect	No effect
Ponatinib	Inhibition	Inhibition	Inhibition	Inhibition	Inhibition	Inhibition	Inhibition
Asciminib	No effect	No effect	No effect	No effect	No effect	No effect	No effect

Platelet Aggregation
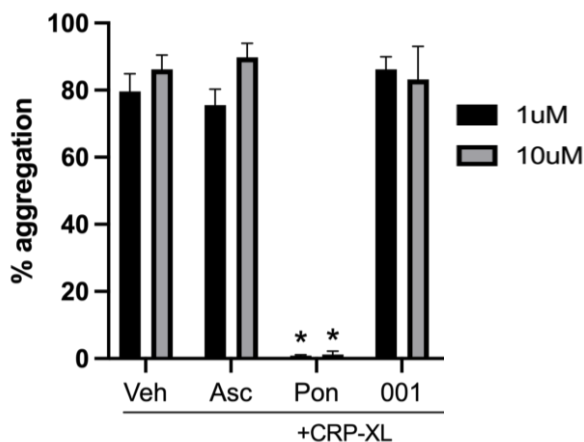
Platelet Spreading
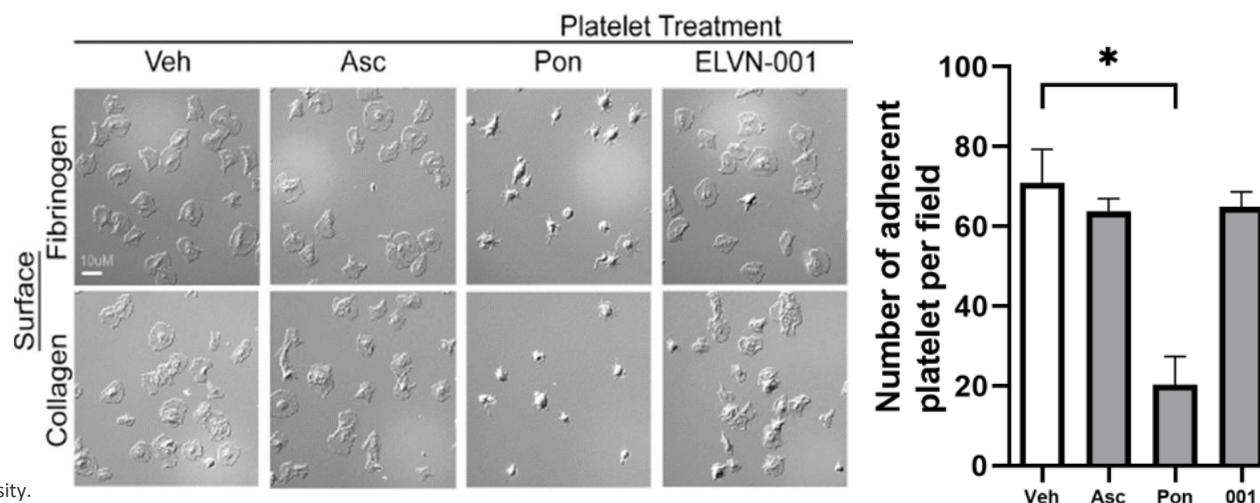
Data courtesy of Owen McCarty, Yiheng Zhang, and Joseph Aslan at Oregon Health & Science University.
PS = Phosphatidyl Serine. VEGFR = Vascular endothelial growth factor receptor.
*Indicates statistical significance.

ELVN-001 + Asciminib Combination Elicits Cures at Physiologically Relevant (Human-Matched) Drug Exposures in Mice

K562 Xenograft

Treatment Stopped (Day 21)

Legend:
- Vehicle + ABT
- Nilotinib 7.5 mg/kg QD
- Asciminib 7.5 mg/kg BID
- Asciminib 10 mg/kg BID + ABT
- ELVN-001 30 mg/kg BID
- ELVN-001 1.5 mg/kg BID + ABT
- ELVN-001 1.5 mg/kg BID + Asciminib 10 mg/kg BID + ABT

8/8 mice cured in combination arm @ Day 111 (90 days after last dose)

Drug Exposure: Mouse vs. Human

	Mouse Dose (mg/kg)	Human Dose (mg)	Ratio of mouse to human exposure
Nilotinib	7.5 QD	400 BID	1.9
Asciminib	7.5 BID	40 BID	1.2
Asciminib	10 BID*	40 BID	1.7
ELVN-001	30 BID	80 QD	1.1
ELVN-001	1.5 BID*	80 QD	1.0

- ELVN-001 elicits anti-tumor activity in this model comparable to asciminib and superior to nilotinib at their respective human-matched drug exposures

- **Combination treatment with ELVN-001 + asciminib** for 21 days at their respective human-matched drug exposures **resulted in 8/8 cures** in this model as of Day 111 (90 days after treatment discontinuation); no cures observed in the monotherapy arms

Phase 1 Data Predicted Pivotal Trial Data
Asciminib vs. Bosutinib in Late-Line CML (ASCEMBL)

Percent MMR at 24 Weeks

Third Line
- Bosutinib: 20% — 6/30
- Asciminib: 29.3% — 24/82

Fourth Line
- Bosutinib: 13.8% — 4/29
- Asciminib: 25% — 11/44

Fifth Line or Later
- Bosutinib: 0% — 0/17
- Asciminib: 16.1% — 5/31

Legend:
- ■ Bosutinib
- ■ Asciminib

Represents most of the patients enrolled in the ELVN-001 Phase 1a Trial

Percent of Major Molecular Response (MMR) at 24 Weeks (x-axis: 0% to 100%)

Probability of MMR Over Time

▲ Censored* ○ Competing Event†

Legend:
- Asciminib (orange)
- Bosutinib (blue)

Y-axis: Probability of MMR (%) (0 to 100)
X-axis: Weeks (0 to 104)

Accelerated Approval 24 weeks

Full Approval 96 weeks
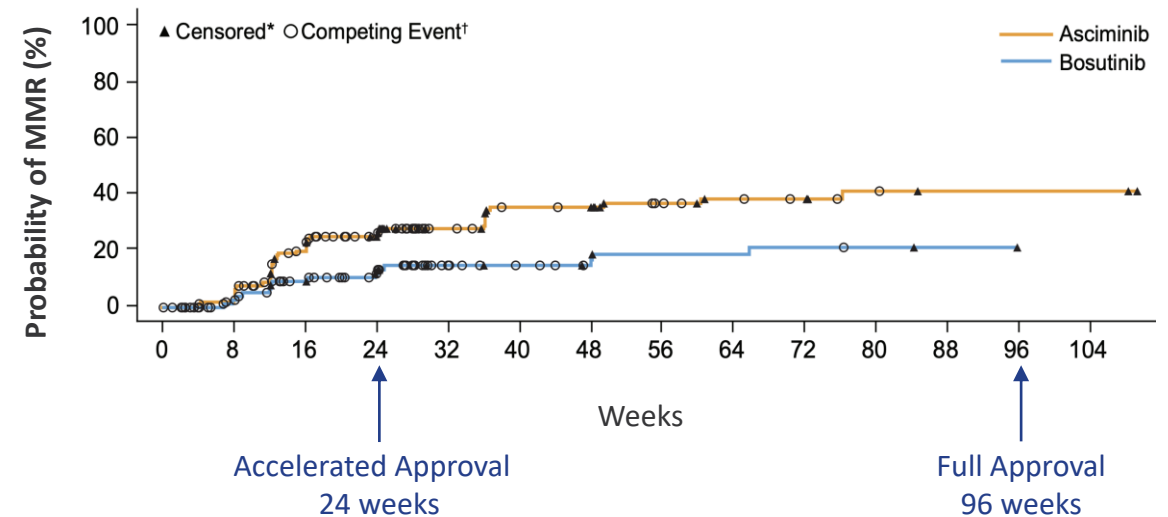
MMR rate decreased with increasing number of prior TKIs	MMR rate increased over time for both drugs

- Cumulative MMR at 24 weeks for asciminib vs. bosutinib was 25% vs. 12%
- Dose reductions due to adverse events: 21% asciminib vs. 42% bosutinib*

CML = Chronic myeloid leukemia. MMR = Major molecular response. TKI = Tyrosine kinase inhibitor.
*Median duration of exposure of 23.7 months for asciminib and 7 months for bosutinib. Note: overall MMR by 24 weeks was 25.5% for asciminib and 13.2% for bosutinib.
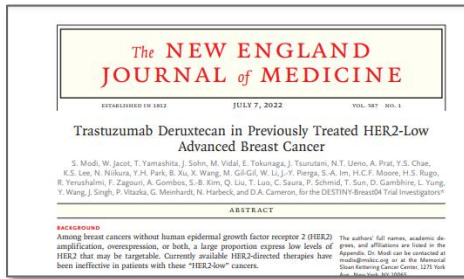**References:** Rea D et al., Blood. 2021.

ELVN-002 Additional Information
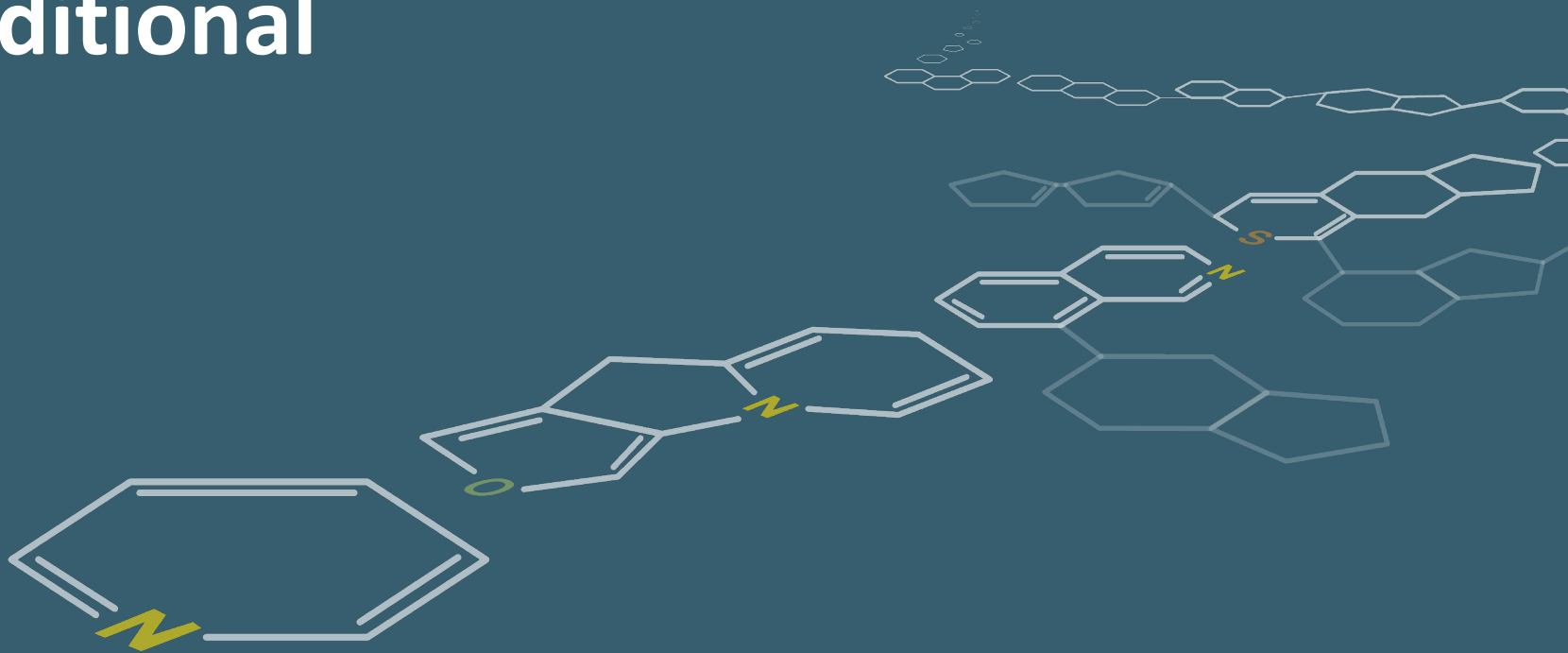
The HER2+ Post-Enhertu® Market is Growing Appreciably

Trastuzumab Deruxtecan (Enhertu®) Is Augmenting the Canonical HER2+ Population

DESTINY-Breast04 trial established Enhertu® as the new SOC post 1L chemo in HER2-low MBC

DAISY trial demonstrated encouraging activity in HER2-low & HER2-non-detected MBC
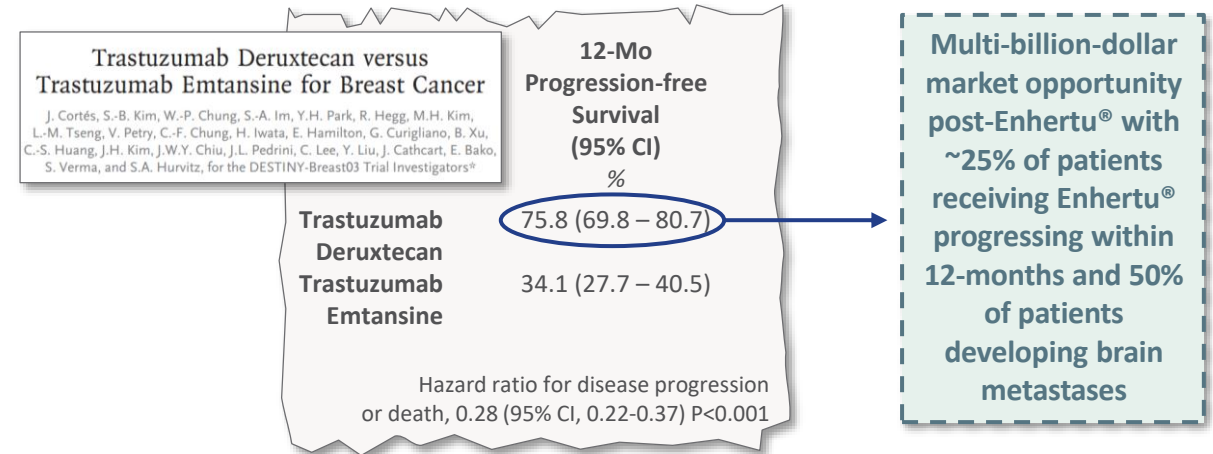
The Advent of HER2-Low Identification Efforts Further Broadens HER2+ Patient Population

1) Deep learning-based image analysis to produce a HER2 Quantitative Continuous Score (QCS), a novel approach to better identify patients with low-level expression who may benefit from a HER2-directed therapy

2) Other AI-mediated approaches designed to detect 'true' HER2 expression in spite of IHC classification through the use of H&E-stained tissue samples

3) Supplementing mass spec-standardized HER2 array with quantitative immunofluorescence to increase sensitivity of genetic amplification beyond conventional assays

Post-Enhertu® Market Is Substantial and Represents a Land Grab Opportunity

	12-Mo Progression-free Survival (95% CI) %
Trastuzumab Deruxtecan	75.8 (69.8 – 80.7)
Trastuzumab Emtansine	34.1 (27.7 – 40.5)

Hazard ratio for disease progression or death, 0.28 (95% CI, 0.22-0.37) P<0.001

Multi-billion-dollar market opportunity post-Enhertu® with ~25% of patients receiving Enhertu® progressing within 12-months and 50% of patients developing brain metastases

Systemic Therapy for Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer: ASCO Guideline Update

"Trastuzumab, pertuzumab, and taxane for first-line treatment and trastuzumab deruxtecan for second-line treatment are recommended. **In the third-line setting, clinicians should offer other HER2-targeted therapy combinations. There is a lack of head-to-head trials; therefore, there is insufficient evidence to recommend one regimen over another.**"

1L = First line. ASCO = American society of clinical oncology. HER2 = human epidermal growth factor receptor 2. H&E = Hematoxylin and eosin. IHC = Immunohistochemistry. MBC = Metastatic breast cancer. SOC = Standard of care.
References: Zhang H, et al. Cancers (Basel). 2022 Dec 25; Cortés J, et al. N Engl J Med. 2022; Journal of Clinical Oncology 40, no. 23 (August 10, 2022) 2612-2635.

56

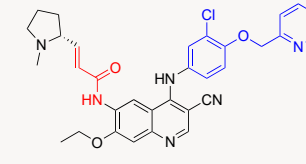# ELVN-002 was >100x More Selective for HER2 YVMA Over EGFR Compared to Dual EGFR/HER2 TKI Competitors
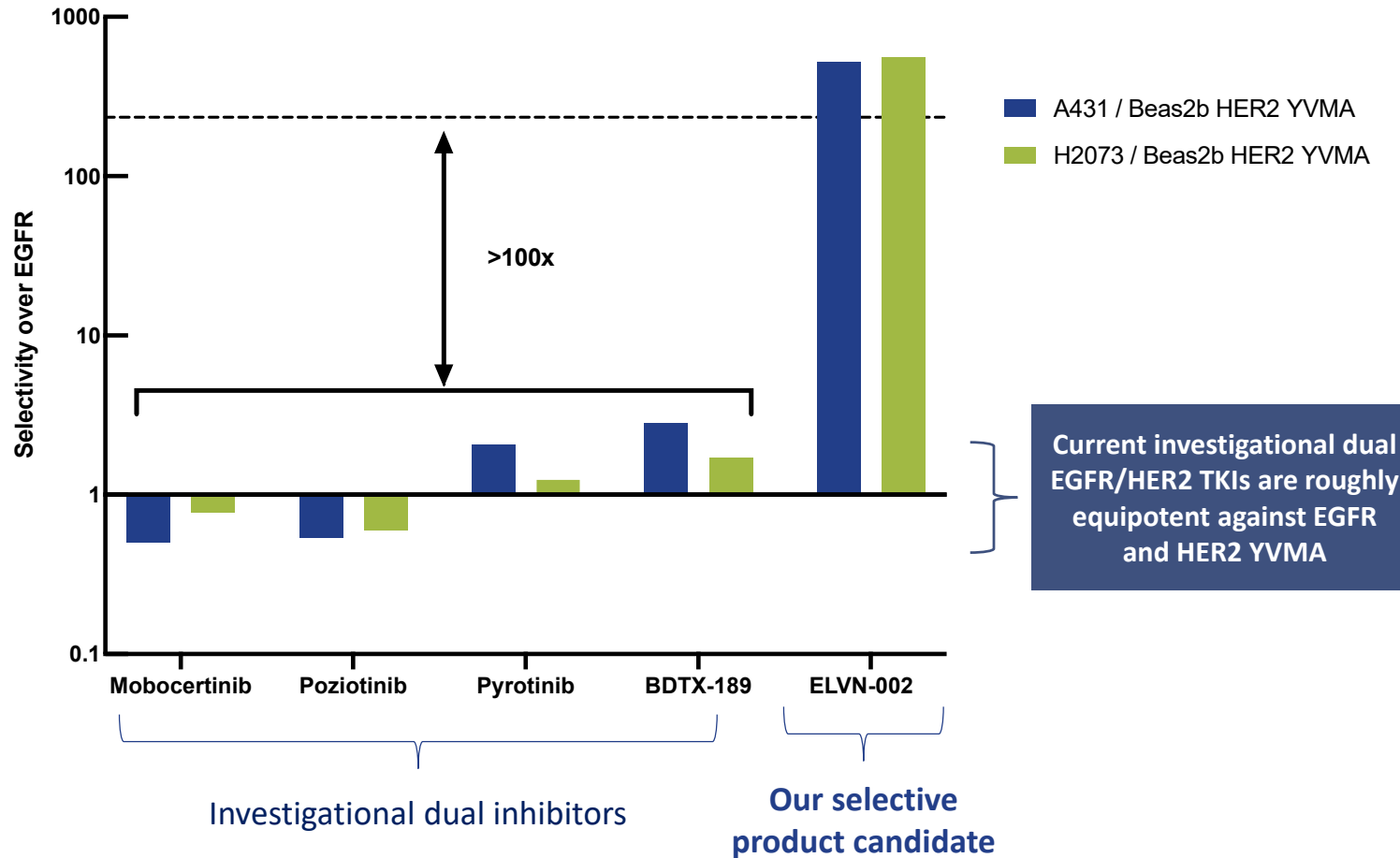
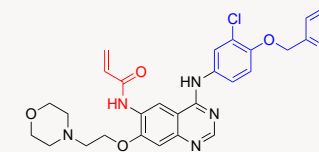## Lack of Differentiation Across Next Generation TKIs
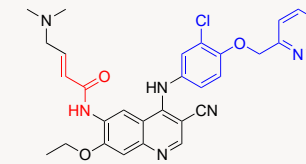
- **Neratinib** — Poor efficacy & tolerability in HER2 mutant setting
- **Pyrotinib** — Phase 1b/2 19% ORR in HER2 mutant NSCLC, poor tolerability
- **BDTX-189** — Poor efficacy & tolerability in HER2 mutant setting

Chart legend:
- A431 / Beas2b HER2 YVMA
- H2073 / Beas2b HER2 YVMA

X-axis categories: Mobocertinib, Poziotinib, Pyrotinib, BDTX-189, ELVN-002

Y-axis: Selectivity over EGFR

>100x

Current investigational dual EGFR/HER2 TKIs are roughly equipotent against EGFR and HER2 YVMA

Investigational dual inhibitors

Our selective product candidate

EGFR = epidermal growth factor receptor. HER2 = human epidermal growth factor receptor 2. NSCLC = Non-small cell lung cancer. ORR = Overall response rate. TKI = Tyrosine kinase inhibitor.
Note: IC values represent an average derived from multiple runs internally with a minimum of two independent experiments.
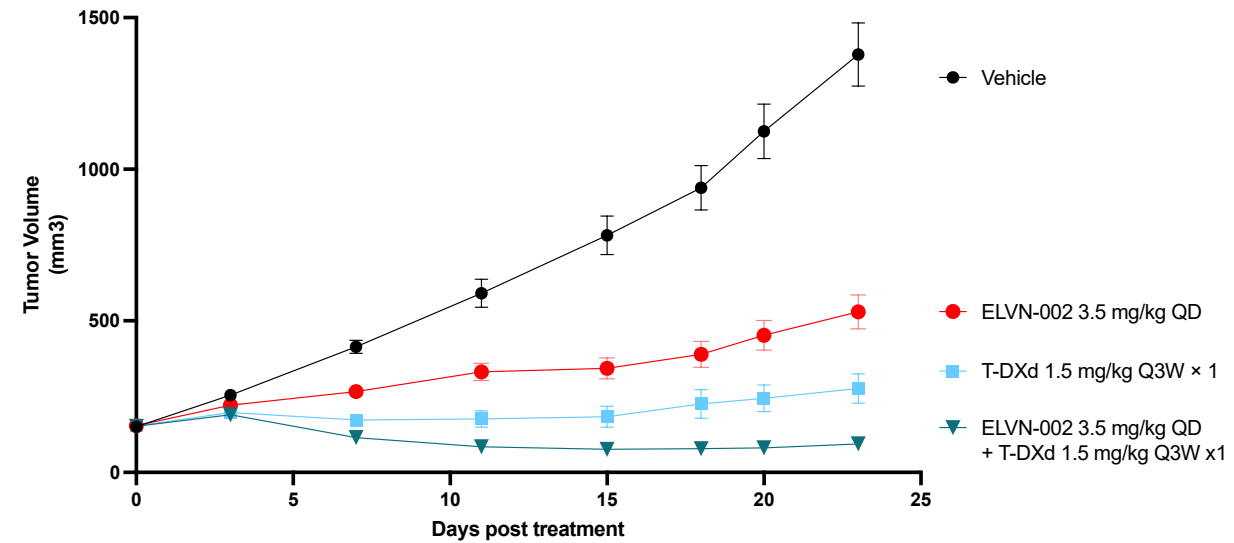
ELVN-002 Demonstrated Robust Anti-Tumor Activity & Additive Activity in Combination with Enhertu® at Well-Tolerated Doses

NCI-N87 HER2^wt Xenograft TGI: ELVN-002 Mono
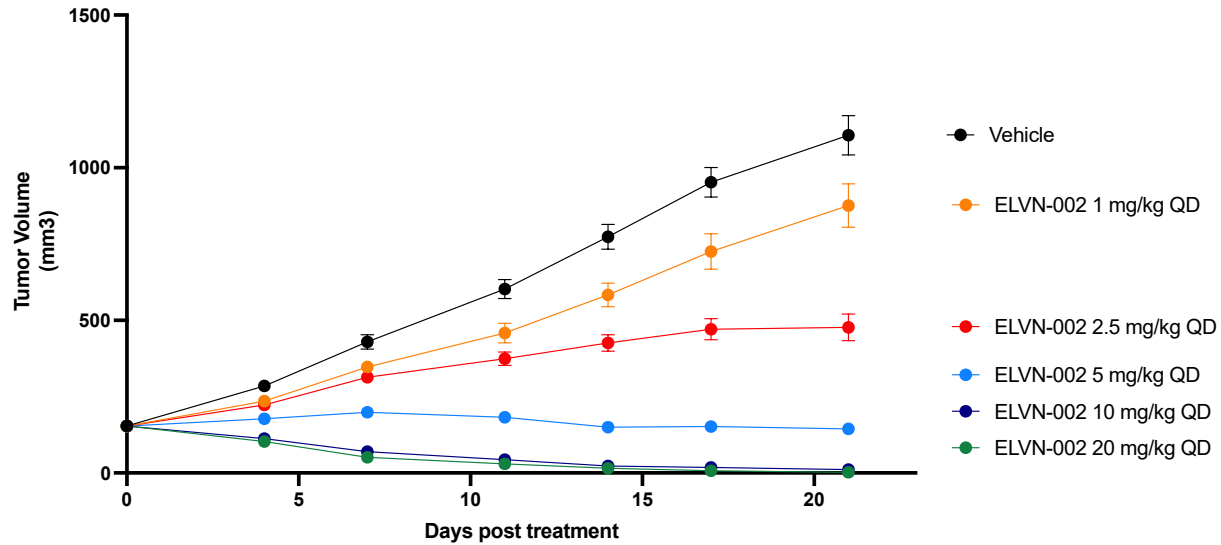
NCI-N87 HER2^wt Xenograft TGI: Enhertu® Combo

- **ELVN-002 yielded deep tumor regressions** in the NCI-N87 xenograft model, and all doses tested were **well-tolerated**

- **Low dose ELVN-002 combined with Enhertu® resulted in additive activity** and deep tumor regressions in the same model

- **In contrast to reversible inhibitors** like tucatinib, irreversible inhibitors have been shown mechanistically to drive increased receptor internalization, and there is both **preclinical and clinical precedent for additive activity upon combining irreversible TKIs with ADCs in HER2-driven settings**