Company Presentation

January 2023

Enliven THERAPEUTICS | imara™

Disclaimer

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This presentation contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (Securities Act)) concerning Enliven, Imara, the proposed transactions and other matters. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Imara and Enliven, as well as assumptions made by, and information currently available to, management of Imara and Enliven. 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The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in Imara's most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the SEC as well as the registration statement on Form S-4 initially filed with the SEC by Imara on November 10, 2022, as amended (the "Form S-4"). Imara and Enliven can give no assurance that the conditions to the proposed transactions will be satisfied. Except as required by applicable law, Imara and Enliven undertake no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

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Important Additional Information Will be Filed with the SEC

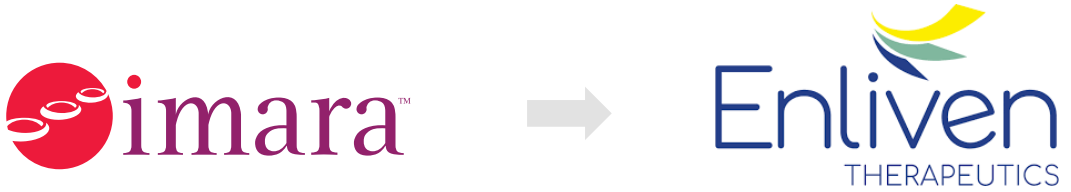
In connection with the proposed transaction between Imara and Enliven, Imara intends to file relevant materials with the SEC, including the Form S-4 that will contain a proxy statement/prospectus of Imara and information statement of Enliven. IMARA AND ENLIVEN URGE INVESTORS AND STOCKHOLDERS TO READ THESE MATERIALS CAREFULLY AND IN THEIR ENTIRETY WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT IMARA, ENLIVEN, THE PROPOSED TRANSACTION AND RELATED MATTERS. Investors and stockholders will be able to obtain free copies of the proxy statement/prospectus/information statement and other documents filed by Imara with the SEC (when they become available) through the website maintained by the SEC at www.sec.gov. In addition, investors and stockholders will be able to obtain free copies of the proxy statement/prospectus/information statement and other documents filed by Imara with the SEC by contacting Imara Inc. at 1309 Beacon Street, Suite 300, Office 341 Brookline, MA 02446. Investors and stockholders are urged to read the proxy statement/prospectus/information statement and the other relevant materials when they become available before making any voting or investment decision with respect to the proposed transaction.

Participants in the Solicitation

Imara, Enliven and their respective directors and executive officers may be considered participants in the solicitation of proxies in connection with the proposed transaction. Information about Imara's directors and executive officers is included in the Form S-4, Imara's most recent Annual Report on Form 10-K, including any information incorporated therein by reference, as filed with the SEC, and the proxy statement for Imara's 2022 annual meeting of stockholders, filed with the SEC on April 22, 2022. Additional information regarding the persons who may be deemed participants in the solicitation of proxies will be included in the proxy statement/prospectus/information statement relating to the proposed transaction when it is filed with the SEC. These documents can be obtained free of charge from the sources indicated above.

Merger with Imara Has the Potential to be Transformative for Enliven

Transition into a clinical-stage, precision oncology company with multiple shots on goal



Enliven Therapeutics opportunity
Provides Imara shareholders with opportunity to participate in the Enliven growth story, at a pivotal time for Enliven

Diversified and clinical-stage portfolio
Two parallel lead programs currently in development, ELVN-001, a highly selective BCR-ABL inhibitor for Chronic Myeloid Leukemia, and ELVN-002, a highly selective HER2 and pan-HER2 mutant irreversible inhibitor for HER2-driven cancers, as well as additional programs in the research pipeline

Multiple near-term milestones
Planned steady stream of company milestones, including early Phase 1 data for ELVN-001 expected by the end of 2023

Strong balance sheet supports runway into 2026
Combined company expected to have approximately $300 million in cash and cash equivalents upon closing; resources expected to fund operations into early 2026

Merger of Enliven and Imara

Transaction Summary

- Merger with Enliven, a privately held precision oncology company
- Strong balance sheet of approximately $300 million of cash and cash equivalents expected to provide funding for operations into early 2026
- Upon close, company expected to be renamed “Enliven Therapeutics, Inc.” trading as Nasdaq: ELVN
- Supported by the Board of Directors of both companies and is subject to shareholder approval and other customary closing conditions

Overview

- Expected ownership is approximately 84% Enliven (including those purchasing Enliven shares in the private financing), 16% Imara, subject to adjustment based on Imara’s net cash at closing
- Projected $82.3 million net cash and cash equivalents from Imara and an additional $164.5 million of cash from concurrent financing
- CVR agreement to provide additional consideration to Imara stockholders if milestone payments are received from the previously announced pending sale of tovinontrine (IMR-687) or a potential sale or license involving IMR-261
- Merger and concurrent financing expected to close in 1Q 2023

Management & Programs

- Existing Enliven management to lead the combined company
- New Board of Directors will include 9 members (8 existing Enliven, 1 existing Imara)
- Combined company will focus on advancing the development of Enliven programs

The Enliven Story

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**

Supported by top tier healthcare investors and a strong balance sheet expected to provide cash runway into early 2026

Highly Distinguished & Industry-Leading Team with Top-Tier Advisors and Investors

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
Goldman Sachs

Stefan Gross, PhD
VP, Biology
blueprint MEDICINES
ARRAY BIOPHARMA

Wei Deng, PhD
VP, Biometrics
FivePrime
GILEAD

Andy Ren, PhD
VP, Chemistry
ARRAY BIOPHARMA

Anne Thomas
VP, Clinical Operations
FivePrime
GILEAD

Ian Scott, PhD
VP, CMC
zentalis
ARRAY BIOPHARMA

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

Board of Directors

Sam Kintz, MBA
Enliven Therapeutics

Joe Lyssikatos, PhD
Enliven Therapeutics

Rishi Gupta, JD
OrbiMed

Andy Schwab
5AM Ventures

Andy Phillips, PhD
Cormorant Asset Management

Mika Derynck, MD
Amunix
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Jake Bauer, MBA
Myokardia

Rich A. Heyman, PhD
Aragon Pharmaceuticals,
Seragon Pharmaceuticals

Rahul Ballal, PhD*
Current CEO of Imara

Scientific Advisors

Brian Druker, MD
Oregon Health &
Science University

Rich A. Heyman, PhD
Aragon Pharmaceuticals,
Seragon Pharmaceuticals

Lori Kunkel, MD
Loxo Oncology,
Pharmacyclics

Kevin Koch, PhD
Array Biopharma,
Edgewise Therapeutics

Current Investors

OrbiMed Healthcare Fund Management
5AM VENTURES
SURVEYOR
Cormorant Asset Management
Roche Venture Fund
Connecting Innovation to Value
SHEATREE CAPITAL
BOXER CAPITAL
LOGOS CAPITAL
Janus Henderson INVESTORS

* To be added to the Board of Directors at the close of the proposed transaction

Leadership Team with Broad Range of Experience and Success

World-Renowned Chemists

- Primarily or co-invented 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

Parallel lead product candidates:

Program	Target	Disease	Differentiation	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Next Milestone	Milestone Expected
ELVN-001	BCR-ABL	CML	Highly selective w/T315I activity						Early Phase 1 Data	YE 2023
ELVN-002	HER2 & mutants	NSCLC, other solid tumors	EGFR sparing, pan-mutant						First Patient Dosed	1H 2023

The following table highlights discovery programs that we are prioritizing:

Target	Disease	Differentiation	Target ID / Validation	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Next Milestone
Target 1	Solid tumors	No approved therapies							Expected to make a product candidate nomination for our 3rd program by 1H 2023
Target 2	Solid tumors	No approved therapies							
Target 3	Solid tumors	No approved therapies							

CML = Chronic myeloid leukemia. CNS = Central nervous system. IND = Investigational new drug. NSCLC = Non-small cell lung cancer.

ELVN-001: Despite Great Advances, a Significant Need Remains for Better Treatment Options for Chronic Myeloid Leukemia

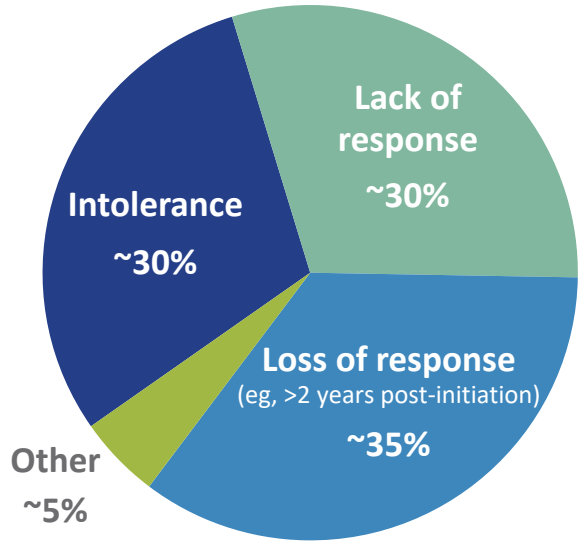
Challenges with Current Standard of Care

- Approximately **1 in 5 patients switch therapy** within the first year and **~40%** of patients switch in the first 5 years (1L & 2L)
- **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 impact efficacy
- Comorbidities, restrictions with concomitant medications, and specific administration requirements **impede long-term patient adherence**
- **Fewer than 10%** of patients successfully achieve sustained treatment-free remission (TFR)

Majority of HCPs (77%) indicated need for more effective, safe, and tolerable agents in CML

Switching Dynamics Demonstrate Unmet Need

Rationale for Treatment Switching



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)

TKI = Tyrosine kinase inhibitors, HCP = Healthcare professional. EU3 = France, UK, Germany.

References: HCP Qualitative & Quantitative Interviews (ClearView); Hochhaus A et al. ASH 2015; Hochhaus A et al. *Leukemia*. 2017; 31(7):1525-1531; Osorio S et al. *Ann Hematol*. 2018; 97(11):2089-2098; Rea et al. *Blood*. 2021; blood.2020009984; Baccarani M and Gale RP. *Leukemia*. 2021; 35:2199-2204; Icsluig® (ponatinib) USPI; Sprycel® (dasatinib) USPI; Tasigna® (nilotinib) USPI.; Bosulif® (bosutinib) USPI

Evolving Chronic Myeloid Leukemia Market Dynamics

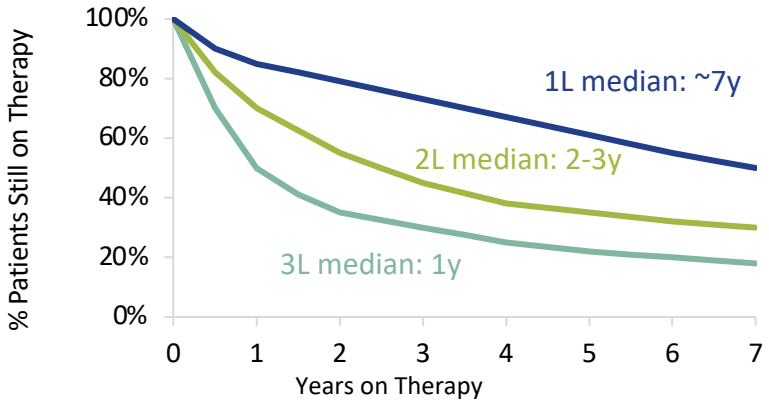
Current Market

- **Growing patient population** due to improved survival, requiring some patients to be **on TKIs for decades**
- Existing **approved drugs have liabilities as chronic therapy**, including poor tolerability due to off-target effects and inability to dose to maximal efficacy resulting in high switch rates
- Nevertheless, the five approved drugs (including generics) drive **annual sales of >$6B,** with **every drug achieving ~$500M** in sales and multiple drugs achieving sales of >$2B

Our Vision

- New drugs with **better tolerability and efficacy** profiles further drive increased switching rates and gain rapid adoption (similar to the HIV market)
- Additional focus from patients and doctors on **deeper molecular responses** (TFR) as well as **tolerability and convenience** factors for long-term treatment
- Chronic nature of CML allows doctors to **freely switch** between therapies, with limited consequences, thereby **blurring lines of therapy**

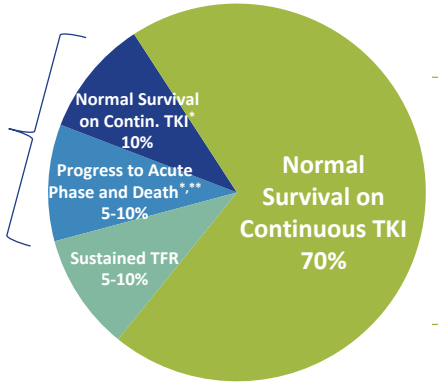
Treatment Duration for SOC by Line of Therapy



CML is a chronic disease requiring many years (even decades) of treatment

Current Outcomes in CML

Treatment decisions are guided by **mutation status,** etc. in only **15-20%** of patients who develop BCR-ABL mutations or other molecular abnormalities



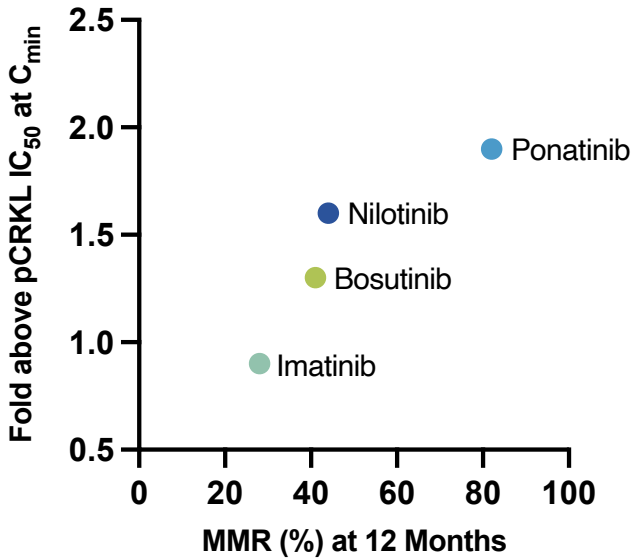
Treatment decisions guided **holistically** based on individual patient (co-meds, co-morbidities, tolerability, etc.) for **>70%** patients

10% overall share (by patients) equates to >$1 billion market opportunity in the U.S. alone†

*Develop BCR/ABL Mutations **Develop other molecular abnormalities. † Assumes current branded pricing
CML = Chronic Myeloid Leukemia. SOC = Standard of care. TFR = Treatment free remission. TKI = Tyrosine kinase inhibitor. Normal survival refers to the expected survival of the age-matched general population.
Reference: Kantarjian HM, et al. *Leukemia*. 2021 Feb; 35(2): 440-453; Hochhaus A et al. *NEJM* 2017; 376:917-927; Hochhaus, A. et al. *Leukemia* 34, 2125–2137 (2020); Giles, et al. *Leukemia* 27, 107–112 (2013); Hochhaus, A. et al. *ASH* 2020; Baccarani M and Gale RP. *Leukemia.* 2021; 35:2199-2204.

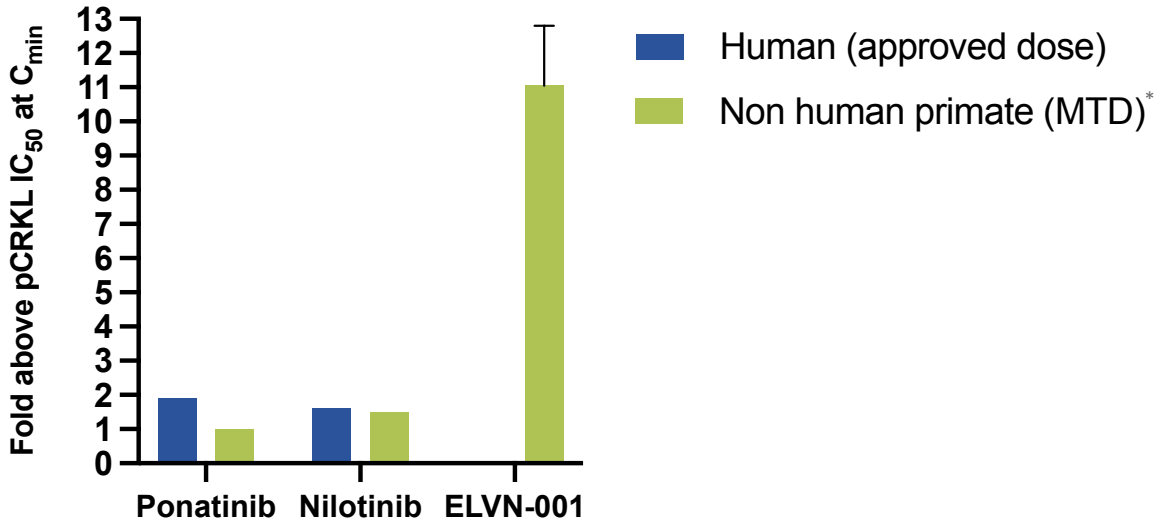
ELVN-001 Potentially Affords an Improved Therapeutic Index

Target Coverage at C_{min} vs. 1L MMR



- Clear correlation between target coverage of the approved agents and major molecular response rate (MMR) at 12 months[1]
- Phosphorylated CRKL or pCRKL IC_{50} represents a robust pharmacodynamic marker for BCR-ABL inhibition

Therapeutic Index vs. NHP Safety Margin



- Toxicology studies with other ABL TKIs show that the maximum tolerated drug exposure is similar between non-human primates and humans
- Data suggests ELVN-001 has the potential for significantly greater therapeutic index than existing TKIs

MMR = Major molecular response. MTD = Maximum tolerated dose. NHP = Non-human primate

[1]Dasatinib was excluded from our analysis due to its short half-life in humans (3-5 hours), however early clinical responses correlated with dasatinib concentrations above its pCRKL IC_{50} for more than 13 hours (Ishida et al. *Eur J Clin Pharmacol.* 2016;72(2):185-93.)

*NHP data for ponatinib, nilotinib, and dasatinib were obtained from the data reported for the maximum tolerated dose (MTD) in their respective NDAs (C_{min} was estimated). NHP data from 28-day GLP tox study for ELVN-001 at 5 mg/kg, a well-tolerated, no adverse event dose (NOAEL)

y-axis: mean C_{min} plasma concentration at the human approved dose (or NHP MTD) divided by K562 pCRKL IC_{50} in 100% human serum

References:

Human C_{min} References: (Imatinib) Peng et al. *J Clin Oncol*. 2004; 22:935-942. DOI: 10.1200/JCO.2004.03.050; (Nilotinib) Kantarjian et al. *NEJM*. 2006; 354:2542-51; (Bosutinib) Abumiya et al. *Nature Scientific Reports*. 2021; 11:6323; (Ponatinib) Iclusig® USPI.

MMR References: (Bosutinib) Cortes JE et al. *J Clin Oncol*. 2012; 30(28):3486-92; (Nilotinib and Imatinib) Saglio G et al. *NEJM*. 2010; 362(24):2251-9; (Ponatinib) Jain P et al. *Lancet Haematol*. 2015; 2(9):e376-83.

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-ABL and T315I mutation (& known asciminib resistant mutations)
- **High selectivity** vs. clinically relevant off-targets
- **Efficacy**: MMR (& MR4.5) greater than approved TKIs driven by an enhanced therapeutic window
- **Tolerability**: fewer dose reductions & discontinuations
- **Safety**: No black box warnings; no edema, effusions, or rash
- **No restrictions** with concomitant medications

Dose Escalation in 3L+ and Expansion

- Progressed/Intolerant CP-CML
- Explore early LoT & combinations
- Seek to demonstrate improved efficacy (CCyR, MMR, MR4.5) and tolerability

4L+ and T315I mutation

- Single-arm study; precedent for approval in last line based on CCyR/MMR by 12m
- T315I mutation in ponatinib or asciminib progressed/intolerant/ineligible

Early Line H2H vs Physician's Choice

- Superiority based on 12m MMR in CP-CML
- Fewer dose reductions/discontinuations vs. approved agents

CCyR = Complete cytogenetic response. CP-CML = Chronic phase CML. H2H = Head-to-head. LoT = Line of therapy. MMR = Major molecular response. MR4.5 = Deep molecular response. TKI = Tyrosine kinase inhibitors

ELVN-002: Opportunity for a Selective Irreversible Pan-Mutant HER2 TKI

Current HER2 TKI Landscape

- The **high degree of structural homology** between EGFR and HER2 makes it difficult to design HER2-selective inhibitors
- Most approved and investigational agents are **dual EGFR/HER2 inhibitors** that are **dose-limited by EGFR-driven toxicity**
- Tucatinib is the **only approved HER2-selective TKI,** but **lacks potency against key mutants,** including HER2 YVMA, the most common Exon 20 insertion mutation (E20IM) in NSCLC, and L755, the most common HER2 breast cancer mutation
- Current HER2 TKIs **do not achieve sufficient CNS free drug levels to address brain metastases,** leading to **disease progression in patients with lung and breast cancer**

Our HER2 Candidate: ELVN-002

- Designed to **irreversibly inhibit** HER2 and **multiple key HER2 mutations**, including HER2 YVMA and L755, and
- Selectively inhibit HER2 while **sparing EGFR** to prevent EGFR-related toxicities, with the potential for **improved efficacy** in NSCLC and other cancers
- Demonstrated **superior pre-clinical activity** in HER2-amplified **subcutaneous and intracranial models**, and an **improved safety margin** in NHPs compared to tucatinib

We believe that ELVN-002, if it achieves the target profile, will be able to achieve an improved therapeutic index compared to current approved and investigational TKIs as well as provide a meaningful therapeutic option to patients with brain metastases

CNS = Central nervous system. IM = Insertion mutation. NSCLC = Non-small cell lung cancer. TKI = Tyrosine kinase inhibitor. NHP = non-human primate.

HER2 Mutant NSCLC May Provide More Rapid Market Entrance Opportunity with Expansion into Other HER2-Driven Cancers to Follow

Initial Focus: HER2 Mutant NSCLC

- Approximately 3% of NSCLC patients harbor HER2 mutations, for which there are **no approved TKIs**
- **~70% of all HER2 mutations** in lung cancer are **HER2 YVMA**
- **High unmet need** in this indication may provide a **fast to market opportunity**

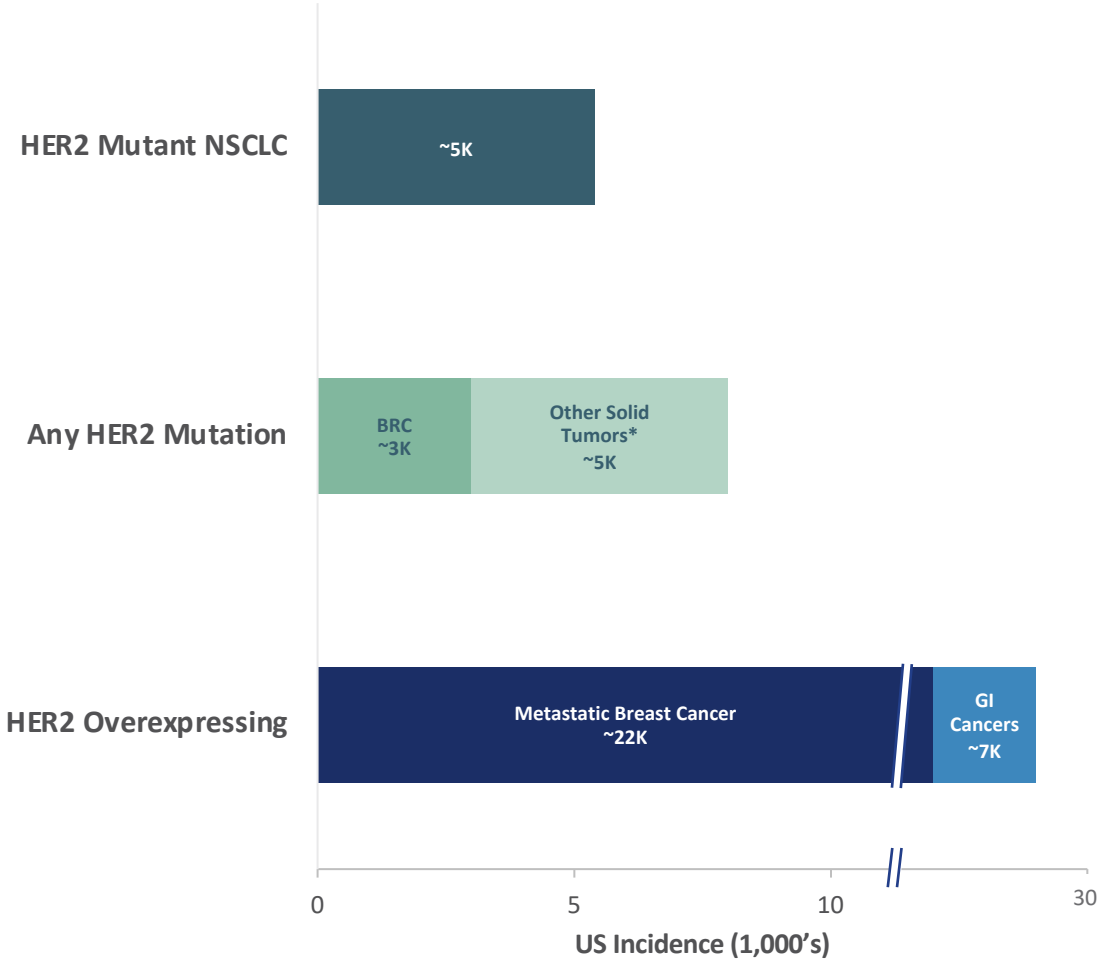
Secondary Focus: Other HER2 Mutant Cancers

- Represents a **larger market** with **limited treatment options**

Indication Expansion: HER2 Amplified or Overexpressing Cancers

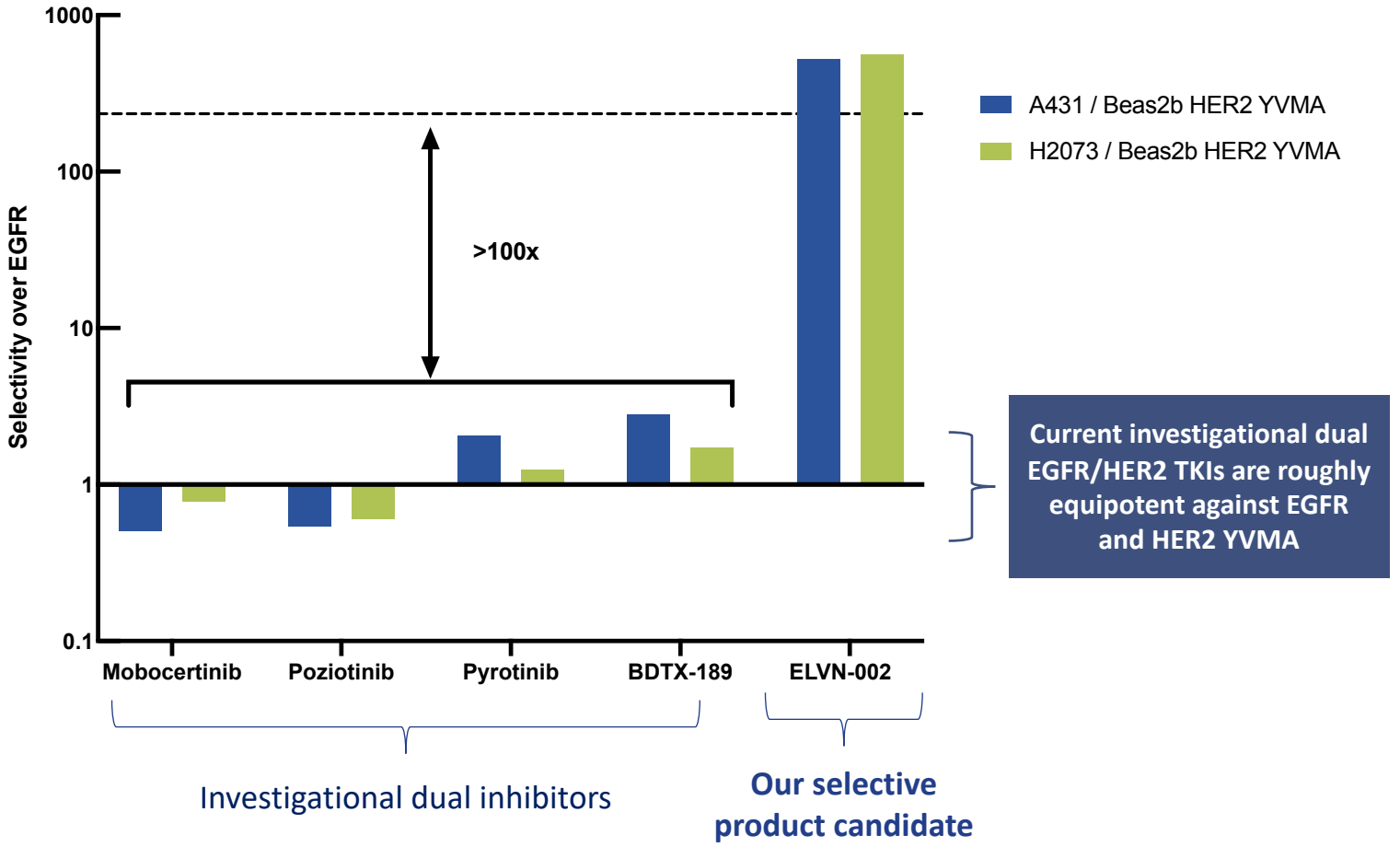
- Largest potential market opportunity, with **nearly 30K metastatic patients across breast, colorectal, and gastric cancers**
- Despite the advances in therapeutic options for HER2+ breast cancer, **~25% of patients experience primary or acquired resistance**, and up to **50%** of patients develop **brain metastasis**
- Despite limitations, **Tukysa (tucatinib) is on a ~$335M revenue run rate** with only a 2L+ HER2+ MBC label

US Market Size Estimates



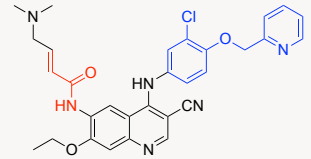
*Other cancers include prostate, endometrial, gastric, stomach, hepatobiliary, etc.
BRC = Breast cancer. GI = Gastrointestinal. NSCLC = Non-small cell lung cancer. MBC = Metastatic breast cancer.
Reference: National Cancer Institute. SEER*Stat software. Bethesda, MD: National Cancer Institute, Surveillance Research Program; Robichaux et al. *Cancer Cell.* 2019;36(4):444-457.e7; SGEN 2Q22 Investor Presentation (28July2022)

ELVN-002 was >100x More Selective for HER2 YVMA Relative to EGFR Than Dual EGFR/HER2 Competitors



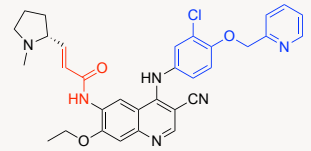
Current investigational dual EGFR/HER2 TKIs are roughly equipotent against EGFR and HER2 YVMA

Lack of Differentiation Across Next Generation TKIs



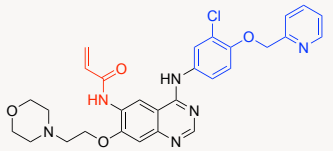
Neratinib

Poor efficacy & tolerability in HER2 mutant setting



Pyrotinib

Phase 1b/2
30% ORR in HER2 mutant NSCLC, poor tolerability



BDTX-189

Poor efficacy & tolerability in HER2 mutant setting

ORR = Overall response rate. NSCLC = Non-small cell lung cancer. TKI = Tyrosine kinase inhibitor.

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., L775)
  - HER2 amplified and/or overexpressed tumors (breast, CRC, etc.)
  - Brain metastases
- **Selective** vs. wild-type EGFR
- **Safety/tolerability**: minimal GI and skin toxicity (avoid EGFR-tox)
- **Combinable:** with SOC including ADCs across HER2-driven tumors
- **Convenient:** oral QD or BID

Dose Escalation in solid tumors with HER2 alterations

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

Expansion: 2L+ HER2 mutant NSCLC

- Single-arm study with potential to support accelerated approval

Multiple Indication Opportunities

- 1L HER2 mutant NSCLC +/- SOC
- Evaluate HER2+ CRC and HER2+ Breast in combination with SOC
- Explore other HER2 mutant solid tumors with “basket study”

ADC = Antibody drug conjugate. BID = twice daily. CNS = Central nervous system. CRC = Colorectal cancer. GI = Gastrointestinal. NSCLC = non-small cell lung cancer. SOC = Standard of care. TKI = Tyrosine kinase inhibitors. QD = once daily.

Expected Near-term Clinical Milestones for Parallel Lead Product Candidates

2022 2023 2024

2H22

ELVN-001 Ph1a initiation (completed)
ELVN-002 IND acceptance (completed)

1H23

ELVN-002 Ph1a initiation

2H23

ELVN-001 Ph1 early clinical data

1H24

ELVN-002 Ph1a data

ELVN-001

ELVN-001 Potential Pivotal Studies

- Late line single arm
- T315I single arm ponatinib or asciminib intolerant / ineligible
- **Early line H2H vs. Physician's Choice**

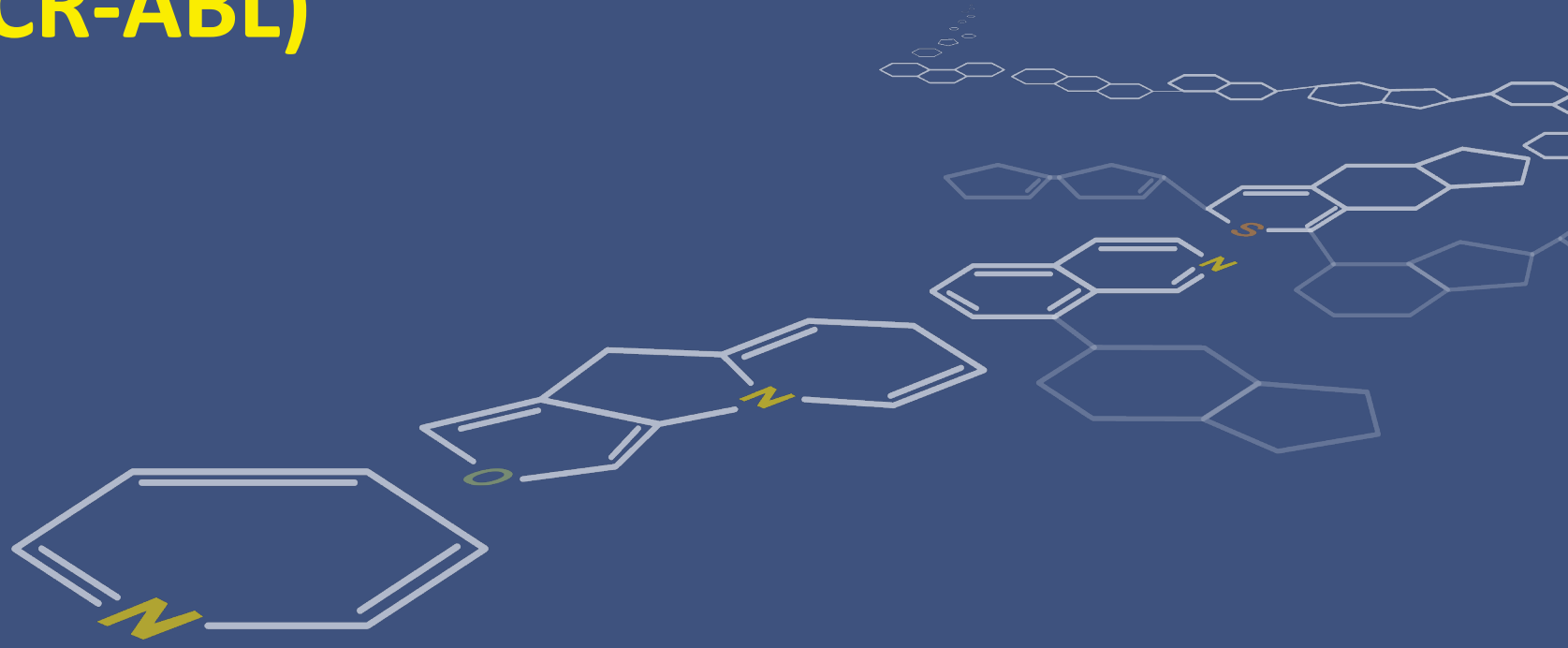
ELVN-002

ELVN-002 Potential Pivotal Studies

- **2L+ NSCLC HER2 mutant monotherapy**
- HER2 amplified MBC monotherapy & combinations
- HER2 mutant basket, HER2-amp CRC, etc.

CRC = Colorectal cancer. IND = Investigational new drug. NSCLC = non-small cell lung cancer. MBC = metastatic breast cancer. H2H = Head-to-head

ELVN-001 (BCR-ABL)



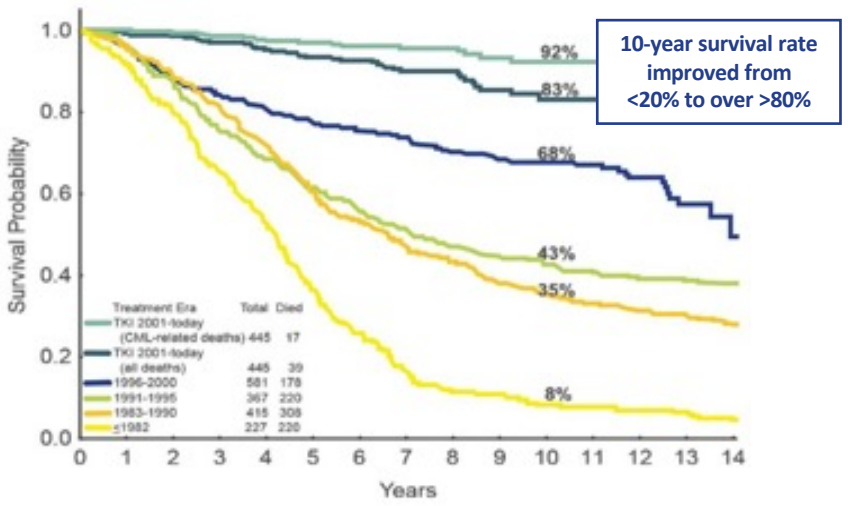
Chronic Myeloid Leukemia

A **big success story** for precision oncology, but needs remain as **treatment goals have evolved**

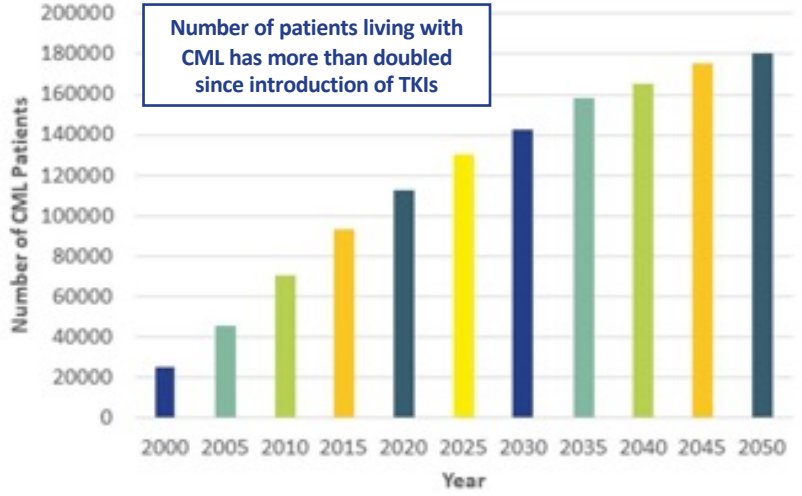
Prior to imatinib the annual CML mortality rate:

<20%

CML 10-Year Survival Rate Over Time



Estimated Prevalence of CML in the US Over Time



1985
BCR-ABL protein identified

1987
HTS yielded the discovery of STI-571 (imatinib)

1998
Imatinib FIH study initiated

2001
Imatinib approved

2006
Dasatinib approved

2007
Nilotinib approved

2012
Ponatinib and Bosutinib approved

2013
NCCN Update (MMR)

2016
Generic imatinib becomes available

2017
Emerging Treatment Goals (MR4.5, TFR)

2021
Asciminib 3L approval

CML = Chronic myeloid leukemia. FIH = First-in-human. MMR = Major molecular response. TFR = Treatment-free reemission.

References: Huang X et al. *Cancer*. 2012;118:3213-3127. DOI: 10.1002/cncr.26679; Kantarjian et al. Chronic Myeloid Leukemia, In: Harrison's Principles of Internal Medicine. 2014.

Significant Need Remains for Better Treatment Options for CML

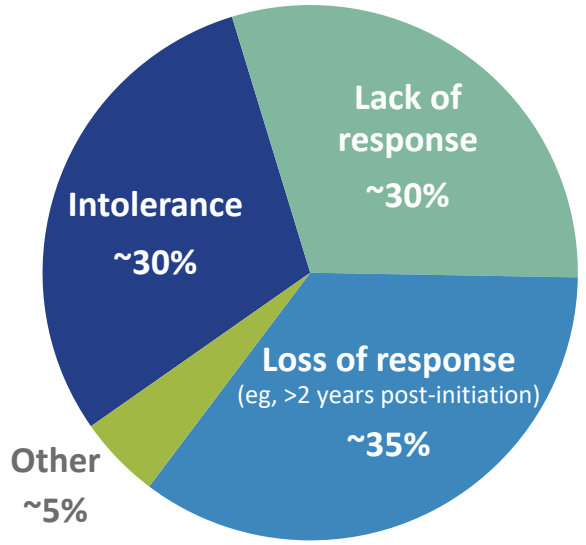
Challenges with Current Standard of Care

- Approximately **1 in 5 patients switch therapy** within the first year and **~40%** of patients switch in the first 5 years (1L & 2L)
- **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 impact efficacy
- Comorbidities, restrictions with concomitant medications, and specific administration requirements **impede long-term patient adherence**
- **Fewer than 10%** of patients successfully achieve sustained treatment-free remission (TFR)

Majority of HCPs (77%) indicated need for more effective, safe, and tolerable agents in CML

Switching Dynamics Demonstrate Unmet Need

Rationale for Treatment Switching



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)

TKI = Tyrosine kinase inhibitors, HCP = Healthcare professional. EU3 = France, UK, Germany.

References: HCP Qualitative & Quantitative Interviews (ClearView); Hochhaus A et al. ASH 2015; Hochhaus A et al. *Leukemia*. 2017; 31(7):1525-1531; Osorio S et al. *Ann Hematol*. 2018; 97(11):2089-2098; Rea et al. *Blood.* 2021; blood.2020009984; Baccarani M and Gale RP. *Leukemia.* 2021; 35:2199-2204; Icsluig® (ponatinib) USPI; Sprycel® (dasatinib) USPI; Tasigna® (nilotinib) USPI.; Bosulif® (bosutinib) USPI

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

Compound	Company	T315I Coverage	Off Target(s) & Treatment-Related AEs		BCR-ABL Coverage†	1L Efficacy	Drug & Administration Requirements	2021 FY Sales (USD)‡
Imatinib (Gleevec®)[1]	Novartis	X	c-KIT, CSFR-1, PDGFR	Myelosuppression: 20-25% Gr 3+ Fluid Retention/Edema: 68% Myalgia/Arthralgia: 50% GI-related: 50%	+	28% MMR 3% MR4.5	Avoid strong CYP3A inhibitors or inducers	**$1.0B**
Dasatinib (Spyrcel®)[2-4]	BMS	X	SRC family, c-KIT, PDGFR-αβ	Myelosuppression: 10-20% Gr 3+ Edema/Effusions: 15-30%	N/A	46% MMR 5% MR4.5	Avoid strong CYP3A inhibitors or inducers, PPIs, antacids, and H2 blockers	**$2.1B**
Nilotinib (Tasigna®)[5-7]	Novartis	X	c-KIT, PDGFR, CSFR-1, DDR-1 (hERG Channel)	Myelosuppression: 10-20% Gr 3+ Hypertension: 10% **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	**$2.0B**
Bosutinib (Bosulif®)[8,9]	Pfizer	X	SRC family	Diarrhea: 82% Nausea: 39% Vomiting: 32% Increased LFTs: 20%	++	41% MMR 7.5% MR4.5	Avoid strong CYP3A inhibitors or inducers, PPIs, antacids, and H2 blockers	**$500M**
Ponatinib (Iclusig®)[10,11]	Takeda	✓	KDR, FGFR, c-KIT, RET, FLT3, PDGFR	Myelosuppression: 50% Gr 3+ Hypertension: 70% **Black Box:** Arterial Occlusive Events, Heart Failure, VTE, Hepatoxicity	+++	82% MMR* 56% MR4.5	Avoid strong CYP3A inhibitors or inducers	**$500M**

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

1L = Front line. GI = Gastrointestinal. Gr = Grade. FY = Fiscal Year. LFTs = Liver function tests. MMR = Major Molecular Response. MR4.5 = Deep Molecular Response. PPI = Proton pump inhibitors. MMR and MR4.5 at 12 months. VTE = Venous thromboembolism.
† The "BCR-ABL Coverage" column refers to BCR-ABL coverage at median trough plasma concentrations at the approved dose of the respective TKI. See Figure 14 and the accompanying text for further information regarding BCR-ABL coverage of the various TKIs.
‡ 2021 FY Sales (USD) are approximate figures (B = billions, M = millions). Company Investor Reports.
* Based on Ponatinib's discontinued 1L CML study; Ponatinib is not approved for use in 1L CML.

References: 1. Gleevec® (imatinib) USPI; 2. Sprycel® (dasatinib) USPI; 3. Kantarjian H et al. *NEJM*, 2010; 362(24):2260-70; 4. Cortes JE et al. *J Clin Oncol*. 2016; 34(20):2333-40; 5. Tasigna® (nilotinib) USPI; 6. Saglio G et al. *NEJM* 2010; 362(24):2251-9; 7. Hochhaus A et al. *Leukemia*. 2016; 30(5):1044-54; 8. Bosulif® (bosutinib) USPI. 9. Cortes JE et al. *J Clin Oncol*, 2012; 30(28):3486-92; 10. Iclusig® (ponatinib) USPI; 11. Jain P et al. *Lancet Haematol*; 2015; 2(9):e376-83.

Review of Asciminib (Scemblix®), 4th Generation Allosteric TKI

Observations

- Approved in US based on 3L+ ASCEMBL Trial
- **Strong launch & blockbuster sales projections in 3L+ alone** demonstrate the size of the market (1L Ph3 readout 2024)
- **~30% discontinued** due to lack of efficacy/AE by 48 wk
- **~50% discontinued** by 96 wk, but only **1.2% due to PD/death**
- **T315I dosed 5x higher** resulting in more dose reductions, enhanced pancreatic toxicity (25%) & elevated liver enzymes
- **Drug-drug interactions**: CYP3A4, CYP2C9
- Potential **off-target resistance liabilities:** PgP & BCRP
- **Requires fasting** 2 hours before and 1 hour after each dose

Emerging BCR-ABL mutations upon discontinuation due to lack of efficacy or progressive disease

	Asciminib (n=39)	Bosutinib (n=30)
No mutations	22 (56%)	20 (67%)
ATP Binding Site	M244V (n=3), E355G, F359V, T315I	T315I, V299L
Myristol Binding Pocket	A337T (n=3), P465	None

Mutations at baseline & end of treatment

ATP Binding Site	F359C/V (n=3), F317L (n=2), Y253H	M244V (n=2), E255V, F317L, Q252H

PD = Progressive disease. TKI = Tyrosine kinase inhibitor.

References: Hochhaus et al. ASH 2020; Cortes et al. ASH 2020; ASH 2021; Novartis Q2 2021 IR; Scemblix (Asciminib) USPI; ASCO 2022; Eadie et al Oncotarget 2018.

Evolving Chronic Myeloid Leukemia Market Dynamics

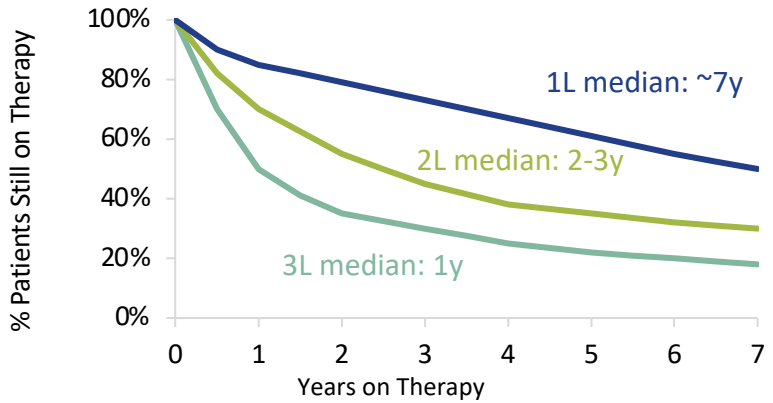
Current Market

- **Growing patient population** due to improved survival, requiring some patients to be **on TKIs for decades**
- Existing **approved drugs have liabilities as chronic therapy**, including poor tolerability due to off-target effects and inability to dose to maximal efficacy resulting in high switch rates
- Nevertheless, the five approved drugs (including generics) drive **annual sales of >$6B,** with **every drug achieving ~$500M** in sales and multiple drugs achieving sales of >$2B

Our Vision

- New drugs with **better tolerability and efficacy** profiles further drive increased switching rates and gain rapid adoption (similar to the HIV market)
- Additional focus from patients and doctors on **deeper molecular responses** (TFR) as well as **tolerability and convenience** factors for long-term treatment
- Chronic nature of CML allows doctors to **freely switch** between therapies, with limited consequences, thereby **blurring lines of therapy**

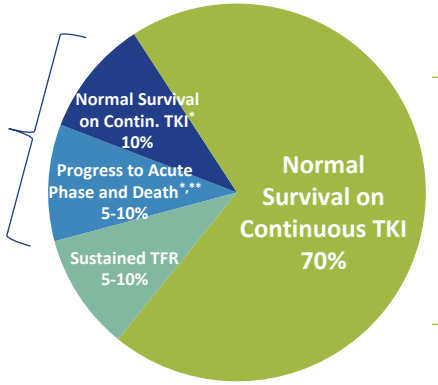
Treatment Duration for SOC by Line of Therapy



CML is a chronic disease requiring many years (even decades) of treatment

Current Outcomes in CML

Treatment decisions are guided by **mutation status,** etc. in only **15-20%** of patients who develop BCR-ABL mutations or other molecular abnormalities



Treatment decisions guided **holistically** based on individual patient (co-meds, co-morbidities, tolerability, etc.) for **>70%** patients

10% overall share (by patients) equates to >$1 billion market opportunity in the U.S. alone†

*Develop BCR/ABL Mutations **Develop other molecular abnormalities. † Assumes current branded pricing
CML = Chronic Myeloid Leukemia. SOC = Standard of care. TFR = Treatment free remission. TKI = Tyrosine kinase inhibitor. Normal survival refers to the expected survival of the age-matched general population.
Reference: Kantarjian HM, et al. *Leukemia*. 2021 Feb; 35(2): 440-453; Hochhaus A et al. *NEJM* 2017; 376:917-927; Hochhaus, A. et al. *Leukemia* 34, 2125–2137 (2020); Giles, et al. *Leukemia* 27, 107–112 (2013); Hochhaus, A. et al. *ASH* 2020; Baccarani M and Gale RP. *Leukemia.* 2021; 35:2199-2204.

Our Strategy and Initial Positioning in an Evolving CML Market

Treatment Paradigm				Market Insights	Market Size (US)
1L (50%)	**1st Gen TKI** Imatinib 28% MMR	**2nd Gen TKIs** Nilotinib, Dasatinib, Bosutinib ~45% MMR		**~50% of patients start on 2nd Gen TKIs**, driven by faster & deeper molecular responses **Further improvement in efficacy** may still allow for **new entrants in 1L** setting	**~30K+**
2L (30%)	**2nd Gen TKIs** ~35% MMR	**2nd Gen TKIs** ~20-25% MMR	**ELVN-001** 30-40%+ MMR Target*	HCPs consistently express high interest in prescribing **novel agents with improved safety/tolerability and efficacy in 2L+**	**~18K+**
3L+ (20%)	**2nd** Bosutinib ~20% MMR	**3rd & 4th Gen TKIs** Ponatinib 35% MMR; Asciminib ~33% MMR		Asciminib has the potential to become the **preferred option in earlier lines of therapy** HCPs report up to **~25% of patients** end up back on **imatinib** in 3L+ setting	**~12K+**
T315I	**3rd Gen TKI** Ponatinib 58% MMR	**4th Gen TKI** High Dose Asciminib 58% MMR**	**ELVN-001** >50% MMR Target	Potentially **more tolerable choice for T315I patients** and has the potential to displace ponatinib High dose asciminib is now an option in the US, but risks remain	**~2K+**

1L = First line. 2L = Second line. 2L+ = Second or later line. 3L+ = Third or later line. 2nd Gen TKIs = Nilotinib, Dasatinib, Bosutinib. MMR = Major Molecular Response at ~12 months. HCP = Health Care Provider.
*Depending on patient population
**Ponatinib-naïve patients (n = 21)

References: HCP Qualitative & Quantitative Interviews (ClearView); Gleevec® (imatinib) USPI; Tasigna® (nilotinib) USPI; Sprycel® (dasatinib) USPI; Bosulif® (bosutinib) USPI; Icsluig® (ponatinib) USPI; Hochhaus et al. ASH 2020; Cortes JE et al. *Blood.* 2020; 136(Supplement1):47-50.

< $500M USD > $2B USD

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-ABL and T315I mutation (& known asciminib resistant mutations)
- **High selectivity** vs. clinically relevant off-targets
- **Efficacy**: MMR (& MR4.5) greater than approved TKIs driven by an enhanced therapeutic window
- **Tolerability**: fewer dose reductions & discontinuations
- **Safety**: No black box warnings; no edema, effusions, or rash
- **No restrictions** with concomitant medications

Dose Escalation in 3L+ and Expansion

- Progressed/Intolerant CP-CML
- Explore early LoT & combinations
- Seek to demonstrate improved efficacy (CCyR, MMR, MR4.5) and tolerability

4L+ and T315I mutation

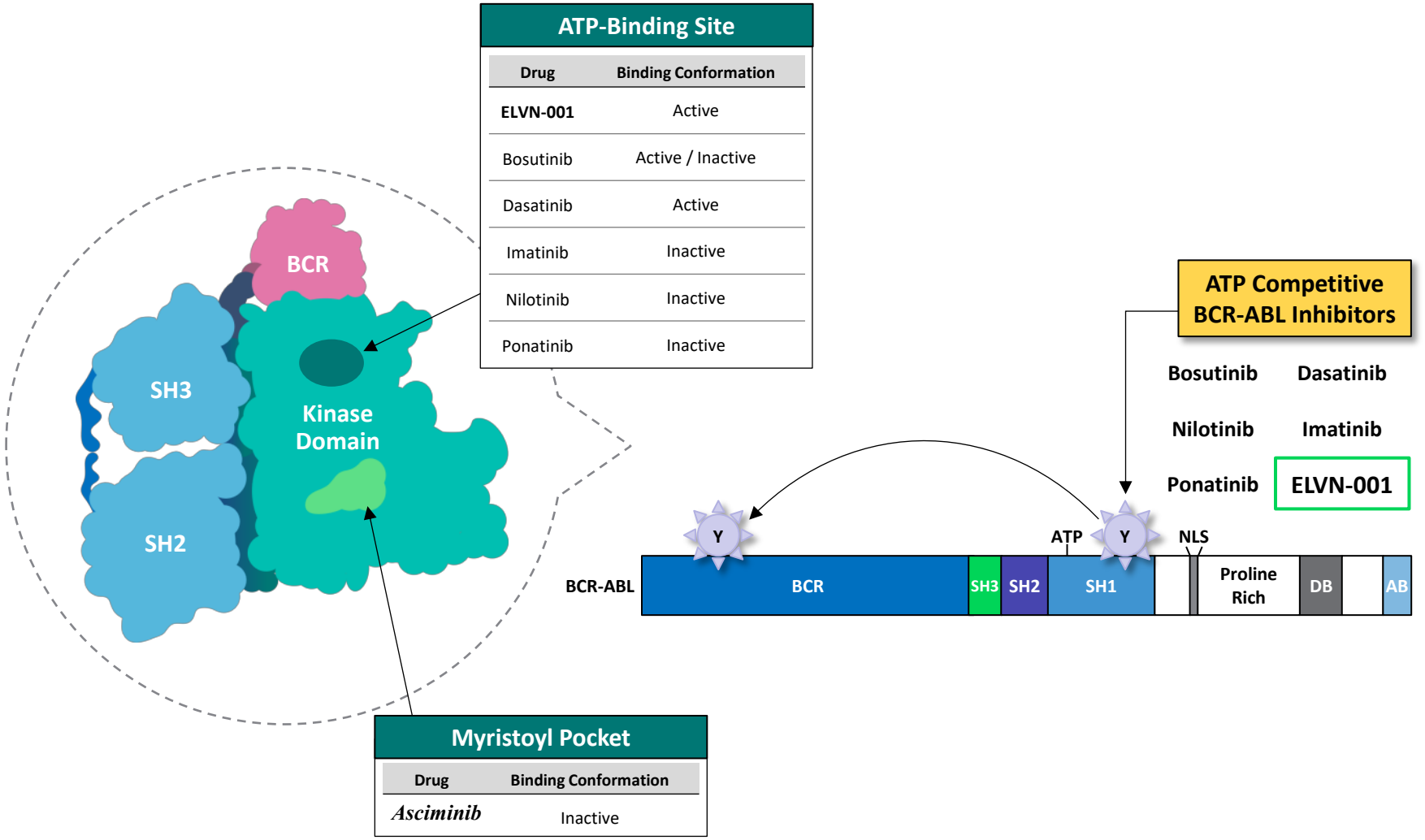
- Single-arm study; precedent for approval in last line based on CCyR/MMR by 12m
- T315I mutation in ponatinib or asciminib progressed/intolerant/ineligible

Early Line H2H vs Physician's Choice

- Superiority based on 12m MMR in CP-CML
- Fewer dose reductions/discontinuations vs. approved agents

CCyR = Complete cytogenetic response. CP-CML = Chronic phase CML. H2H = Head-to-head. LoT = Line of therapy. MMR = Major molecular response. MR4.5 = Deep molecular response. TKI = Tyrosine kinase inhibitors.

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



Y=Tyrosine; NLS=Nuclear Localization Signal; SH1=Src Homology 1 Domain; SH2=Src Homology 2 Domain; SH3=Src Homology 3 Domain; DB=DNA-Binding Region; AB=Actin-Binding Region; BCR=Breakpoint cluster region

References: Braun T. et al. *Cancer Cell* 2020 2020 Apr 13;37(4):530-542.

ELVN-001 Has a Differentiated and Attractive Profile for CML

	Asciminib	Ponatinib	Nilotinib	ELVN-001
KCL-22 (BCR-ABL^{wt}) cytotox IC_{50} (50% human serum)	7 nM	1 nM	90 nM	19 nM
KCL-22 (BCR-ABL^{T315I}) cytotox IC_{50} (50% human serum)	>1,150 nM	14 nM	> 10,000 nM	131 nM
K-562 (BCR-ABL^{wt}) cytotox IC_{50} (50% human serum)	85 nM	4 nM	228 nM	65 nM
K-562 pCRKL IC_{50} (100% human serum)	**N/A**	**36 nM**	**1,080 nM**	**112 nM**
HL-60 cytotox IC_{50} (10% FBS)	12,200 nM	366 nM	5,050 nM	3,550 nM
Human Hepatocyte stability, extraction ratio	64	62	62	**0**
Plasma Protein Binding (% unbound)	~2	< 1	< 1	40
CYPs (% inhibition @ 10 µM)	All < 50%	All < 50%	2C8, 2C9, 3A4, 2C19 > 50%	All < 50%
hERG IC_{50}	25 µM	2.3 µM	0.13 µM	> 30 µM
BCRP Substrate	Yes	Yes	Yes	**No**

Strong correlation to MMR in humans

BCRP may play a role in off-target resistance

- **Good potency** in the presence of human serum against native BCR-ABL and T315I (smaller potency shift compared to ponatinib & asciminib)
- Designed for safe and flexible use including **reduced risk of DDIs**, appropriate for a chronic disease setting
- Predicted human PK will enable **maximal target coverage** through the full dosing window

DDI = Drug-drug interaction
Note: IC values represent an average derived from multiple runs internally with a minimum of two independent experiments. ADMET data were generated internally or obtained from literature including NDAs. Results of a head-to-head comparison may differ from those set forth herein.

ELVN-001 is Selective for ABL1

- ELVN-001 has a very **selective** kinase profile
  - Clean vs. key off-targets in cells
  - 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

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

ELVN-001 (100 µM ATP)

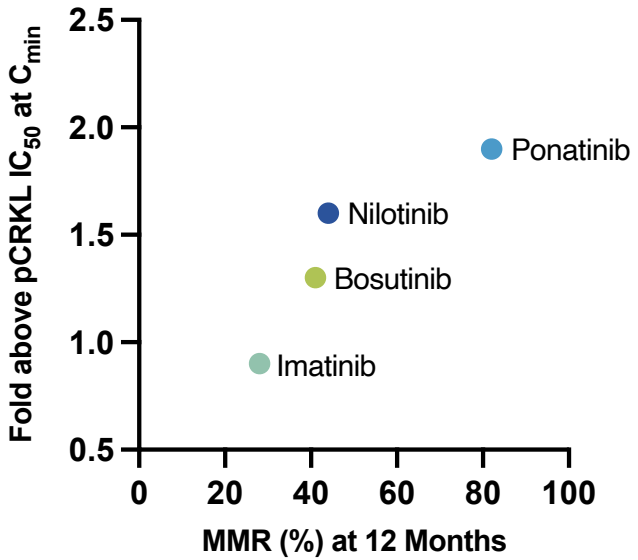
Kinase	IC_{50} (nM)
ABL1	**1**
ABL2/ARG	31
TRKC	41
TNIK	110
LOK/STK10	183
LRRK2	486
FGR	550
ACK1	698
FYN	725
HGK/MAP4K4	973
LCK	>1,000

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

Reference: Abl kinases are required for vascular function, Tie2, and angiopoietin-1-mediated survival. Pendergast et al. *PNAS*. 2013;110(30):12432-7.

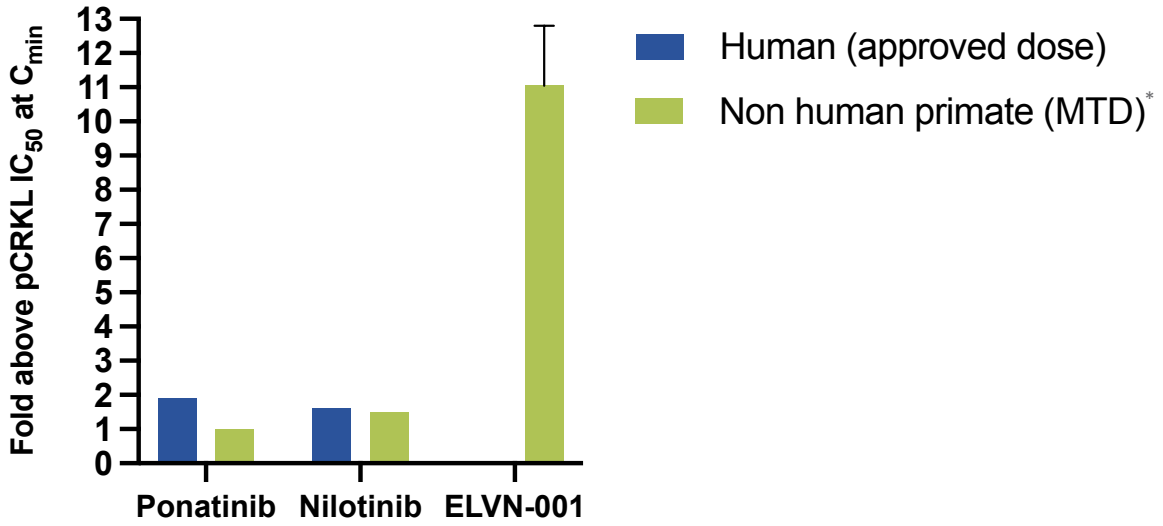
ELVN-001 Potentially Affords an Improved Therapeutic Index

Target Coverage at C_{min} vs. 1L MMR



- Clear correlation between target coverage of the approved agents and major molecular response rate (MMR) at 12 months[1]
- Phosphorylated CRKL or pCRKL IC_{50} represents a robust pharmacodynamic marker for BCR-ABL inhibition

Therapeutic Index vs. NHP Safety Margin



- Toxicology studies with other ABL TKIs show that the maximum tolerated drug exposure is similar between non-human primates and humans
- Data suggests ELVN-001 has the potential for significantly greater therapeutic index than existing TKIs

MMR = Major molecular response. MTD = Maximum tolerated dose. NHP = Non-human primate.
[1]Dasatinib was excluded from our analysis due to its short half-life in humans (3-5 hours), however early clinical responses correlated with dasatinib concentrations above its pCRKL IC_{50} for more than 13 hours (Ishida et al. *Eur J Clin Pharmacol.* 2016;72(2):185-93.)
*NHP data for ponatinib, nilotinib, and dasatinib were obtained from the data reported for the maximum tolerated dose (MTD) in their respective NDAs (C_{min} was estimated). NHP data from 28-day GLP tox study for ELVN-001 at 5 mg/kg, a well-tolerated, no adverse event dose (NOAEL)
y-axis: mean C_{min} plasma concentration at the human approved dose (or NHP MTD) divided by K562 pCRKL IC_{50} in 100% human serum

References:
Human C_{min} References: (Imatinib) Peng et al. *J Clin Oncol*. 2004; 22:935-942. DOI: 10.1200/JCO.2004.03.050; (Nilotinib) Kantarjian et al. *NEJM*. 2006; 354:2542-51; (Bosutinib) Abumiya et al. *Nature Scientific Reports*. 2021; 11:6323; (Ponatinib) Iclusig® USPI.
MMR References: (Bosutinib) Cortes JE et al. *J Clin Oncol*. 2012; 30(28):3486-92; (Nilotinib and Imatinib) Saglio G et al. *NEJM*. 2010; 362(24):2251-9; (Ponatinib) Jain P et al. *Lancet Haematol*. 2015; 2(9):e376-83.

ELVN-001 Clinical Development Strategy

Phase 1

TRIAL

- CP-CML intolerant / resistant
- T315I mutation

GOALS

- Demonstrate potential for efficacy superior to 2nd Gen TKIs (at least as good as asciminib & ponatinib) at well tolerated dose(s)
- Identify dose(s) for Phase 1b and beyond

Phase 1b / 2

TRIAL

- Late line single arm & T315I single arm
- Explore based on data (MMR/MR4.5)
  - Earlier lines of therapy
  - Combinations with approved TKIs (e.g., asciminib)

GOALS

- Establish PoC for deep and durable responses in early line CML
- Demonstrate efficacy and safety profile suitable for initiating early line H2H

Registrational / Phase 3

TRIAL

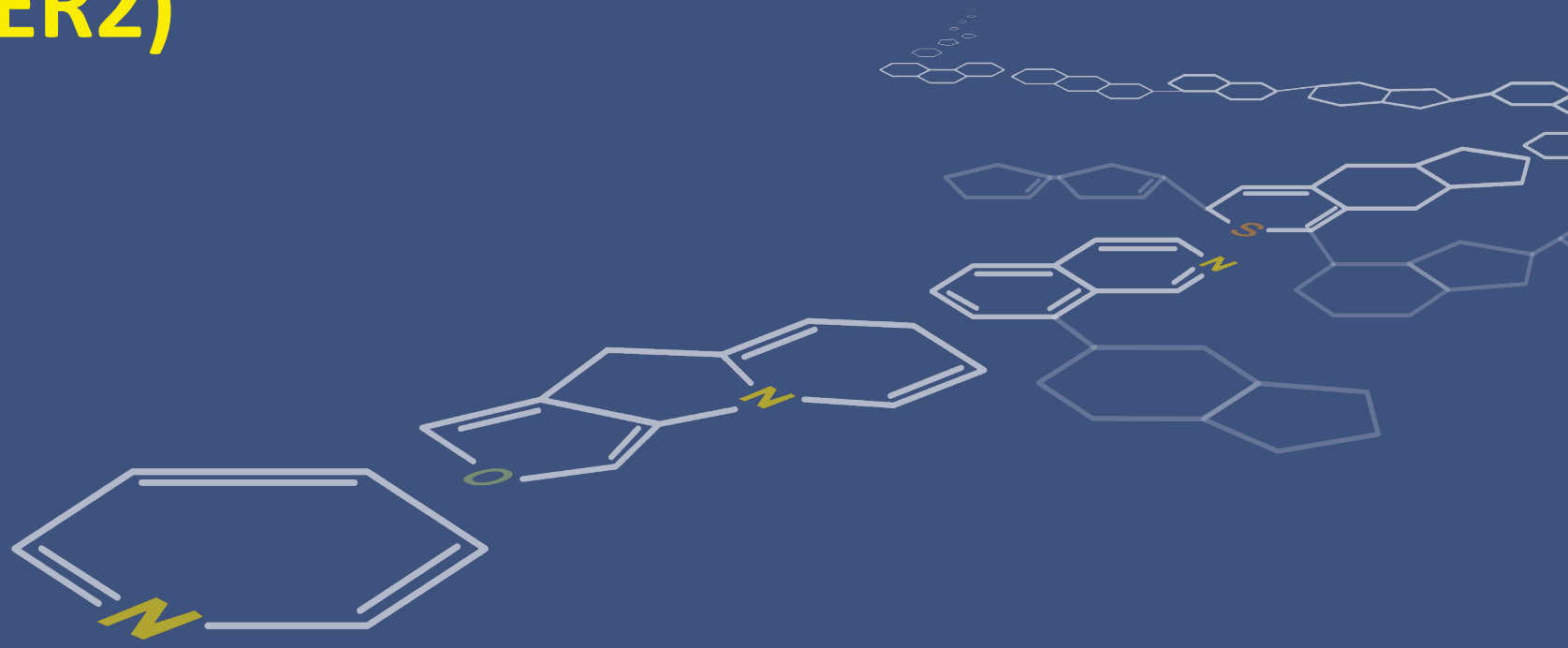
- File on 4L+ and T315I single arm data
- Initiate early line H2H vs. Physician's Choice

GOALS

- Accelerated Approval in late line CP-CML
- Initiate early line H2H for broad label accelerated approval in CP-CML

CP-CML = Chronic-phase CML. H2H = Head-to-head. MMR = Major molecular response. MR4.5 = Deep molecular response. PoC = Proof of concept.

ELVN-002 (HER2)



ELVN-002: Opportunity for a Selective Irreversible Pan-Mutant HER2 TKI

Current HER2 TKI Landscape

- The **high degree of structural homology** between EGFR and HER2 makes it difficult to design HER2-selective inhibitors
- Most approved and investigational agents are **dual EGFR/HER2 inhibitors** that are **dose-limited by EGFR-driven toxicity**
- Tucatinib is the **only approved HER2-selective TKI,** but **lacks potency against key mutants,** including HER2 YVMA, the most common Exon 20 insertion mutation (E20IM) in NSCLC, and L755, the most common HER2 breast cancer mutation
- Current HER2 TKIs **do not achieve sufficient CNS free drug levels to address brain metastases,** leading to **disease progression in patients with lung and breast cancer**

Our HER2 Candidate: ELVN-002

- Designed to **irreversibly inhibit** HER2 and **multiple key HER2 mutations**, including HER2 YVMA and L755, and
- Selectively inhibit HER2 while **sparing EGFR** to prevent EGFR-related toxicities, with the potential for **improved efficacy** in NSCLC and other cancers
- Demonstrated **superior pre-clinical activity** in HER2-amplified **subcutaneous and intracranial models**, and an **improved safety margin** in NHPs compared to tucatinib

We believe that ELVN-002, if it achieves the target profile, will be able to achieve an improved therapeutic index compared to current approved and investigational TKIs as well as provide a meaningful therapeutic option to patients with brain metastases

CNS = Central nervous system. IM = Insertion mutation. NSCLC = Non-small cell lung cancer. TKI = Tyrosine kinase inhibitor. NHP = non-human primate.

HER2 Mutant NSCLC May Provide More Rapid Market Entrance Opportunity with Expansion into Other HER2-Driven Cancers to Follow

Initial Focus: HER2 Mutant NSCLC

- Approximately 3% of NSCLC patients harbor HER2 mutations, for which there are **no approved TKIs**
- **~70% of all HER2 mutations** in lung cancer are **HER2 YVMA**
- **High unmet need** in this indication may provide a **fast to market opportunity**

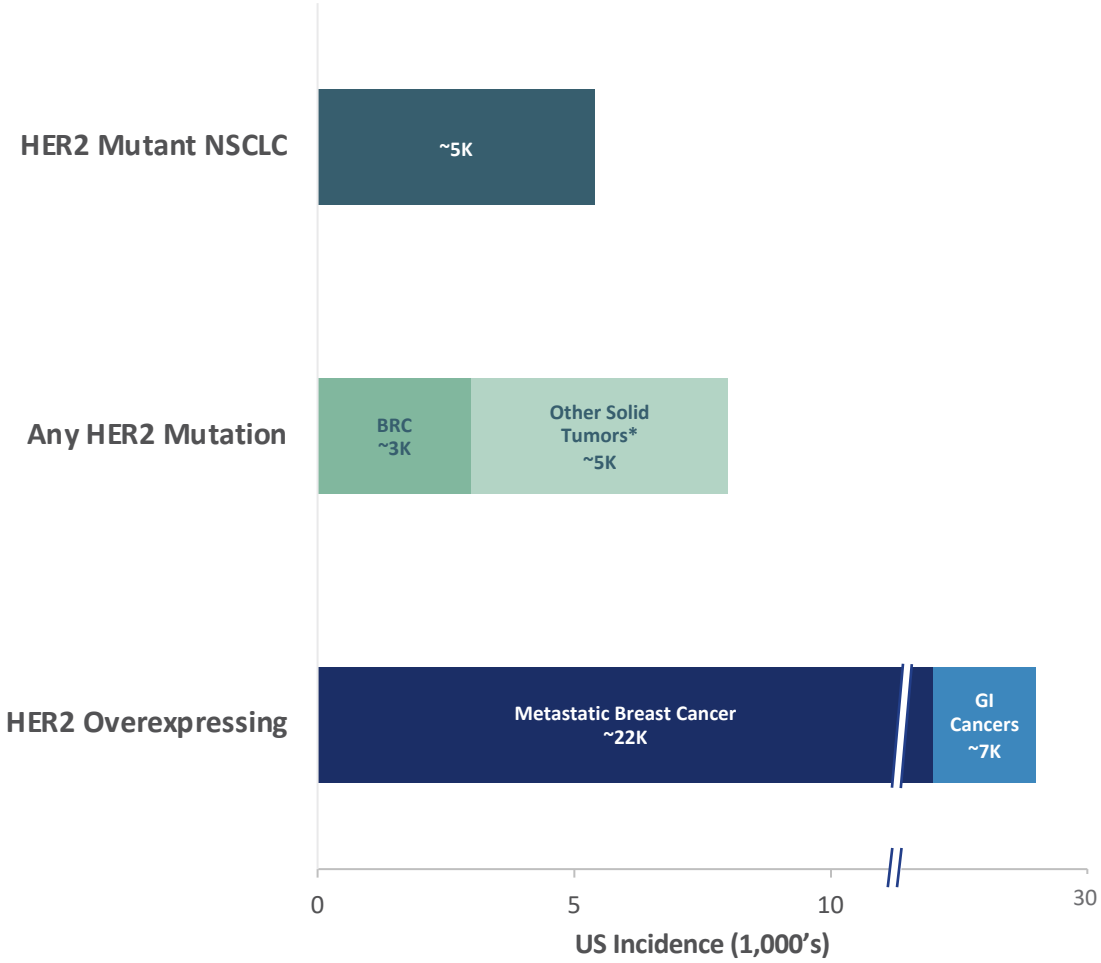
Secondary Focus: Other HER2 Mutant Cancers

- Represents a **larger market** with **limited treatment options**

Indication Expansion: HER2 Amplified or Overexpressing Cancers

- Largest potential market opportunity, with **nearly 30K metastatic patients across breast, colorectal, and gastric cancers**
- Despite the advances in therapeutic options for HER2+ breast cancer, **~25% of patients experience primary or acquired resistance**, and up to **50%** of patients develop **brain metastasis**
- Despite limitations, **Tukysa (tucatinib) is on a ~$335M revenue run rate** with only a 2L+ HER2+ MBC label

US Market Size Estimates



*Other cancers include prostate, endometrial, gastric, stomach, hepatobiliary, etc.
BRC = Breast cancer. GI = Gastrointestinal. NSCLC = Non-small cell lung cancer. MBC = Metastatic breast cancer.
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; SGEN 2Q22 Investor Presentation (28July2022)

HER2 Mutant NSCLC Landscape: No Approved Selective TKIs

Compound	Company	Stage	MoA	Selectivity vs. EGFR^{WT}	HER2mut NSCLC Efficacy	Safety / Tolerability
CURRENT & POTENTIAL FUTURE STANDARD OF CARE						
Platinum-doublet[1]	N/A	N/A	Chemo	N/A	ORR: ~25-35% mPFS: 4-7m	Gr 3+ Neutropenia: 19% Nausea: 52% Constipation, diarrhea, vomiting, cough, dyspnea, decreased appetite (20-30% each)
Trastuzumab deruxtecan (Enhertu®)[2]	Daiichi Sankyo	FDA Approved (2L+)	HER2-ADC topoisomerase payload	HER2-specific	ORR: 58% DOR: 8.7m	Gr 3+ Neutropenia: 16%; Black Box Warning: 12% ILD/pneumonitis (all grades) All Grade Nausea (61%), Anemia (34%), Fatigue (32%) **Dose discontinuation due to AE: 8%**
INVESTIGATIONAL TKIs						
Poziotinib[3]	Spectrum	Received FDA CRL Nov. 2022	Irreversible, EGFR/HER2	< 1x	ORR: ~28% mPFS: 5.5m	Gr 3+: Rash (49%); Diarrhea (26%); Stomatitis (25%) All Grade Rash (91%); Diarrhea (82%); Stomatitis (69%); Paronychia (38%) **Dose modifications due to AEs: 91%** | **Dose discontinuations due to AEs: 13%**
Pyrotinib[4]	Jiangsu HengRui Medicine	Phase 3	Irreversible, EGFR/HER2	≤ 1x	ORR: 19% mPFS: 5.6m	Gr 3+: Diarrhea (17%) All Grade Diarrhea (86%); Fatigue (58%); Anemia (36%); Dizziness (33%); Decreased appetite (32%, Hand-foot syndrome (32%); Nausea (32%) **Dose modification due to AEs: 8%**
BI-1810631[5]	Boehringer Ingelheim	Phase 1a	Irreversible, HER2	> 100x	50% ORR (n=14)	Phase 1a in progress – As of October 2022, 29 pts dosed (QD and BID arm). MTD not reached. 1 DLT: Gr 2 oedema; 59% TRAE (28% diarrhea Gr 1/2) Additional clinical pharmacology studies underway to bridge to a new formulation and assess food / PPI effect.

Poor TKI selectivity of dual inhibitors resulting in EGFR-driven toxicities limits efficacy

2L+ = Second or later line of therapy. AE = Adverse event. CRL = Complete Response Letter. DOR = Duration of response. Gr = Grade. ILD = Interstitial lung disease. m = Months. N/A = Not applicable. NSCLC = Non-small cell lung cancer. ORR = Overall response rate. mPFS = Median progression free survival. PPI = Proton pump inhibitor. TKI = Tyrosine kinase inhibitor. MoA = Mechanism of action

References: 1. Wang et al. *BMC Cancer* (2018) 18:326; 2. Enhertu® (fam-trastuxumab deruxtecan) USPI; 3. Le, et al. *J. Clin Oncol* 2021, 40:710-718**; 4.** Song et al. *BMC Medicine* (2022) 20:42; 5. Opdam et al. *ENA* 2022, NCT04886804, NCT05380947.

HER2 Breast Landscape: No Irreversible, Highly Selective TKI Option

Compound	Company	MoA	Clinical Usage	HER2+ BRC Efficacy	Safety / Tolerability
ANTIBODY DRUG CONJUGATES					
Enhertu (fam-trastuzumab deruxtecan)[1]	Daiichi Sankyo	HER2-ADC topoisomerase payload	2L	mPFS: NR (18.5-NE) ORR: 80%	Gr 3+: Neutropenia: 20% All Grade: ILD (11%); Nausea (72%); Alopecia, Anemia, Vomiting (30-40% each) **Discontinuation due to AE: 13% (median txt duration: 14m)**
Kadcyla (ado-trastuzumab emtansine)[1]	Roche	HER2-ADC DM1 toxin payload	2L	mPFS: 6.8m ORR: 35%	Gr 3+: Thrombocytopenia: 25% All Grade: Nausea, Fatigue, AST/ALT increase (20-30% each) **Discontinuation due to AE: 5% (median txt duration 7m)**
TYROSINE KINASE INHIBITORS					
Tukysa (tucatinib + trastuzumab + capecitabine)[2]	Seagen	Reversible, HER2 TKI	3L+ (CNS mets)	mPFS: 7.8m ORR: 40.6% mOS: 21.9m	Gr 3+: PPE / Diarrhea (12-13% each) All Grade: Diarrhea (80%); PPE (63%); Fatigue, Nausea (~50% each) **Discontinuation due to AE: 6% (median txt duration 7m)**
Tucatinib (single agent)[3,4]	Seagen	Reversible, HER2 TKI	N/A	ORR: 11% CBR: 22% (med prior tx: 6)	Gr 3+: ALT increase (4%); Rash (4%); Diarrhea (0%) All Grade: Diarrhea (26-33%); Nausea (33%); Fatigue (18%)
CHEMOTHERAPY					
Xeloda (capecitabine)[5]	Roche	Chemo	3L+	ORR: 25% DoR: 5m	Gr 3+: Diarrhea (15%); PPE (11%); Nausea, Vomiting (4% each) All Grade: PPE / Diarrhea (57% each); Nausea (53%); Vomiting (37%) **Discontinuation due to AE: 8% (median txt duration 3.8m)**

No selective, irreversible TKI to meaningfully address brain metastases

1L = First line of therapy. 2L = Second line of therapy. 2L+ = Second or later line of therapy. 3L+ = Third or later line of therapy. AE = Adverse event. ADC = Antibody drug conjugate. AST = Aspartate aminotransferase. ALT = Alanine transaminase. CBR = Clinical benefit rate. CNS mets = Central Nervous System metastases. DoR = Duration of response. Gr = Grade. ILD = Interstitial lung disease. NE = Not evaluable. NR = Not reached. N/A = Not applicable. ORR = Overall response rate. mPFS = Median progression free survival. PPE = Palmar-plantar erythrodysesthesia. mOS = Median overall survival. TKI = Tyrosine kinase inhibitor. Tx or Txt = Treatment. MoA = Mechanism of action

References: 1. Cortes J et al. *N Engl J Med* 2022; 386:1143-1154; 2. Murthy RK et al. *N Engl J Med* 2020; 382:597-609; 3. Moulder S et al. *Clin Cancer Res*; 23(14); 4. Stricker et al. *ESMO* 2022; 5. Xeloda® USPI, 2015.

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., L775)
  - HER2 amplified and/or overexpressed tumors (breast, CRC, etc.)
  - Brain metastases
- **Selective** vs. wild-type EGFR
- **Safety/tolerability**: minimal GI and skin toxicity (avoid EGFR-tox)
- **Combinable:** with SOC including ADCs across HER2-driven tumors
- **Convenient:** oral QD or BID

Dose Escalation in solid tumors with HER2 alterations

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

Expansion: 2L+ HER2 mutant NSCLC

- Single-arm study with potential to support accelerated approval

Multiple Indication Opportunities

- 1L HER2 mutant NSCLC +/- SOC
- Evaluate HER2+ CRC and HER2+ Breast in combination with SOC
- Explore other HER2 mutant solid tumors with “basket study”

ADC = Antibody drug conjugate. BID = twice daily. CNS = Central nervous system. CRC = Colorectal cancer. GI = Gastrointestinal. NSCLC = non-small cell lung cancer. SOC = Standard of care. TKI = Tyrosine kinase inhibitors. QD = once daily.

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
HER2 Exon20 Insertion Mutations	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
Common HER2 Point Mutations	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

YVMA: 71% E20IM NSCLC

VC: 11% E20IM NSCLC

22% $HER2^{mut}$ BRC

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

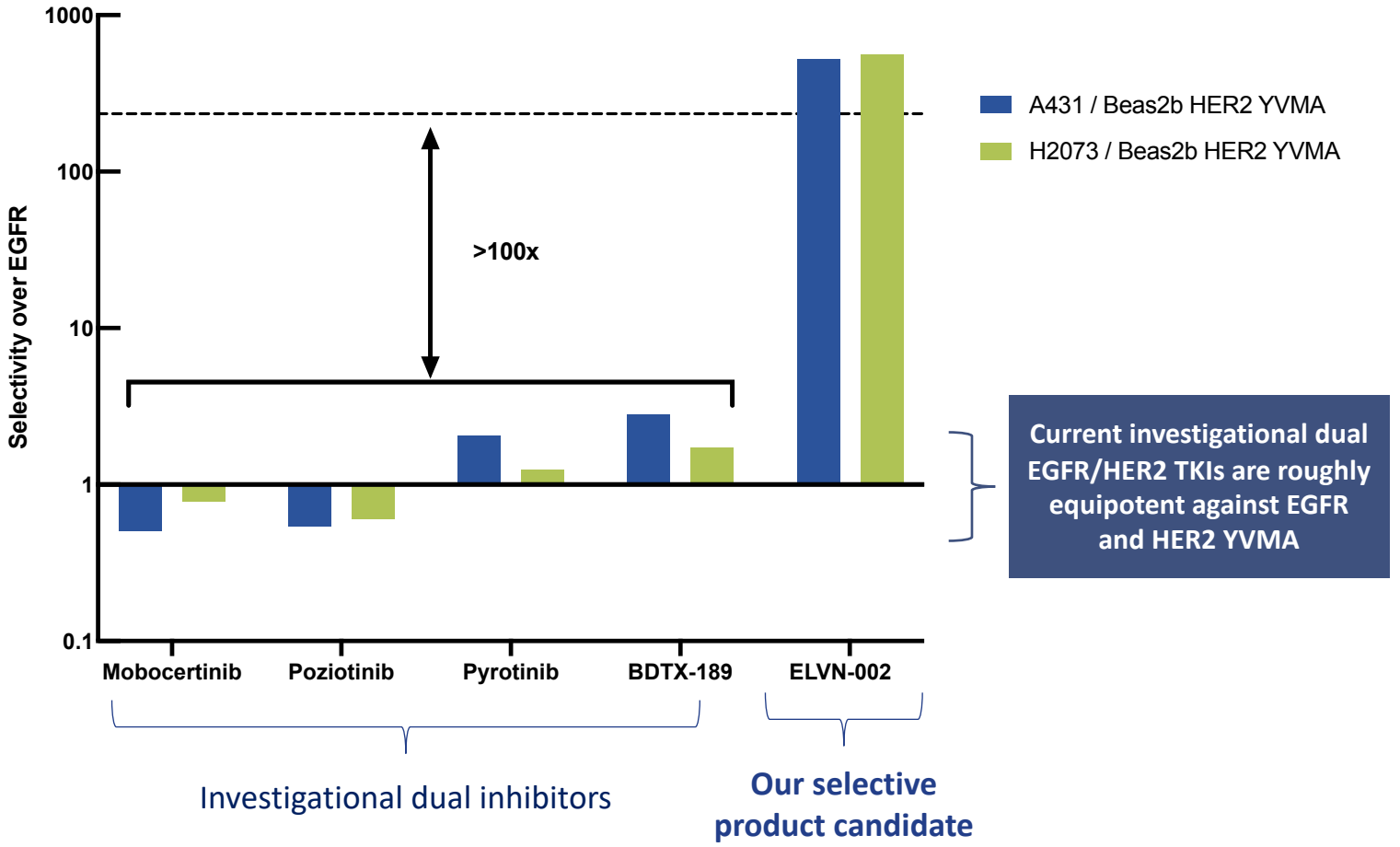
	Poziotinib	Pyrotinib	Tucatinib	ELVN-002
BT474 $HER2^{WT}$ pHER2 IC_{50}	3.5	13	12	13
Beas2b $HER2^{S310F}$ pHER2 IC_{50}	1.9	2	16	2.8
Beas2b $HER2^{L755S}$ pHER2 IC_{50}	**4**	**3.5**	**99**	**4.7**
Beas2b $HER2^{YVMA}$ pHER2 IC_{50}	**2.1**	**5**	**127**	**4.2**
Beas2b $HER2^{YVMA}$ pHER2 IC_{50} in 100% human serum (fold shift)	69 (33x)	324 (65x)	>1000 (~10x)	33 (8x)
BT474 ($HER2^{wt}$) cytotox IC_{50}	0.9	2.3	22	3.9
NCI-N87 ($HER2^{wt}$) cytotox IC_{50}	0.4	2.6	44	3.3
Ba/F3 $HER2^{YVMA}$ cytotox IC_{50}	1.5	3.2	119	5.1
H2073 ($EGFR^{wt}$) pEGFR IC_{50}	1.4	6.4	>10000	2160
A431 ($EGFR^{wt}$) pEGFR IC_{50}	1.3	10	>10000	2290
A431 ($EGFR^{wt}$) cytotox IC_{50}	0.6	75	>10000	*3530*
Human Hepatocyte stability, extraction ratio	68	74	76	22
GSH in human liver cytosol, (% remaining @ 1h)	80%	34%	-	70%
Kinetic Solubility pH 7.4 (uM)	5.6	< 0.1	9.3	260

In contrast to tucatinib, potent pharmacodynamic activity for HER2 YVMA (71% of E20IM NSCLC) & HER2 L755 (22% HER^{mut} BRC)

In contrast to dual inhibitors, our candidates spare EGFR

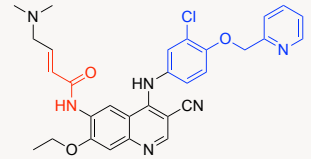
ELVN-002 has exceptional drug like properties and PK profile for a covalent TKI

ELVN-002 was >100x More Selective for HER2 YVMA Relative to EGFR Than Dual EGFR/HER2 Competitors



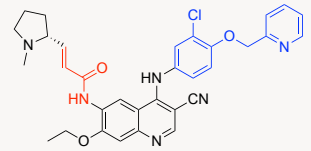
Current investigational dual EGFR/HER2 TKIs are roughly equipotent against EGFR and HER2 YVMA

Lack of Differentiation Across Next Generation TKIs



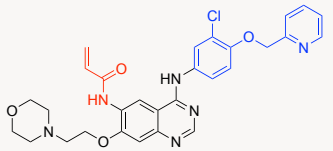
Neratinib

Poor efficacy & tolerability in HER2 mutant setting



Pyrotinib

Phase 1b/2
30% ORR in HER2 mutant NSCLC, poor tolerability



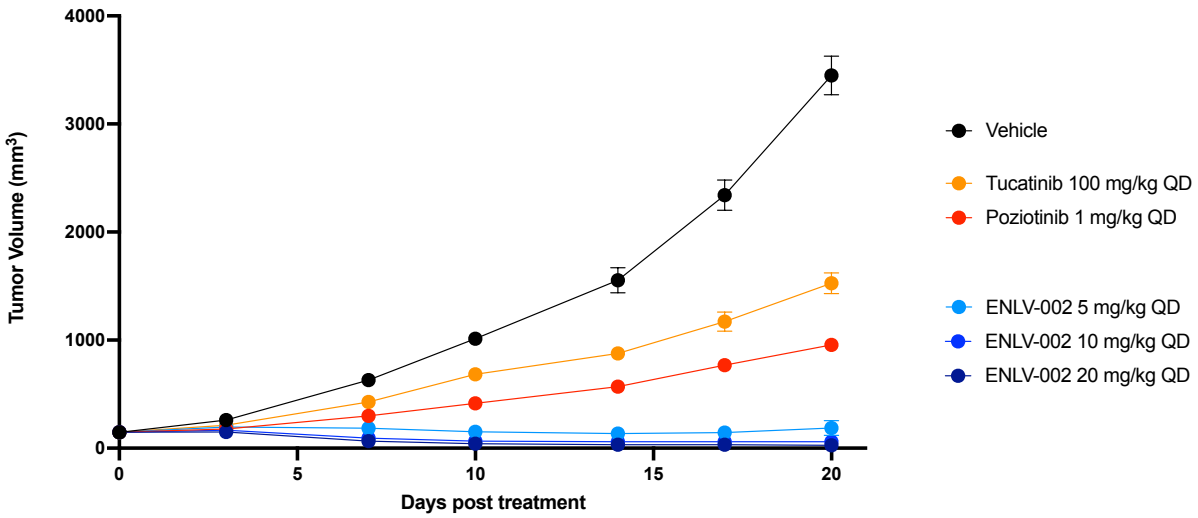
BDTX-189

Poor efficacy & tolerability in HER2 mutant setting

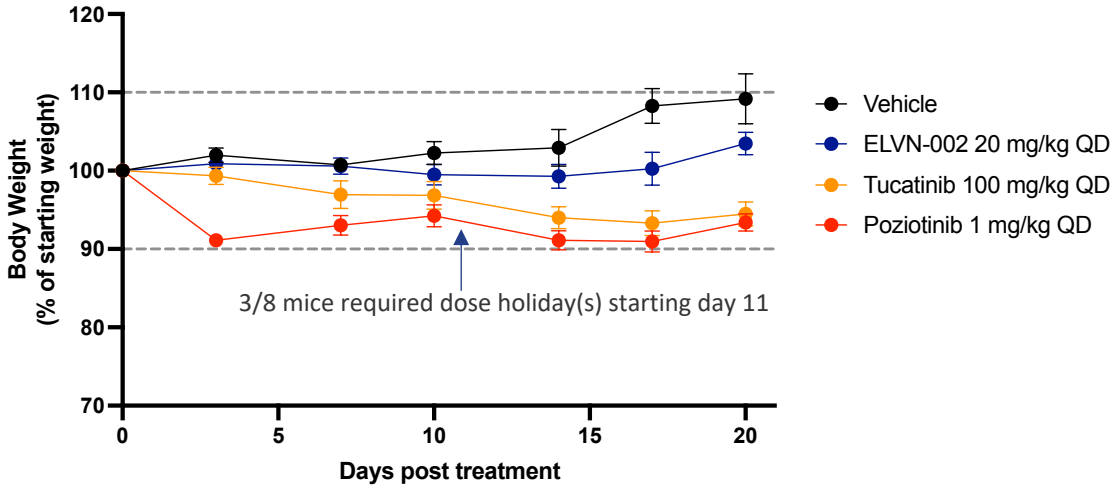
ORR = Overall response rate. NSCLC = Non-small cell lung cancer. TKI = Tyrosine kinase inhibitor.

ELVN-002 Demonstrated Robust Anti-Tumor Activity in Beas2b HER2 YVMA Xenograft Model at Well-Tolerated Doses

Beas2b HER2 YVMA Xenograft TGI



Beas2b HER2 YVMA Xenograft Body Weight Change

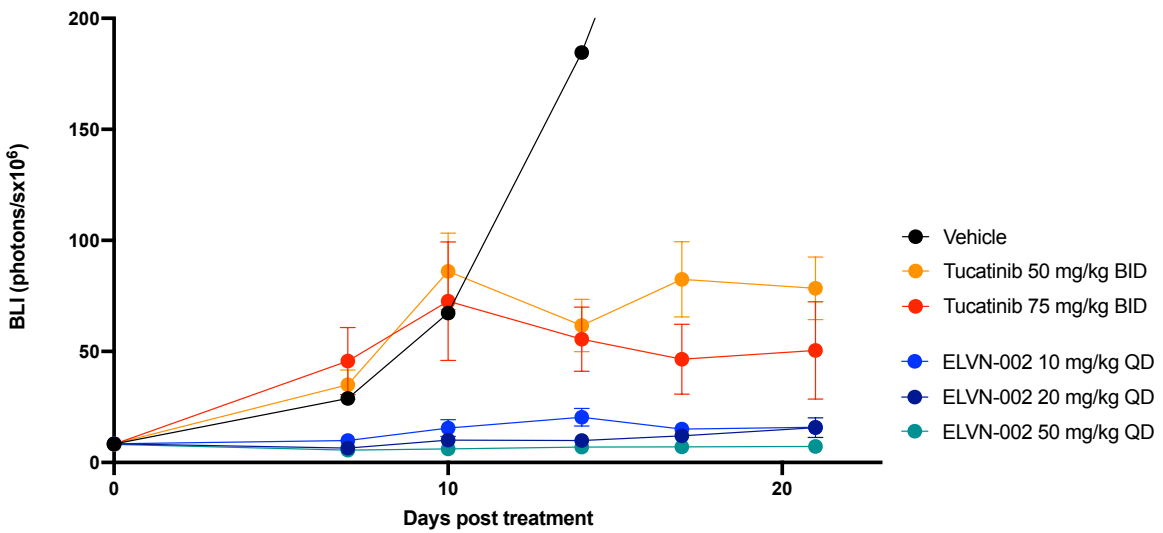


- **Poziotinib's MTD** in this model was 1 mg/kg, and this dose yielded an exposure **~8x its human exposure** at 16 mg QD
- **ELVN-002 yielded deep tumor regressions**, and all doses tested were **well-tolerated**
- **Minimal TGI** vs. YVMA observed with **tucatinib** treatment up to **~14x its human exposure** at 300 mg BID

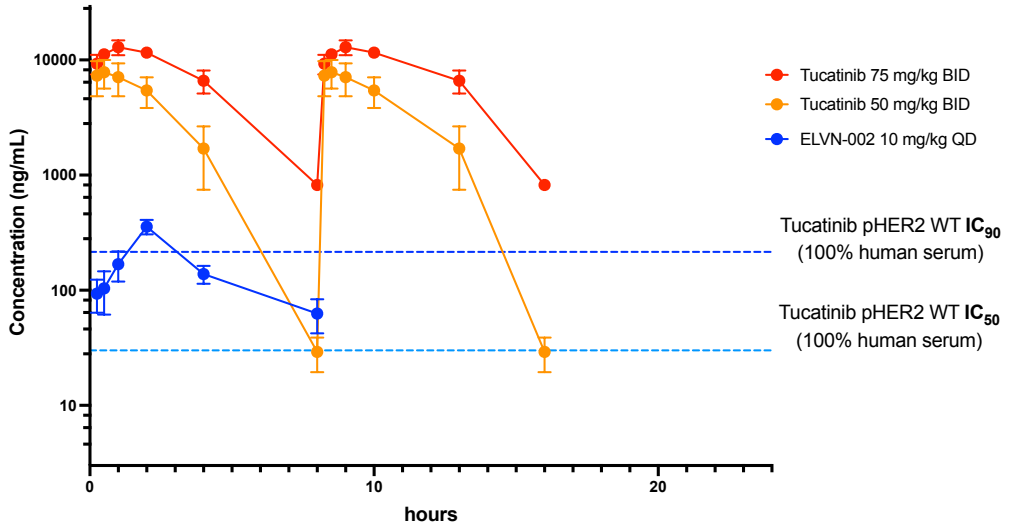
BID = Twice a day. MTD = Maximum tolerated dose. TGI = Tumor growth inhibition. QD = Once a day.

ELVN-002 Demonstrated Robust CNS Anti-Tumor Activity in NCI-N87 HER2 amp Intracranial Model at Well-Tolerated Doses

NCI-N87 HER2^{wt} Intracranial (CNS) Model



Tucatinib vs. ELVN-002 Nude Mouse PK

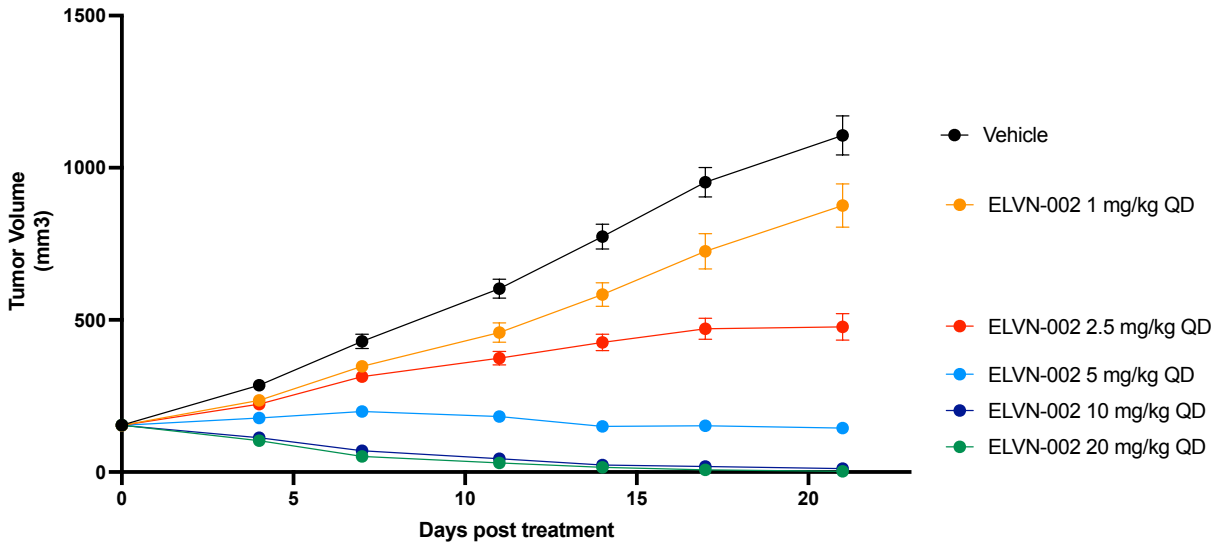


- **ELVN-002 yielded sustained tumor regressions in the NCI-N87 intracranial model**, and all doses tested were **well-tolerated**
- **Tucatinib** treatment of 50 & 75 mg/kg BID results in **~4.5x & ~12x its human exposure** at 300 mg BID
- ELVN-002 exhibited **superior CNS anti-tumor activity at ~40-100x lower exposures** compared to tucatinib in this model

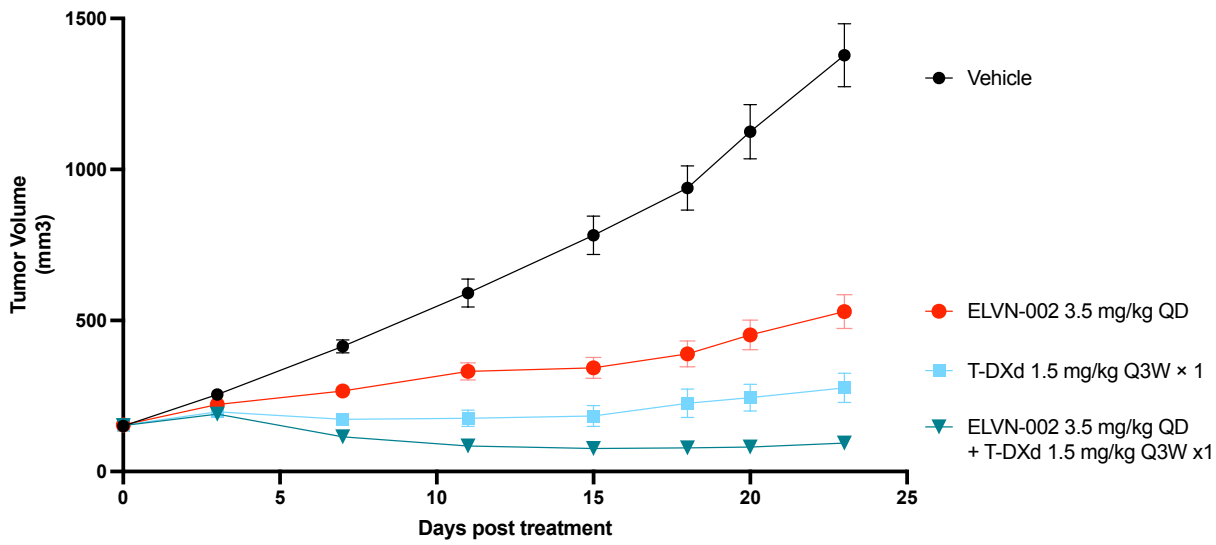
BID = Twice a day. QD = Once a day.

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

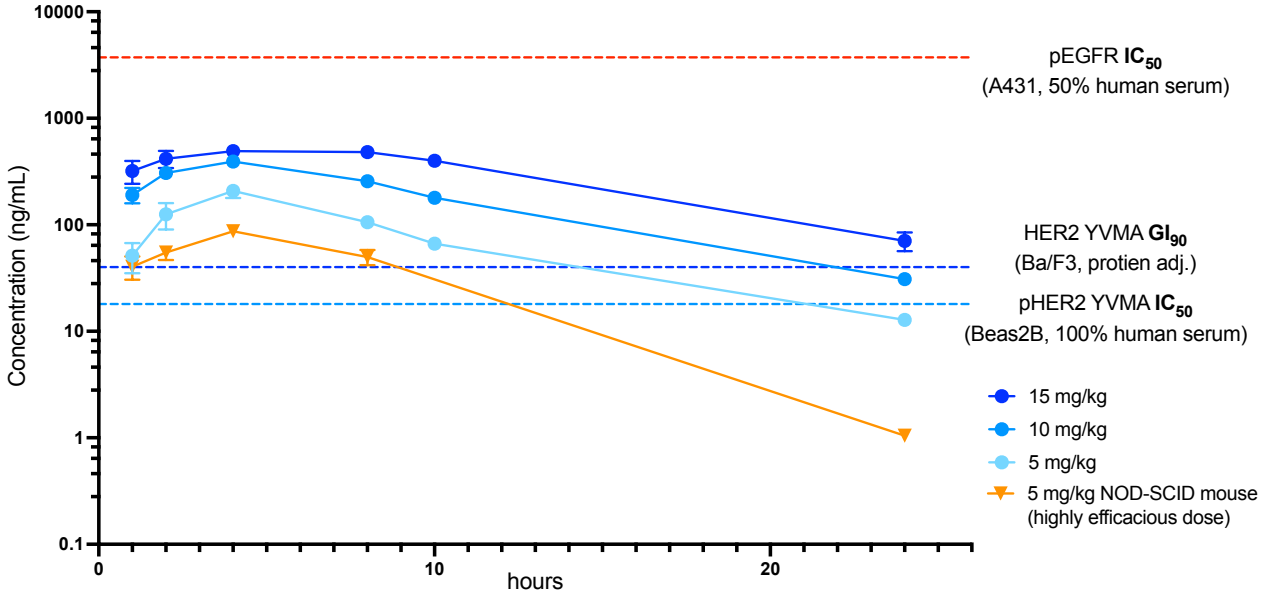


- **ELVN-002 yielded deep tumor regressions** in the NCI-N87 xenograft model, and all doses tested were **well-tolerated**
- **Low dose ELVN-002 combined with Enhertu resulted in additive activity** and deep tumor regressions in the same model
- **In contrast to reversible inhibitors** like tucatinib, 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**

References: Li et al. Cancer Disc 2020; Abraham et al. J Clin Oncol 2019.

ELVN-002 Achieved a Wide Safety Margin in Preclinical Species

ELVN-002 28-day GLP Tox NHP TK



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 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**

NHP = Non-human primate. NOAEL = No observed adverse event level.
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 linearly extrapolated AUC of ELVN-002 at 2.5 mg/kg in Nude mouse, which roughly matches the TGI of Tucatinib at 20 mg/kg BID measured in an NCI-N87 xenograft model
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 1

TRIAL

- 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

TRIAL

- Late line HER2-mutant NSCLC
- Explore based on data
  - Earlier lines of therapy
  - Combinations with approved ADCs (e.g., trastuzumab deruxtecan)

GOALS

- Establish PoC for HER2-mutant NSCLC
- Evaluate intracranial activity and combinability with approved ADCs
- Explore potential beyond NSCLC in other HER2-driven solid tumors (i.e., MBC, CRC, etc.)

Registrational / Phase 3

TRIAL

- File on Late line HER2-mutant NSCLC
- Initial registrational studies H2H against standard of care as mono or combination with HER2 ADC in NSCLC and breast

GOALS

- Accelerated Approval in late line HER2-mutant NSCLC
- Initiate registrational studies in early line MBC and HER2-mutant NSCLC

ADC = Antibody drug conjugate. CRC = Colorectal cancer. MBC = Metastatic breast cancer. NSCLC = Non-small cell lung cancer. PoC = Proof of concept.

Thank You