

# Company Overview

J.P. Morgan 2026 Healthcare Conference

THE NEXT LEAP FORWARD IN PRECISION MEDICINE



**BLOSSOMHILL**  
THERAPEUTICS



**Intelligently designed small molecules  
to address the challenges of cancer treatment resistance with the  
potential for deeper, longer response**



Jun 2020

**\$71M**  
Preferred Series A

Mar 2021

**\$100M**  
Preferred Series B



Feb 2024

**CLK**  
Inhibitor  
(BH-30236)  
First in human

Jun 2024

**OMNI-EGFR™**  
Inhibitor  
(BH-30643)  
First in human

Jan 2025

**\$84M**  
Preferred Series B+



Dec 2025



# Experienced Leadership, Proven Drug Design Expertise

## J. Jean Cui, PhD

Scientific Founder, President and CEO



### Sustained Recognition

Elected to the National Academy of Engineering .....2024

American Chemical Society Heroes of Chemistry .....2013 & 2021

38<sup>th</sup> Annual Inventor of the Year .....2011

## 3 FDA-Approved Cancer Therapeutics

  
**XALKORI®**  
(crizotinib)

Multi-**\$Billion**  
lifetime revenues

2011

  
**LORBRENA®**  
(lorlatinib)

~**\$1Billion**  
annual revenues

2018

Scientific Founder,  
CSO of:

  
**AUGTYRO®**  
(repotrectinib)

Acquired  
by BMS in 2022

2023

## 30 Years of Drug Design and Development



## Our Differentiated, Global, Wholly-Owned Pipeline

Target	Candidate	Indication/Therapeutic Area	Differentiation/Opportunity	Discovery	IND Enabling	Phase 1 Dose Escalation	Phase 1 Dose Expansion
EGFR	BH-30643	EGFR-mutant NSCLC	<ul style="list-style-type: none"><li>• Mutant-selective, non-covalent, macrocyclic OMNI-EGFR inhibitor</li><li>• Potent against classical, atypical, resistance mutations</li></ul>				
CLK	BH-30236	R/R AML and HR-MDS	<ul style="list-style-type: none"><li>• First-in-class opportunity</li></ul>				
	BH-30236 + Venetoclax	R/R AML and HR-MDS	<ul style="list-style-type: none"><li>• Strong pre-clinical synergy</li></ul>				
KRAS	Undisclosed	Oncology	<ul style="list-style-type: none"><li>• Novel chemical scaffold</li></ul>				
Undisclosed Validated Targets	Discovery	Oncology, metabolic and autoimmune diseases	<ul style="list-style-type: none"><li>• Highly selective, macrocycle molecules</li></ul>				



# BH-30643: OMNI-EGFR™ Inhibitor

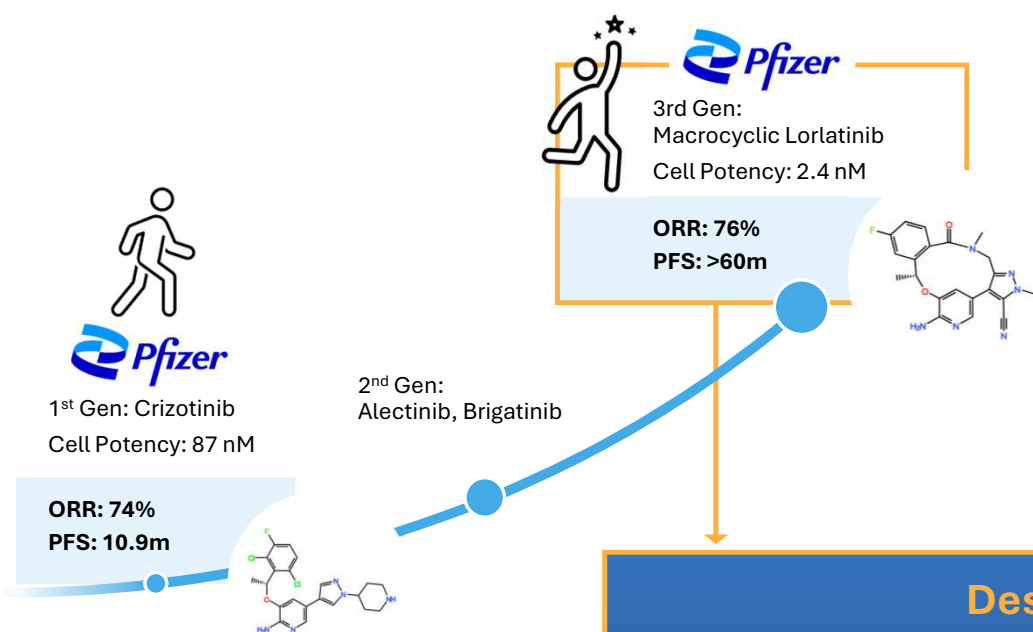
Novel macrocyclic, non-covalent, targeting mutant EGFR active conformation



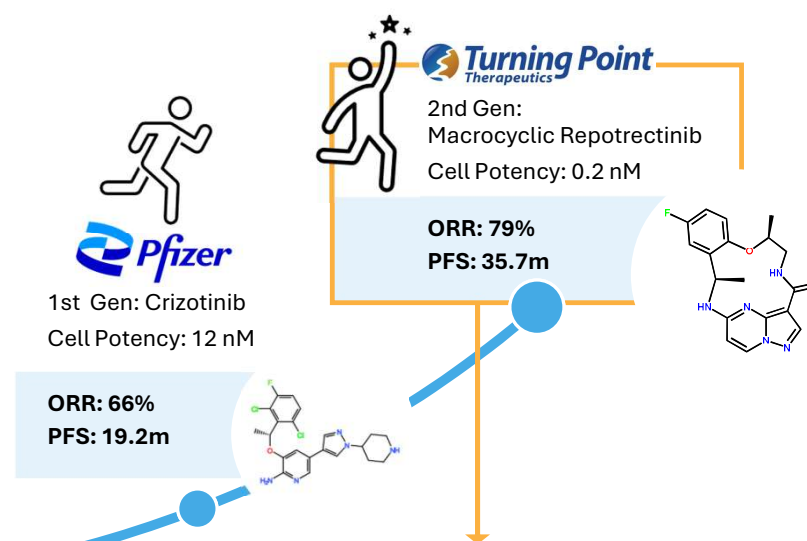
# Making a Leap in Patient Treatment Outcomes

ACHIEVING LONGER PFS AND PRE-EMPTION OF RESISTANCE WITH SUPER-POTENCY

## EML4-ALK Inhibitors in *ALK*<sup>+</sup> NSCLC



## ROS1 Inhibitor in *ROS1*<sup>+</sup> NSCLC



### Design Approach and Attributes

- Macrocyyclic design for conformationally restricted chemotype and precision interactions with target
- Super-potency against both primary and secondary mutations
- Better drug-like properties



# Our Goal: Making the Leap in *EGFR*-mutant NSCLC

## Limitations of Existing *EGFR* TKIs:

- Suboptimal efficacy constrained by wildtype *EGFR*/HER2 toxicity
- Liable to on-target resistance (e.g. T790M, C797S, etc.)
- Targeting only a subset of *EGFR* mutations (eg, classical, PACC, exon 20 insertion, etc.)



1<sup>st</sup> Gen: Gefitinib  
Cell Potency: 20 nM

**PFS: 10-12 months**  
**Resistance: T790M**



2<sup>nd</sup> Gen: Afatinib  
Cell Potency: 1-2 nM

**PFS: 11.3 months**  
**Resistance: T790M**



3<sup>rd</sup> Gen: Osimertinib  
Cell Potency: 8-10 nM

**PFS: 18.9 months**  
**Resistance: C797S**



## Our Goal

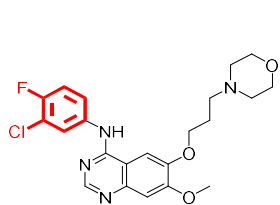
### Making the Leap

There is an urgent medical need for a noncovalent, super potent, mutant-selective OMNI-*EGFR* inhibitor with broad activity, wildtype selectivity, and clean safety profile

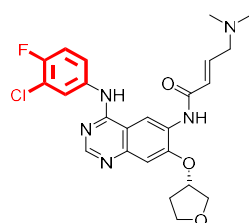


# Existing EGFR Tyrosine Kinase Inhibitors Share Structure Similarities and Common Functional Liabilities

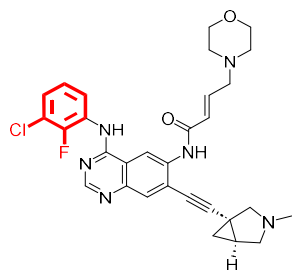
## T790M-resistance



Gefitinib



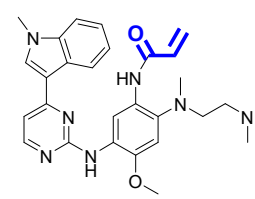
Afatinib



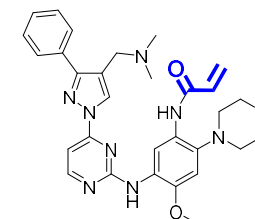
BDTX-1535

Newer EGFR inhibitors commonly iterate on prior designs, **inheriting the same limitations**

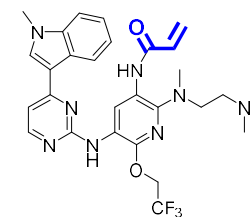
## C797S-resistance



Osimertinib



Lazertinib



Firmonertinib

Many TKIs use a **back-pocket motif** for potency

Gefitinib	Afatinib	STX-721
Erlotinib	Dacomitinib	Zipalertinib
Icotinib	BDTX-1535	Enozertinib

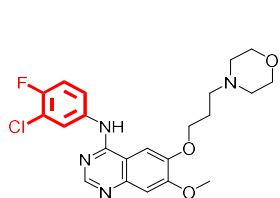
Other TKIs **covalently bind** for potency

Osimertinib	Almonertinib	Mobocertinib
Rociletinib	Aumolertinib	Sunvozertinib
Lazertinib	Olmutinib	Firmonertinib

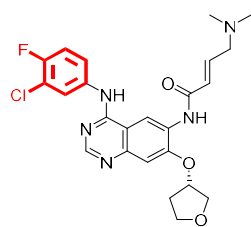


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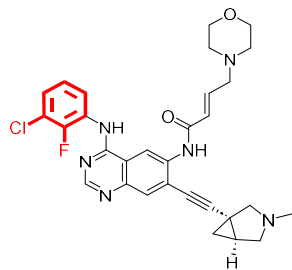
## T790M-resistance



Gefitinib

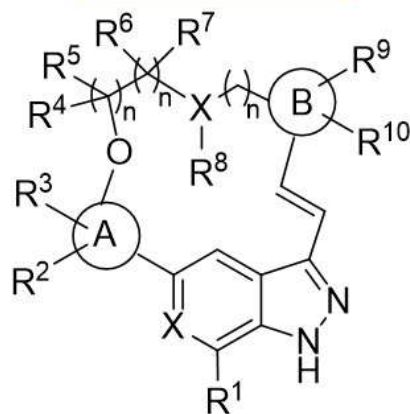


Afatinib



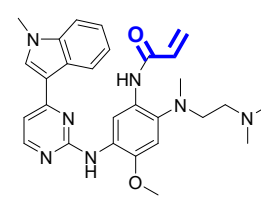
BDTX-1535

## BH-30643

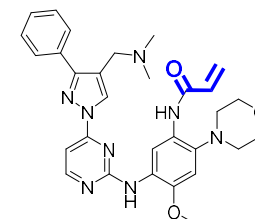


BH-30643 leverages an entirely novel macrocyclic scaffold to uniquely address both T790M and C797S resistance

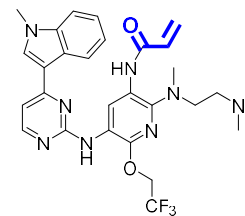
## C797S-resistance



Osimertinib



Lazertinib



Firmonertinib

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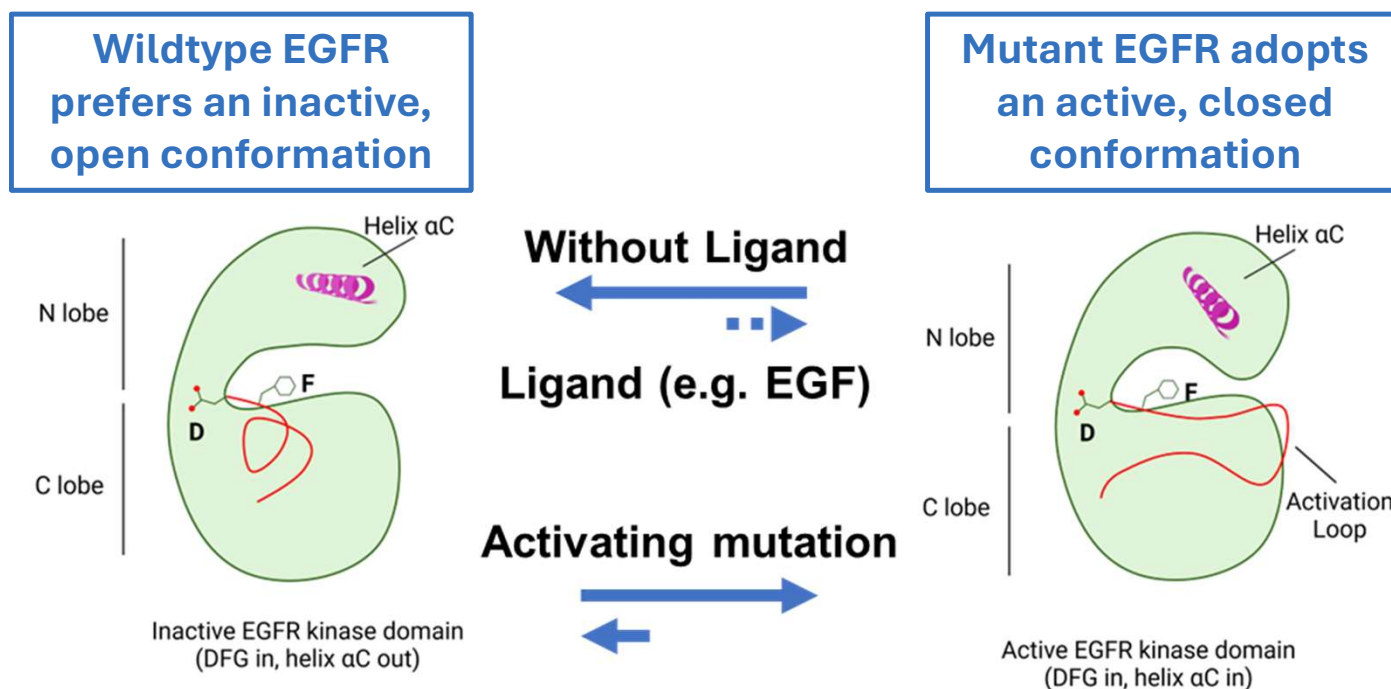
Gefitinib	Afatinib	STX-721
Erlotinib	Dacomitinib	Zipalertinib
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Other TKIs **covalently bind** for potency

Osimertinib	Almonertinib	Mobocertinib
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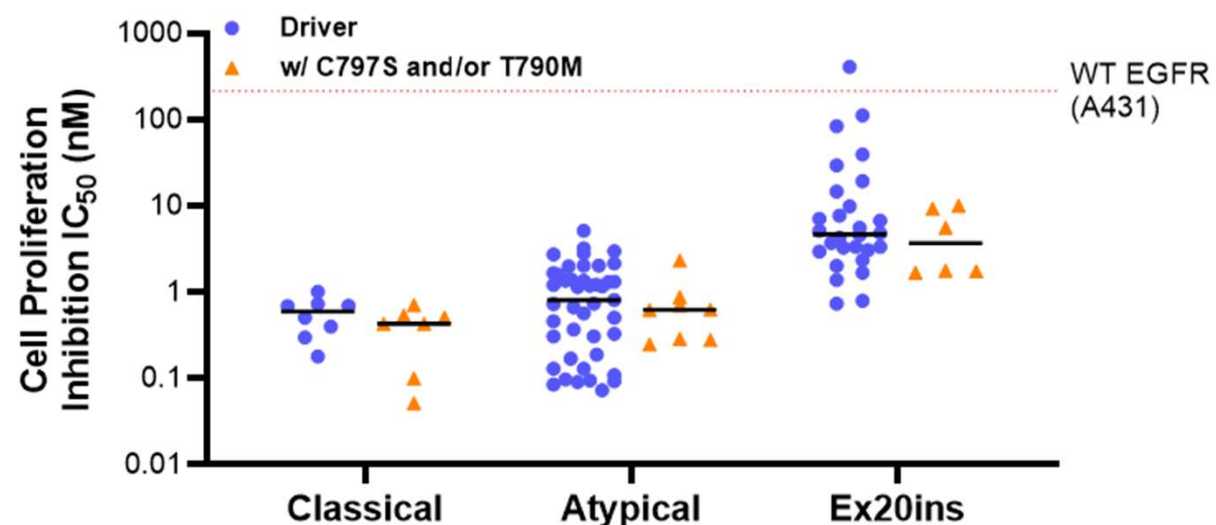
## Design Principle: Targeting the Mutant EGFR Active Conformation



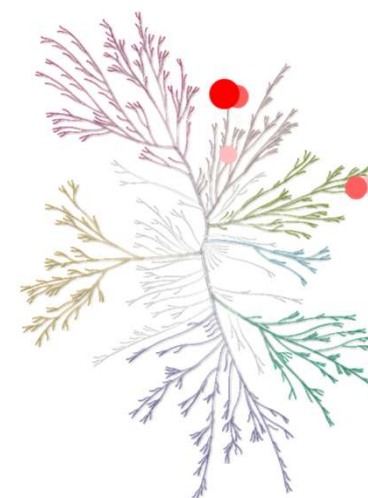
**Targeting the active conformation unlocks the potential for OMNI-EGFR activity**



## BH-30643 Represents a First-in-class OMNI-EGFR Kinase Inhibitor



Selectivity over 371 human WT kinases



EGFR	1	●
HER2, TNIK	1-5 x	●
MINK, HGK, LRRK2	5-20 x	●

$IC_{50}$ (nM): Median (N)	Classical (N=15)	Atypical (N=51)	Ex20ins (N=34)
Driver	0.60 (8)	0.81 (43)	4.73 (28)
w/ C797S and/or T790M	0.43 (7)	0.63 (8)	3.69 (6)

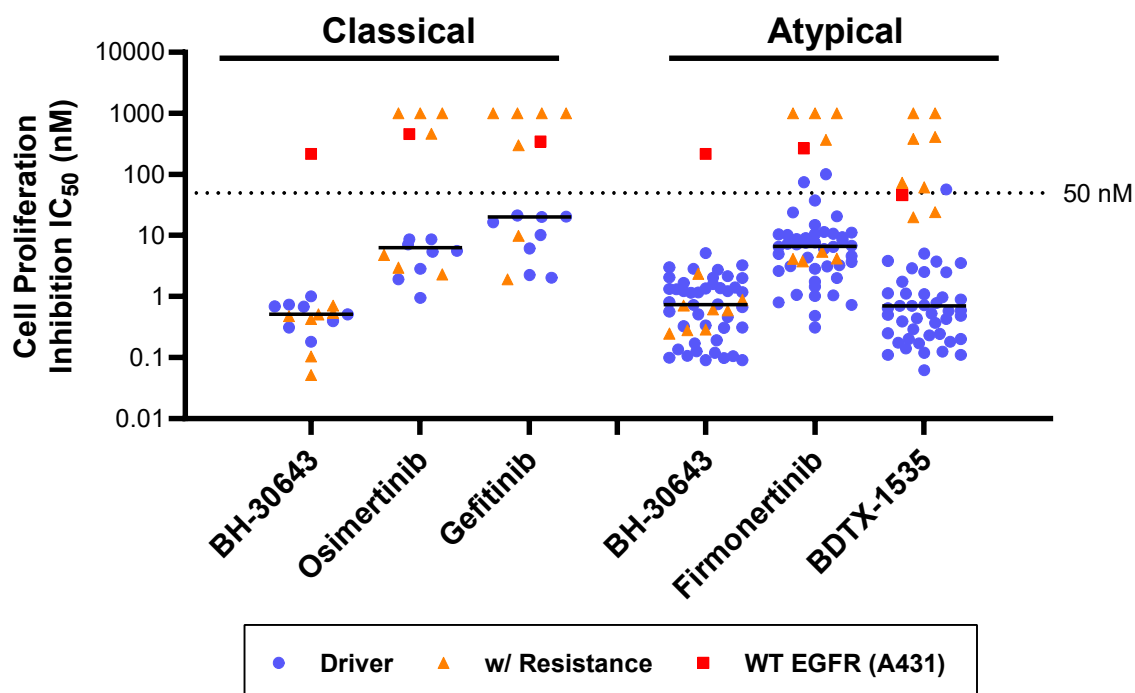
Note: Classical mutations include ex19del, L858R; Atypical mutations with prevalence  $\geq 0.1\%$  (Sisoudiya et al, 2024; *NPI Precision Oncology*) include genetic alterations at G719, L861, S768, E709, L747, V834, L833, V769 and any compounds of these mutations with one another or with classical mutations; Ex20ins mutations include any in-dels in ex20; Resistance mutations include C797S, T790M. The bar in each group indicates median value.



# Unique Design Overcomes the Limitations of Contemporary EGFR TKIs

## BH-30643 has 3 distinguishing features

1. Sub-nM potency against classical EGFR mutations: 10x more potent than osimertinib
2. Wide therapeutic window, avoiding wildtype inhibition and allowing tolerability at high exposures
3. The only molecule which can address both C797S **and** T790M resistance



Note: Classical mutations include ex19del, L858R; Atypical mutations include genetic alterations at G719, L861, S768, E709, L747, V834, L833, V769 and any compounds of these mutations with one another or with classical mutations; Resistance mutations include C797S, T790M. The bar in each group indicates grand median.

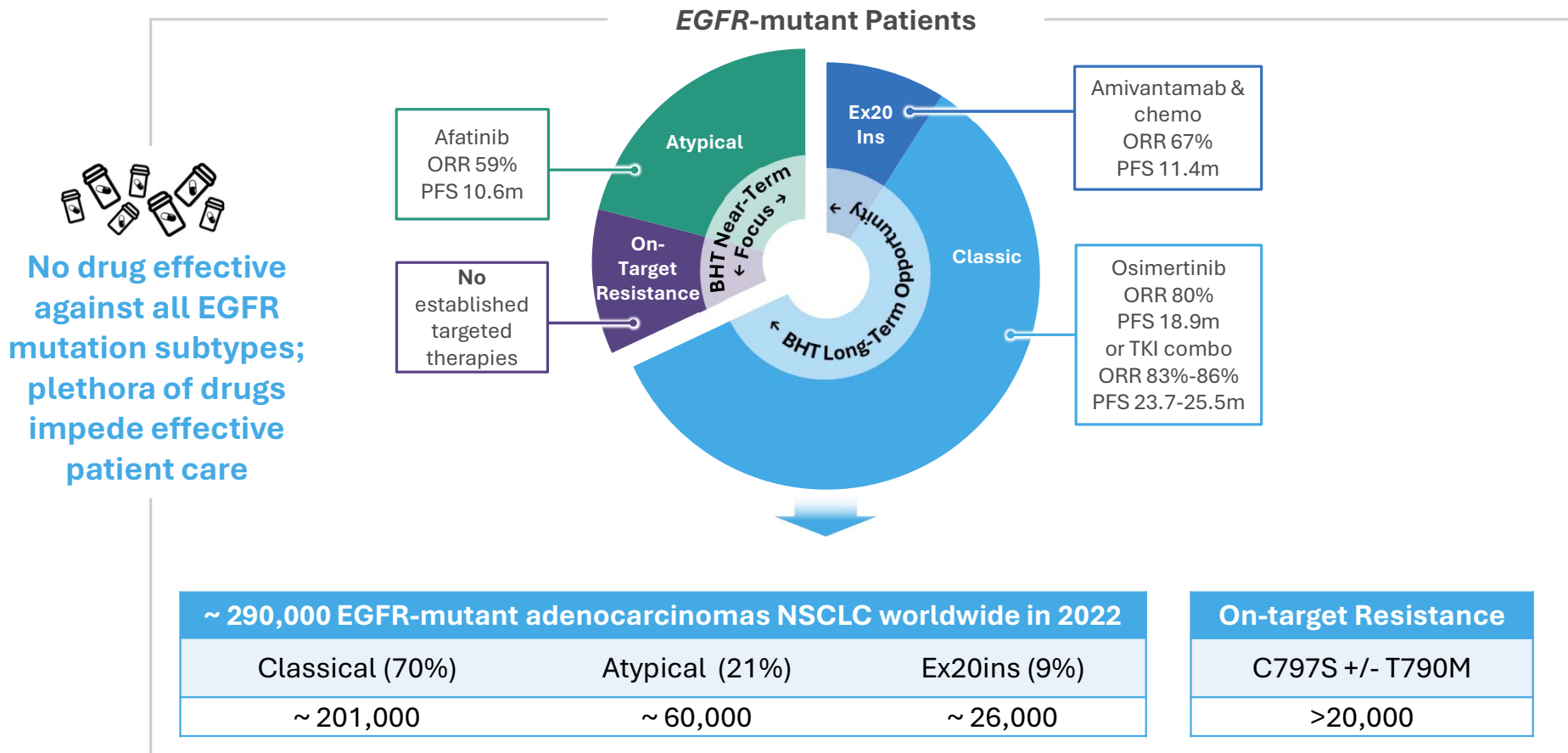


# BH-30643: SOLARA Clinical Trial

Global Phase 1/2 study



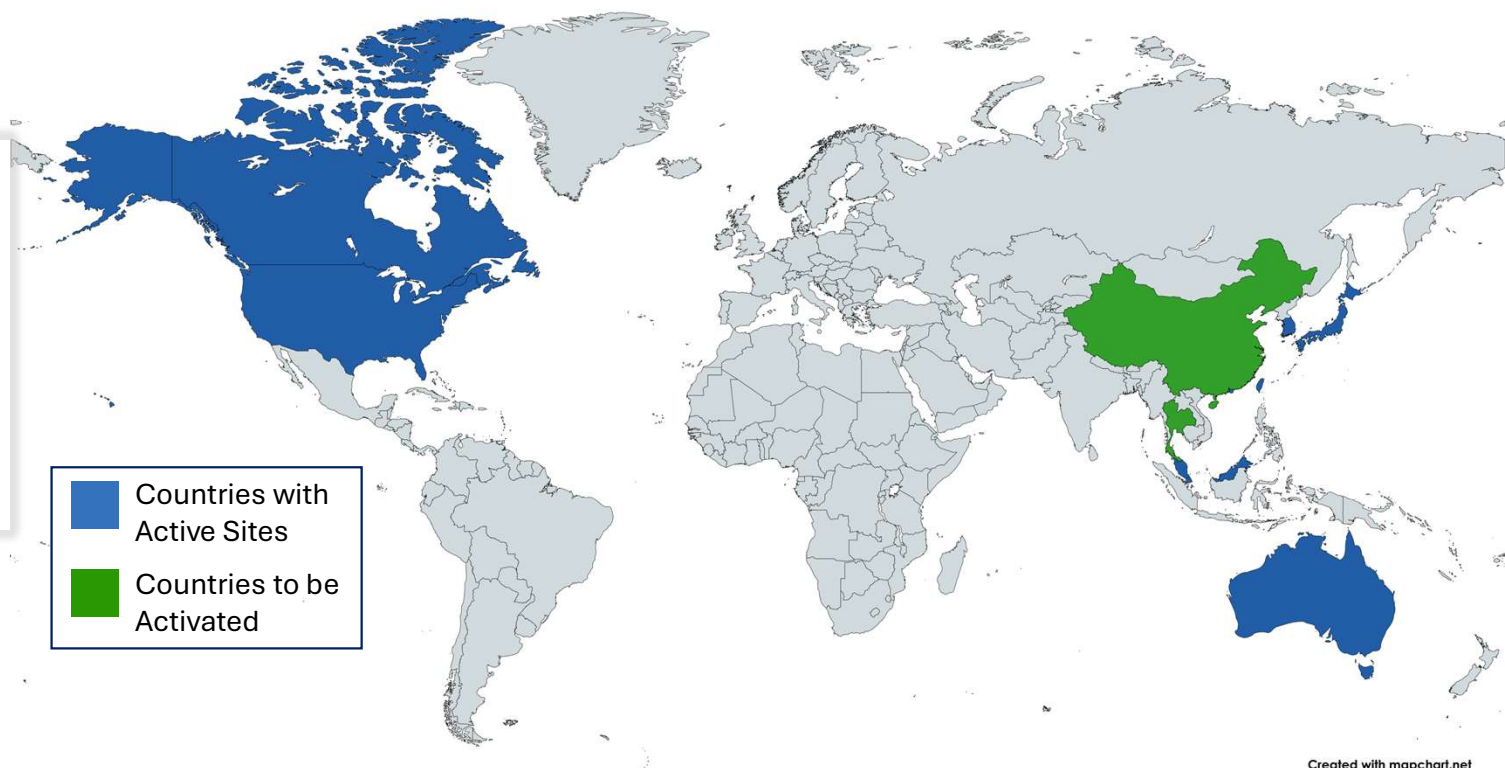
## EGFR-Mutant NSCLC Is a Prevalent Global Disease





## BH-30643-01 (SOLARA) Global Phase 1/2 Clinical Trial

- Global Phase 1/2 trial
- Enrollment initiated January 2025
- Now enrolling at >30 sites in 9 countries

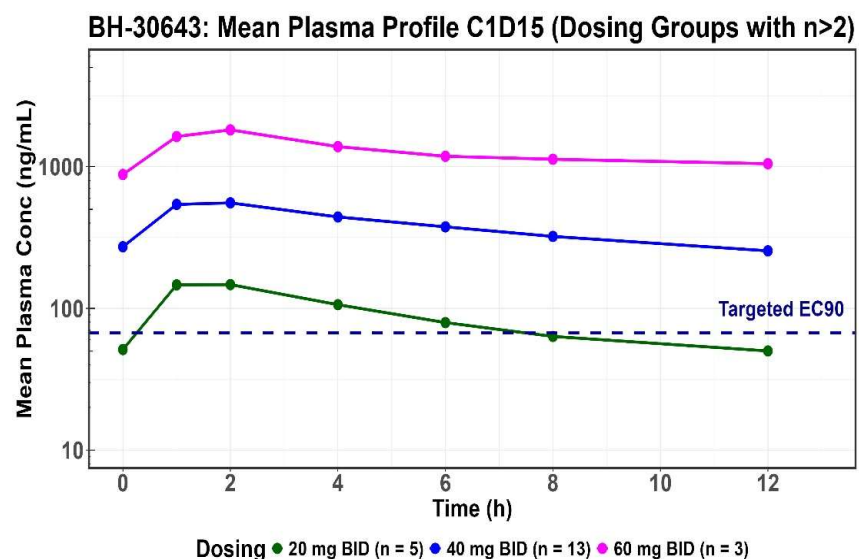


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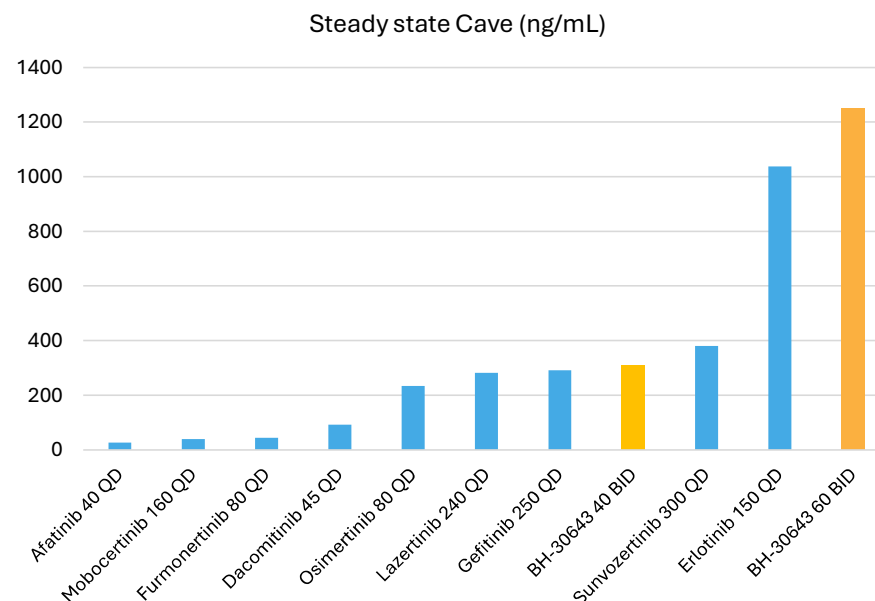


## BH-30643 PK Profile: High and Sustained Exposure

Exposures at doses  $\geq 40$  mg BID well exceed the target  $EC_{90}$



Exposures at candidate dose levels exceed those of many contemporary EGFR TKIs

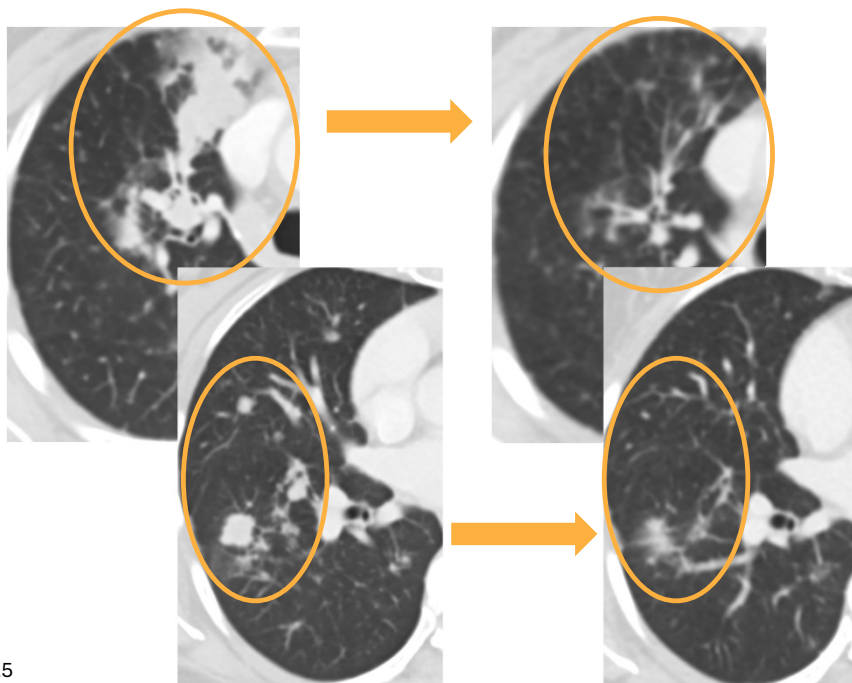


Paired with super-potency, high exposures could permit maximal EGFR inhibition

## Overcomes C797S Resistance Even in the Presence of T790M

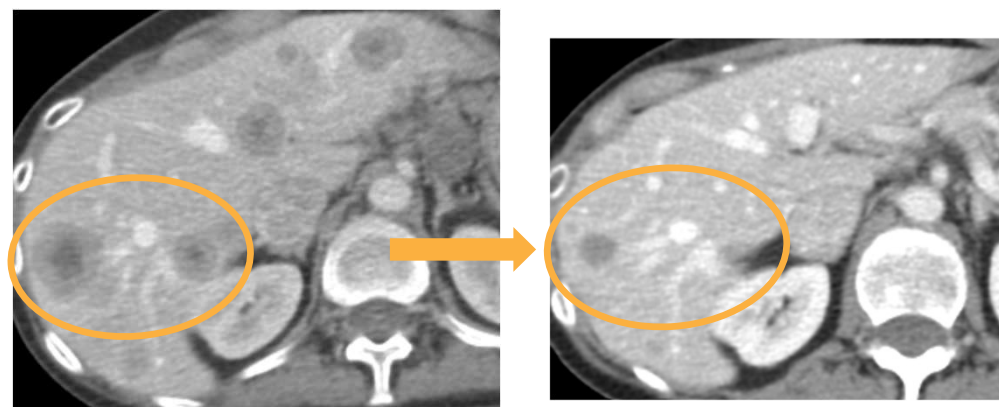
### C797S & exon 19 deletion

- 5 prior lines of therapy including osimertinib, amivantamab, and IO
- Partial response sustained on multiple scans, with therapy ongoing



### C797S & T790M & exon 19 deletion

- 8 prior lines of therapy including osimertinib, investigational TKI, EGFR/met ab, ADC, etc
- Partial response sustained on multiple scans, with therapy ongoing



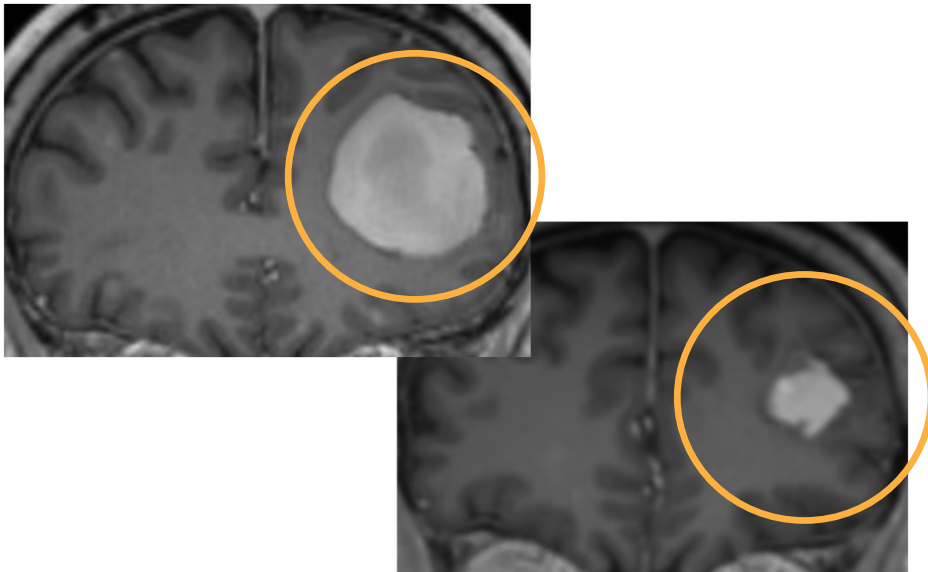
## Breadth of Activity Includes Brain Mets and Atypical EGFR Mutations



18

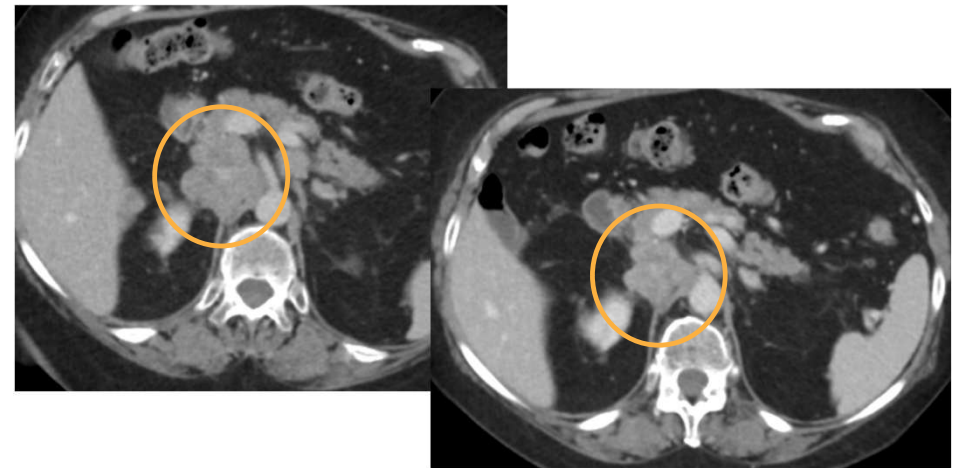
### Exon 20 insertion with brain metastases

- 3 prior lines of chemotherapy
- Partial response sustained on multiple scans, with therapy ongoing
- Sustained CNS improvement in the absence of radiation or steroids



### L861Q (atypical) after multiple TKIs

- 4 prior lines including platinum, erlotinib, osimertinib, and chemo/mobocertinib
- Partial response sustained on multiple scans, with therapy ongoing



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# SOLARA Expansion Cohorts: Now Enrolling Across Multiple Dose Levels



## 6 Expansion Cohorts (n ~20-40 each):

### TKI Pretreated Cohorts

- 1) Classical mutation with C797S resistance
- 2) Atypical mutations after one prior TKI

### TKI-Naive Cohorts

- 3) Classical mutations
- 4) Atypical mutations

### Additional Cohorts

- 5) EGFR exon 20 insertions, up to 2 prior lines
- 6) HER2 mutations, up to 2 prior lines

**Escalation &  
backfill**



**Potentially  
registrational  
Phase 2**

**Each cohort may study multiple doses**



# BH-30236: Macrocyclic CLK Inhibitor

Novel macrocyclic, non-covalent, targeting aberrant alternative splicing

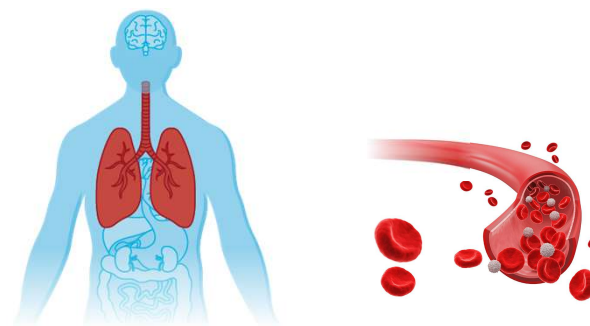
# Targeting Aberrant Alternative Splicing

## Importance of Alternative Splicing



- A single gene can produce multiple forms of a protein via alternative splicing
- Cancer cells can take advantage of this to make proteins that help them grow uncontrollably
- When alternative splicing becomes **dysregulated**, it can **lead to cancer progression and therapeutic resistance**

## Addressing Aberrant Alternative Splicing Extends the Targetable Proteome



### TWO EXAMPLES

#### Lung Cancer

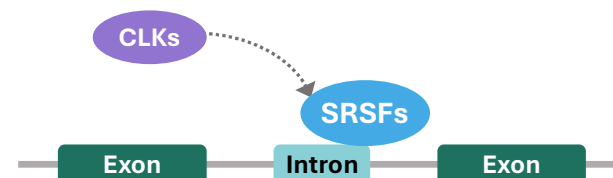
**SRSF1, SRSF6, NUMB, RBM5, RBM6, RBM10, U2AF1**, EGFR, MET, VEGFR, S6K1, MKNK2, AIMP2, BCL2L11, ENHA, KLK8, **DHX9**

#### AML/Blood Cancers

**SF3B1, HNRNPK**, p53, p21, Cebpa, Cebpb, **U2AF1, SRSF2, ZRSR2, PRPF8**, SFPQ/PSF, **DDX41**, CD22, IKZF1, **WT1, SMC1A**

**Red** = Spliceosome genes (mutated/aberrantly expressed)

## Importance of CLK

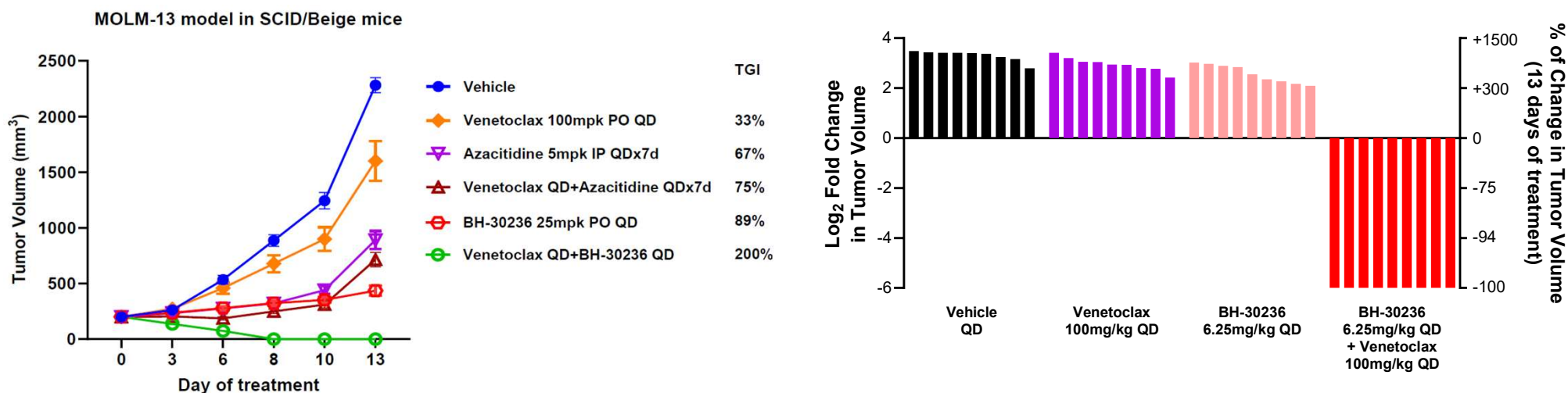


- CDC-like kinases (CLKs) can modulate aberrant splicing via phosphorylation of SRSF proteins
- Restoring normal splicing function is key to overcome off-target resistance in cancer
- Initial CLK inhibitors (eg. CTX-712) have demonstrated proof of concept

## Synergistic Effect of CLK Inhibition in AML Models

- Hematologic malignancies such as AML are especially dependent upon aberrant alternative splicing
- In AML models, CLK inhibition with BH-30236 could overcome venetoclax resistance, even when dosed at low dose levels (6.25 mg QD of BH-30236, equivalent to 30 mg QD in human)

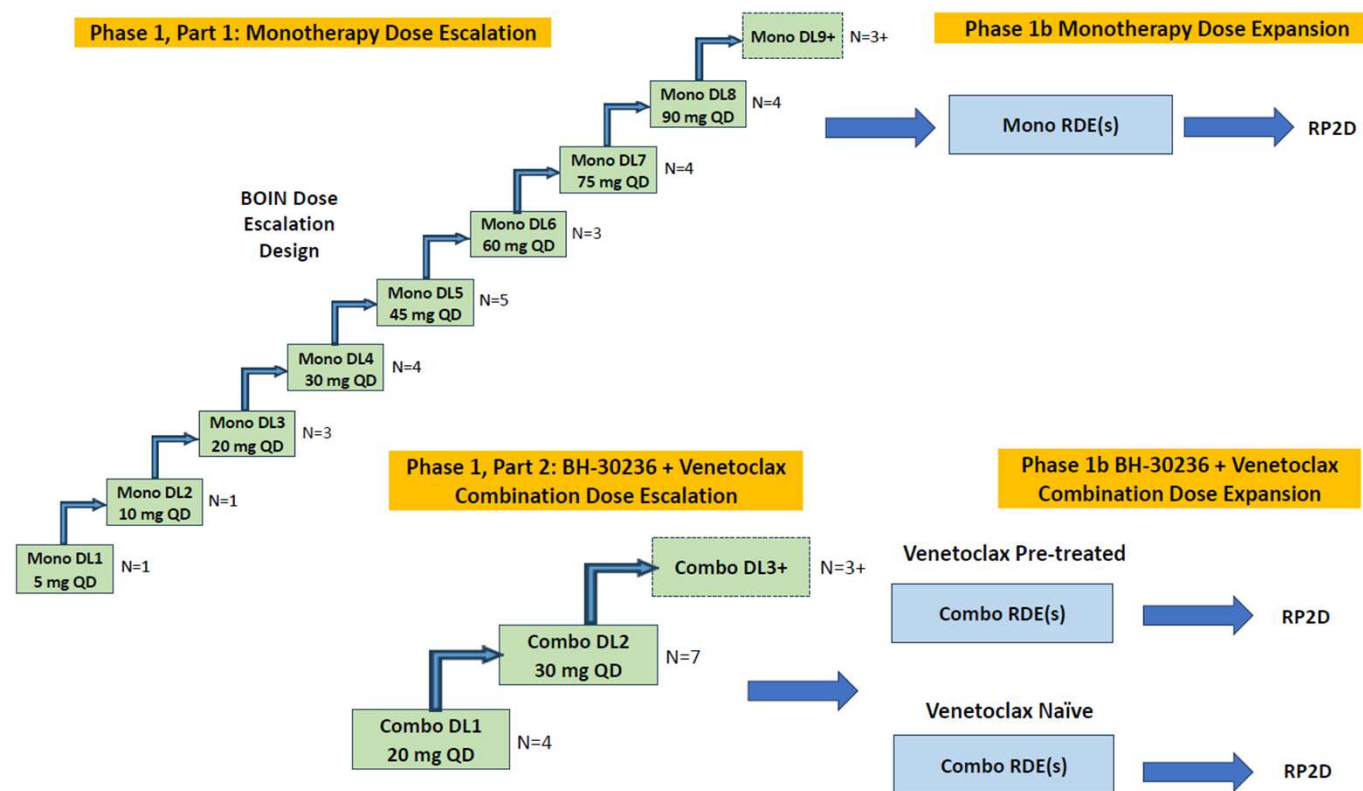
### Anti-tumor Activity of BH-30236 in Combination with Venetoclax in MOLM-13 CDX Tumors



# BH-30236: On-going Phase 1 FIH Study in AML/HR-MDS

**Objective: Evaluate safety & tolerability, identify doses for expansion**

- Monotherapy dose escalation on-going across multiple US sites
- Now studying dose level 9, with no safety limitations seen with continuous daily dosing
- Combination dose escalation with venetoclax (target dose 400 mg daily) has now initiated





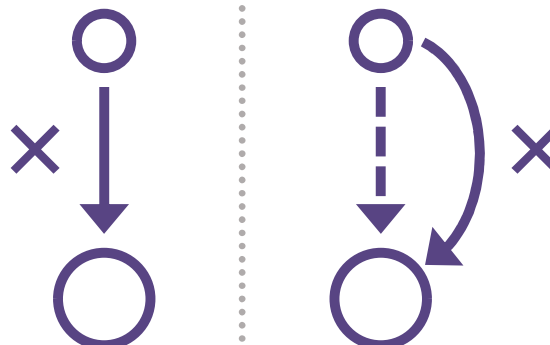
# Making a Transformational Leap in Cancer Therapy

# Intelligently Designed Molecules to Address the Challenges of Cancer Treatment Resistance



## BH-30643

- Novel, non-covalent, brain-active, macrocyclic OMNI-EGFR inhibitor
- Super-potency across broad spectrum of EGFR mutations with good selectivity over wild-type
- Favorable PK & safety profile
- Anti-tumor activity in resistant cancers including CNS activity
- SOLARA trial expansion cohorts are enrolling well in TKI-naïve and TKI-pretreated NSCLC



## BH-30236

- Potent macrocyclic CLK inhibitor
- Modulating splicing, DNA damage repair and apoptosis pathways
- Strong synergy with venetoclax in preclinical models
- No safety limitation with continuous daily dosing
- Combination study with venetoclax is actively enrolling

**Clinical trial data readouts anticipated in 2026**