Company Overview

J.P. Morgan 2026 Healthcare Conference

THE NEXT LEAP FORWARD IN PRECISION MEDICINE

BLOSSOMHILL THERAPEUTICS

BLOSSOMHILL THERAPEUTICS

Intelligently designed small molecules

to address the challenges of cancer treatment resistance with the potential for deeper, longer response

Jun 2020 — BLOSSOMHILL THERAPEUTICS — Founded in San Diego, CA

Mar 2021 — **$71M** Preferred Series A — Cormorant Asset Management, VIVO CAPITAL, orbimed, HERCULES BioVentures

Feb 2024 — **$100M** Preferred Series B — COLT VENTURES, PLAISANCE CAPITAL MANAGEMENT, orbimed, Cormorant Asset Management, VIVO CAPITAL

Jun 2024 — **CLK** Inhibitor (BH-30236) First in human

Jan 2025 — **OMNI-EGFR™** Inhibitor (BH-30643) First in human

Dec 2025 — **$84M** Preferred Series B+ — Janus Henderson INVESTORS, Brahma Capital, BioTrack Capital, Cormorant Asset Management, orbimed, PLAISANCE CAPITAL MANAGEMENT, VIVO CAPITAL

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**

38th Annual Inventor of the Year **2011**

3 FDA-Approved Cancer Therapeutics

2011

Pfizer

XALKORI® (crizotinib)

Multi-$Billion lifetime revenues

2018

Pfizer

LORBRENA® (lorlatinib)

~$1Billion annual revenues

2023

Scientific Founder, CSO of:

Turning Point Therapeutics

AUGTYRO® (repotrectinib)

Acquired by BMS in 2022

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	• Mutant-selective, non-covalent, macrocyclic OMNI-*EGFR* inhibitor • Potent against classical, atypical, resistance mutations				
CLK	BH-30236	R/R AML and HR-MDS	• First-in-class opportunity				
	BH-30236 + Venetoclax	R/R AML and HR-MDS	• Strong pre-clinical synergy				
KRAS	Undisclosed	Oncology	• Novel chemical scaffold				
Undisclosed Validated Targets	Discovery	Oncology, metabolic and autoimmune diseases	• Highly selective, macrocycle molecules				

BH-30643: OMNI-EGFR™ Inhibitor

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

Making a Leap in Patient Treatment Outcomes

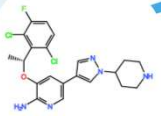
ACHIEVING LONGER PFS AND PRE-EMPTION OF RESISTANCE WITH SUPER-POTENCY

EML4-ALK Inhibitors in *ALK*+ NSCLC

Pfizer

1st Gen: Crizotinib
Cell Potency: 87 nM

ORR: 74%
PFS: 10.9m

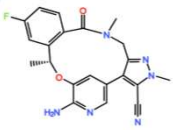


2nd Gen:
Alectinib, Brigatinib

Pfizer

3rd Gen:
Macrocyclic Lorlatinib
Cell Potency: 2.4 nM

ORR: 76%
PFS: >60m

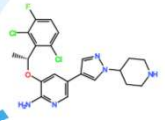


ROS1 Inhibitor in *ROS1*+ NSCLC

Pfizer

1st Gen: Crizotinib
Cell Potency: 12 nM

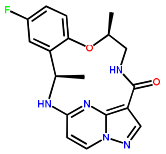
ORR: 66%
PFS: 19.2m



Turning Point Therapeutics

2nd Gen:
Macrocyclic Repotrectinib
Cell Potency: 0.2 nM

ORR: 79%
PFS: 35.7m



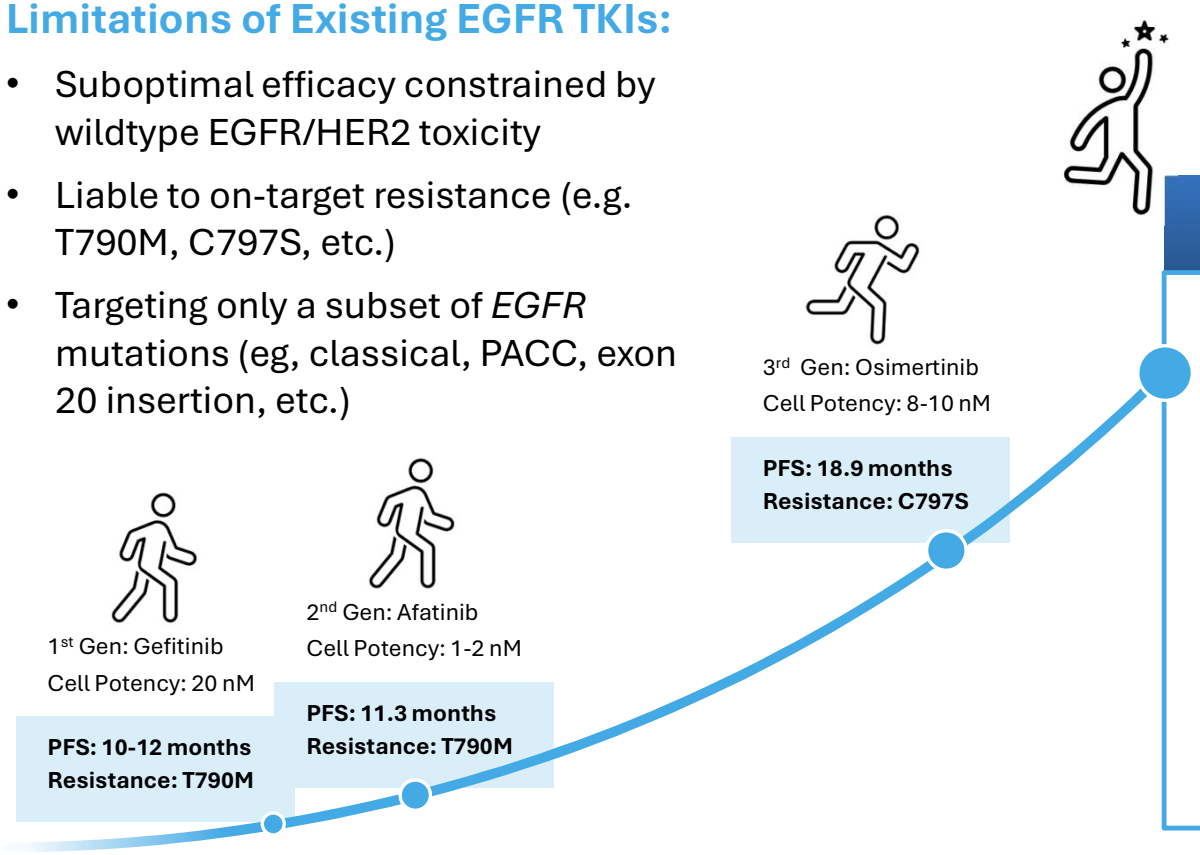
Design Approach and Attributes

- Macrocyclic 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.)



BLOSSOMHILL THERAPEUTICS

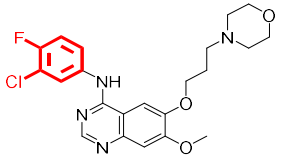
Our Goal

Making the Leap

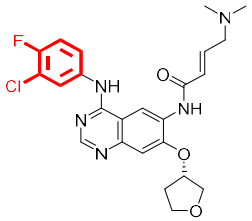
There is an urgent medical need for a noncovalent, super potent, mutant-selective OMNI-EGFR inhibitor with broad activity, wildtype selectivity, and clean safety profile

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

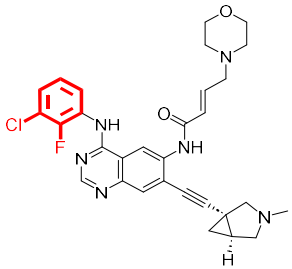
T790M-resistance



Gefitinib

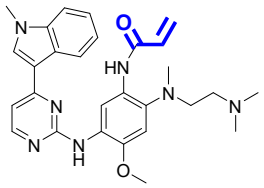


Afatinib

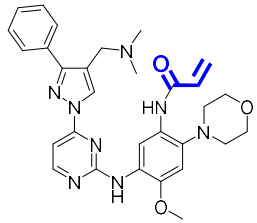


BDTX-1535

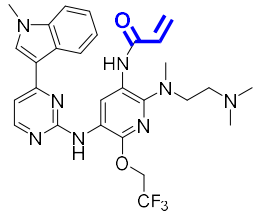
C797S-resistance



Osimertinib



Lazertinib



Firmonertinib

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

Many TKIs use a back-pocket motif for potency

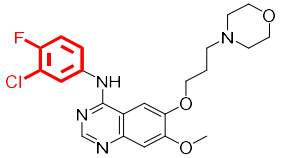
Gefitinib	Afatinib	STX-721
Erlotinib	Dacomitinib	Zipalertinib
Icotinib	BDTX-1535	Enozertinib

Other TKIs covalently bind for potency

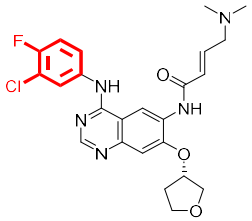
Osimertinib	Almonertinib	Mobocertinib
Rociletinib	Aumolertinib	Sunvozertinib
Lazertinib	Olmutinib	Firmonertinib

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

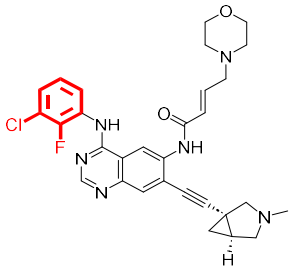
T790M-resistance



Gefitinib

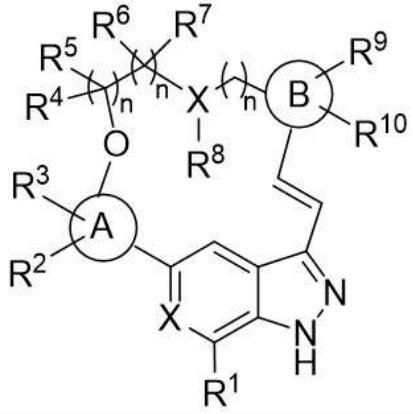


Afatinib



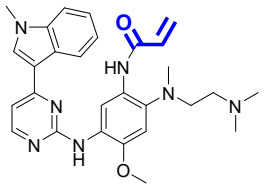
BDTX-1535

BH-30643

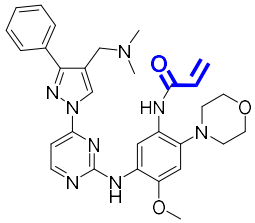


BH-30643 leverages an entirely novel macrocyclic scaffold to uniquely address both T790M and C797S resistance

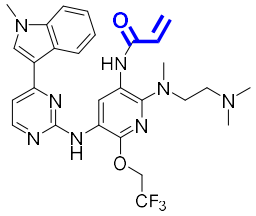
C797S-resistance



Osimertinib



Lazertinib



Firmonertinib

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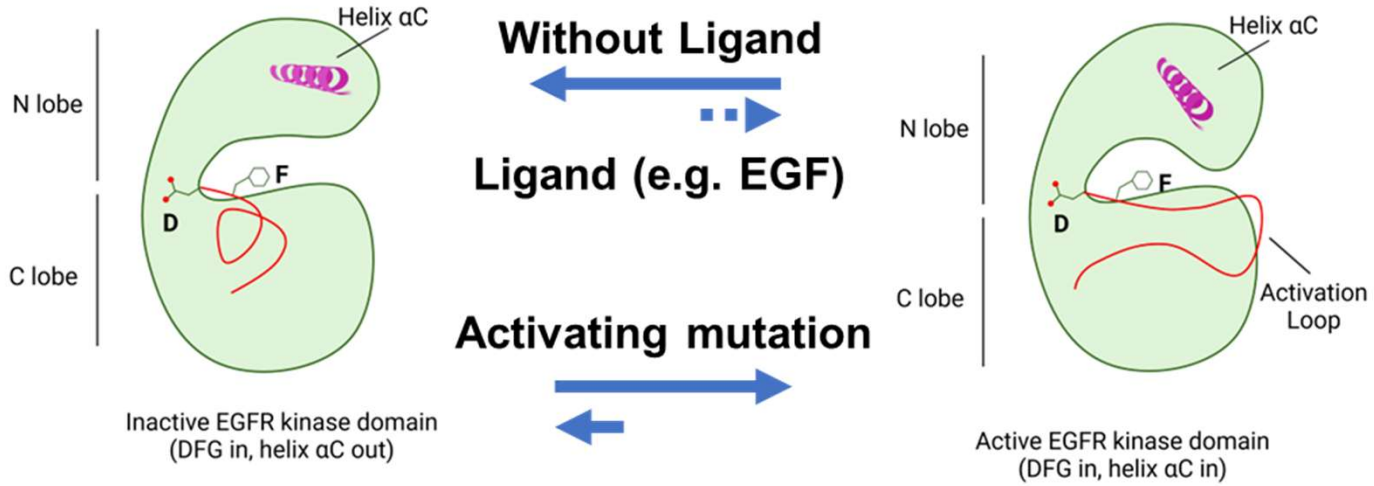
Other TKIs covalently bind for potency

Osimertinib	Almonertinib	Mobocertinib
Rociletinib	Aumolertinib	Sunvozertinib
Lazertinib	Olmutinib	Firmonertinib

Design Principle: Targeting the Mutant EGFR Active Conformation

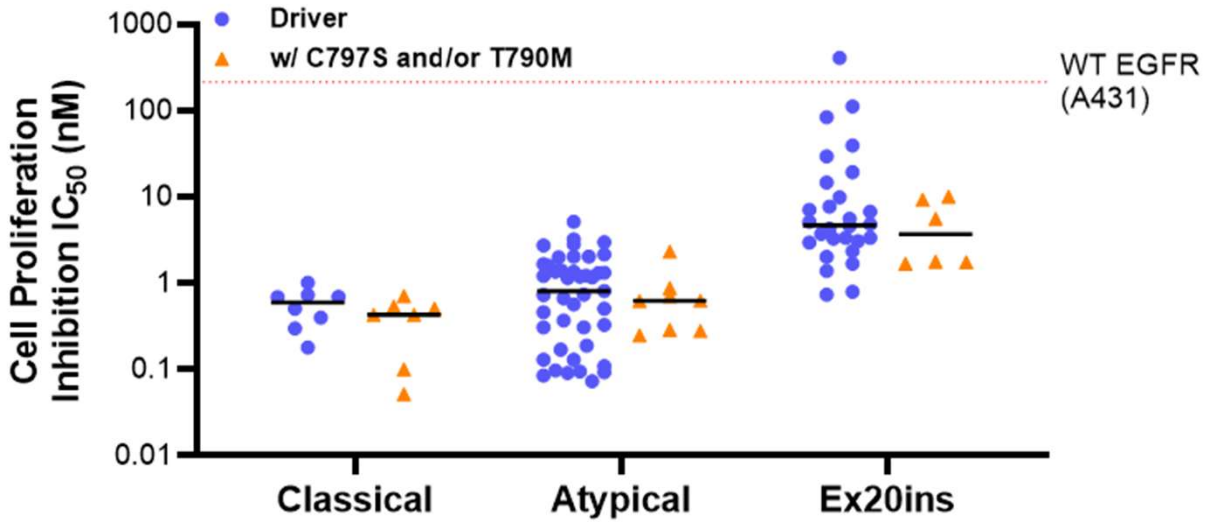
Wildtype EGFR prefers an inactive, open conformation

Mutant EGFR adopts an active, closed conformation



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

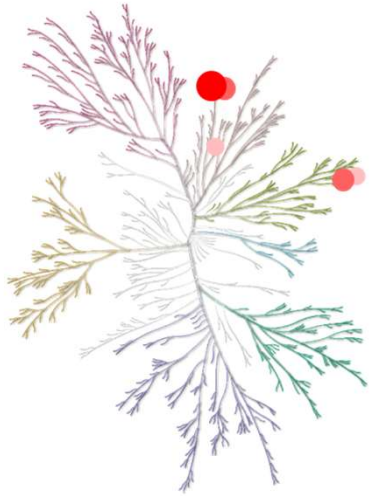
BH-30643 Represents a First-in-class OMNI-EGFR Kinase Inhibitor



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 ≥ 0.1% (Sisoudiya et al, 2024; *NPJ 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.

Selectivity over 371 human WT kinases

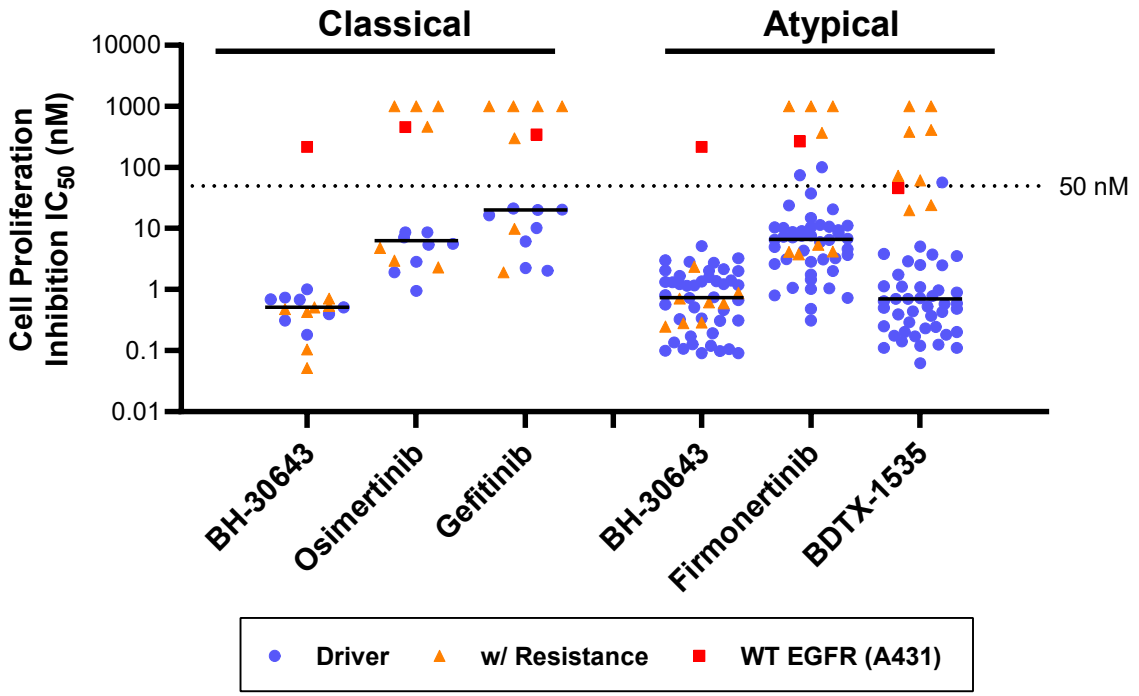


EGFR	1
HER2, TNIK	1-5 x
MINK, HGK, LRRK2	5-20 x

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



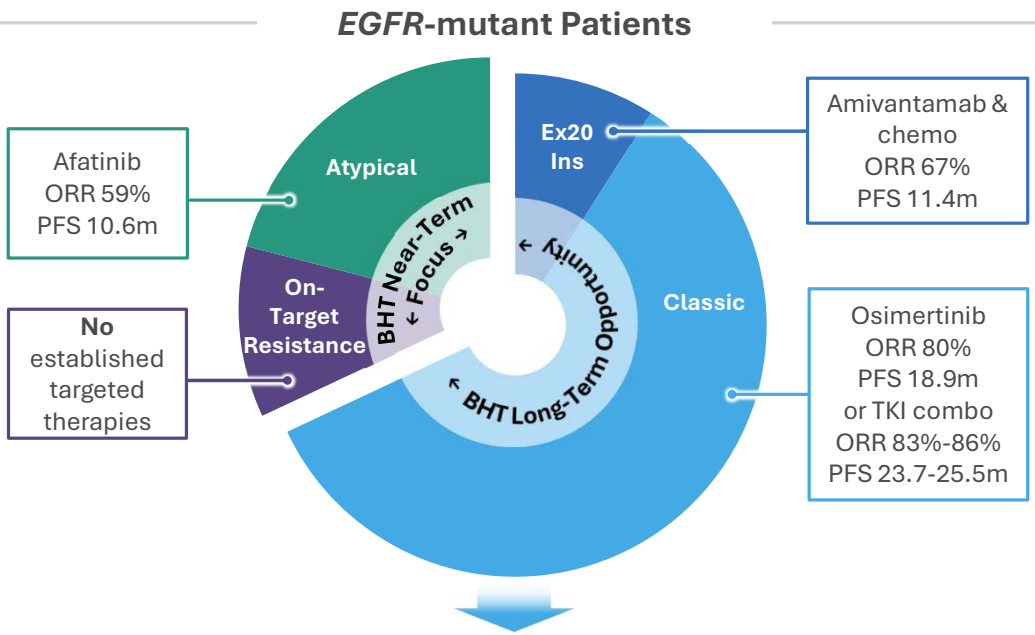
Note: Classical mutations include ex19del, L858R; Atypical mutations include genetic alterations at G719, L861, S768, E709, L747, V834, L833, V769 and any compounds of these mutations with one another or with classical mutations; Resistance mutations include C797S, T790M. The bar in each group indicates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

BH-30643: SOLARA Clinical Trial

Global Phase 1/2 study

EGFR-Mutant NSCLC Is a Prevalent Global Disease

No drug effective against all EGFR mutation subtypes; plethora of drugs impede effective patient care



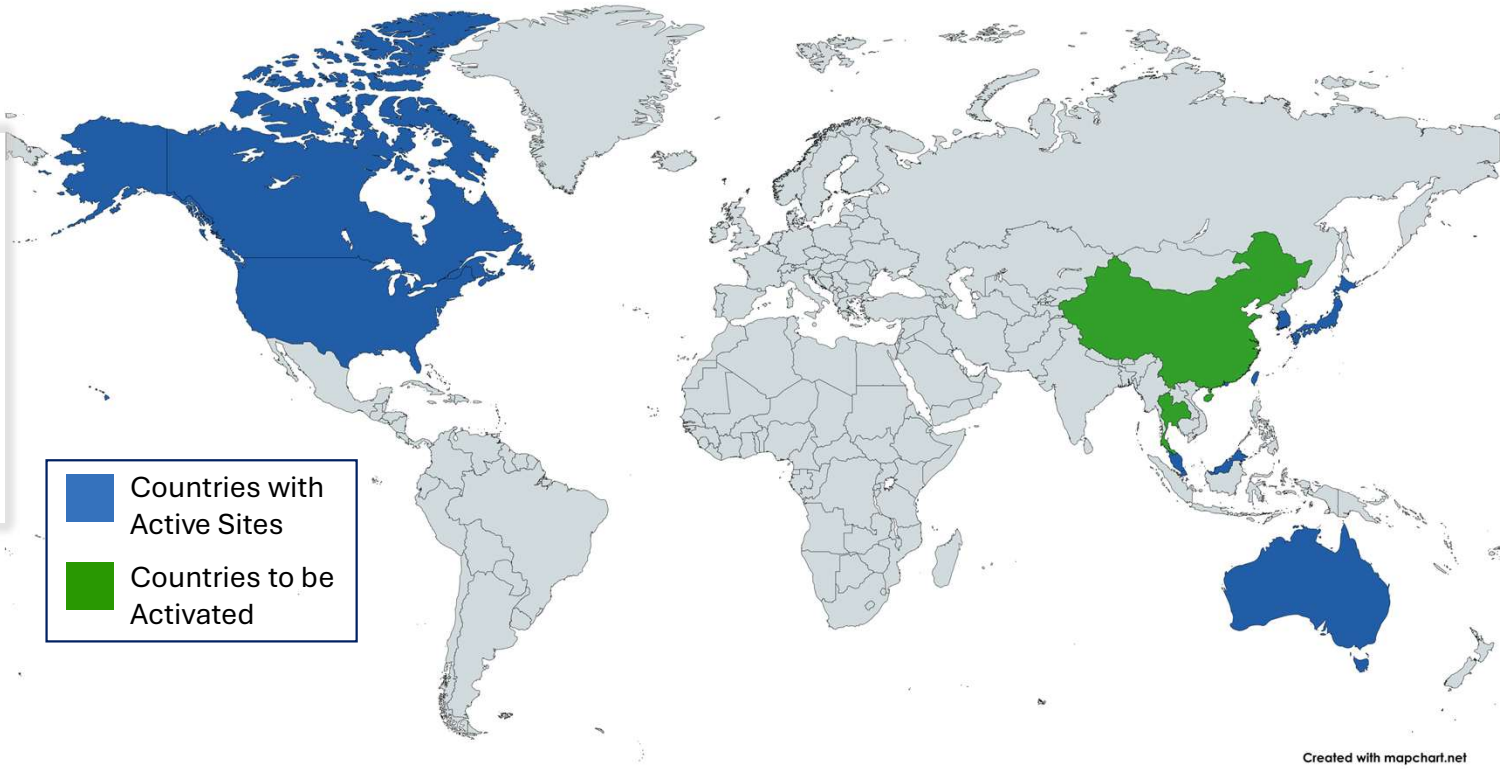
~ 290,000 EGFR-mutant adenocarcinomas NSCLC worldwide in 2022		
Classical (70%)	Atypical (21%)	Ex20ins (9%)
~ 201,000	~ 60,000	~ 26,000

On-target Resistance
C797S +/- T790M
>20,000

Robichaux et al, Nature, 2021; Midha et al, Am J Cancer Res, 2015; La Cava et al, ASCO Ed Book, 2025 https://www.wcrf.org/preventing-cancer/cancer statistics/lung-cancer-statistics/

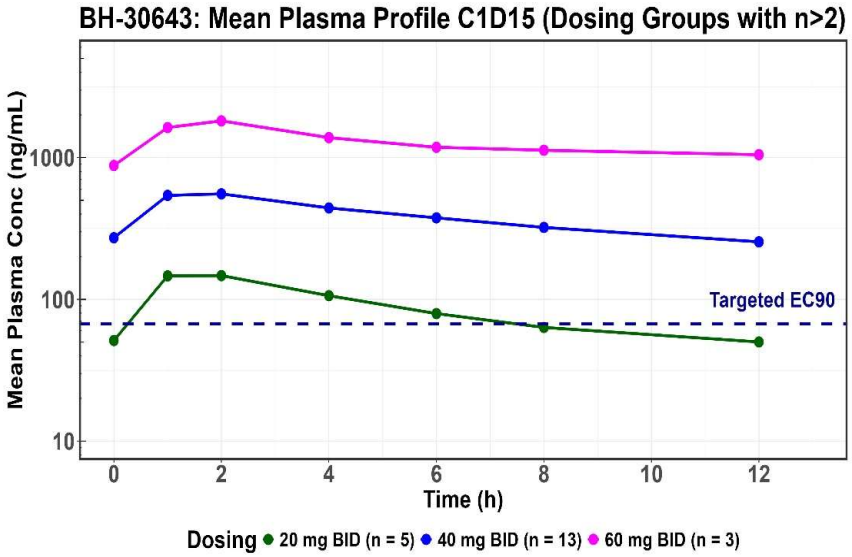
BH-30643-01 (SOLARA) Global Phase 1/2 Clinical Trial

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

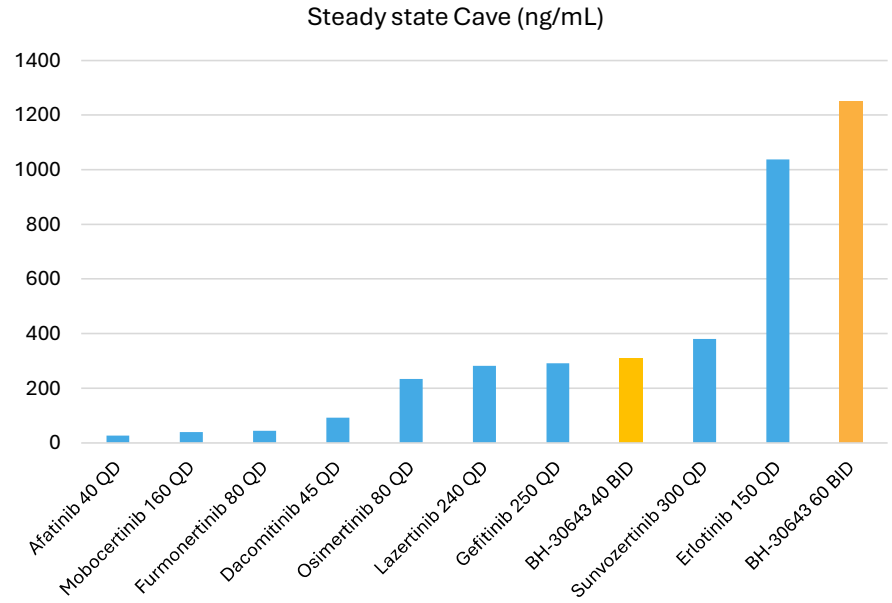


BH-30643 PK Profile: High and Sustained Exposure

Exposures at doses ≥40 mg BID well exceed the target EC_{90}



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

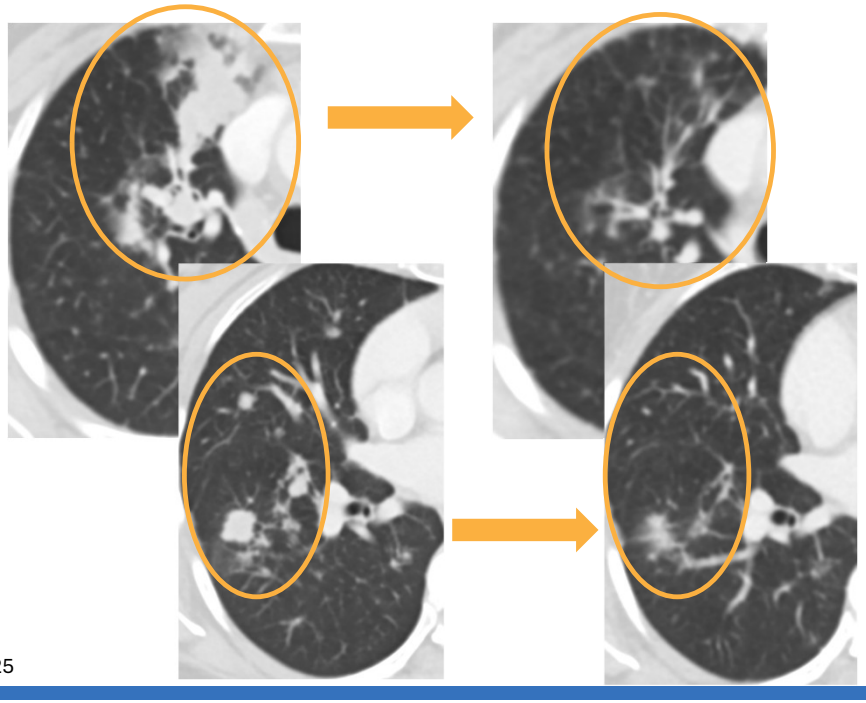


Paired with super-potency, high exposures could permit maximal EGFR inhibition

Overcomes C797S Resistance Even in the Presence of T790M

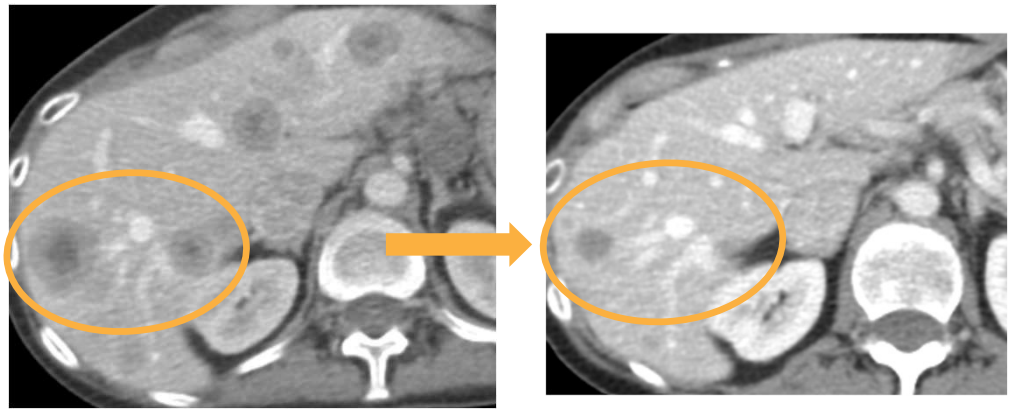
C797S & exon 19 deletion

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



C797S & T790M & exon 19 deletion

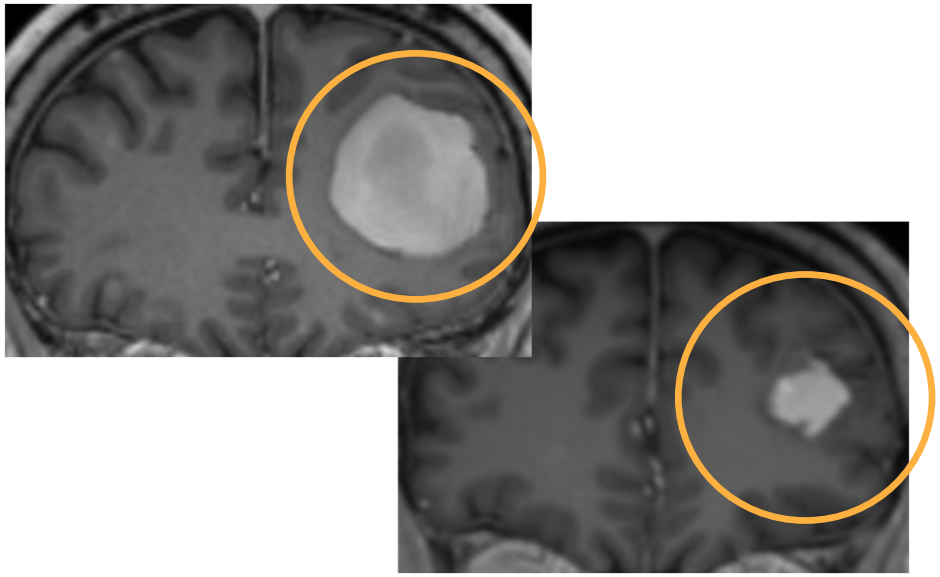
- 8 prior lines of therapy including osimertinib, investigational TKI, EGFR/met ab, ADC, etc
- Partial response sustained on multiple scans, with therapy ongoing



Breadth of Activity Includes Brain Mets and Atypical EGFR Mutations

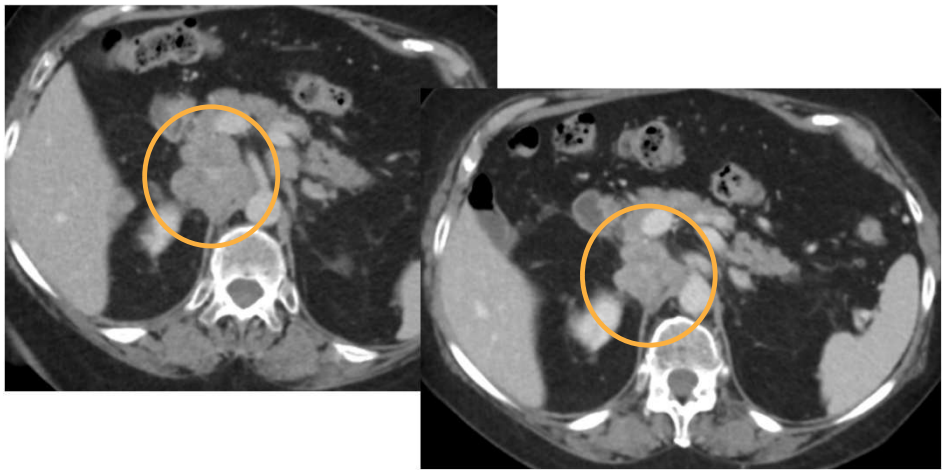
Exon 20 insertion with brain metastases

- 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



SOLARA Expansion Cohorts: Now Enrolling Across Multiple Dose Levels

Escalation & backfill

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

Potentially registrational Phase 2

Each cohort may study multiple doses

ASCO 2025, ENA 2025

BH-30236: Macrocyclic CLK Inhibitor

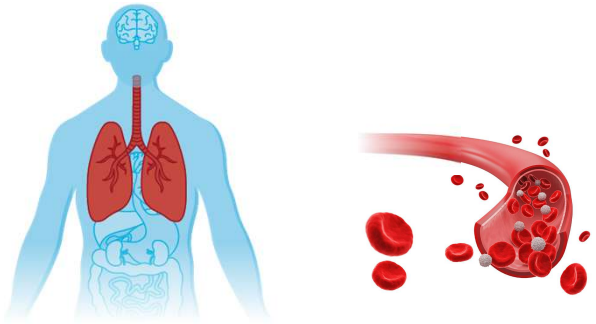
Novel macrocyclic, non-covalent, targeting aberrant alternative splicing

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

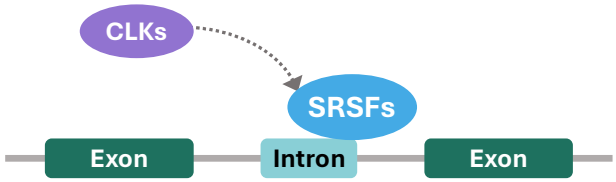


TWO EXAMPLES

Lung Cancer	AML/Blood Cancers
SRSF1, SRSF6, NUMB, RBM5, RBM6, RBM10, U2AF1, EGFR, MET, VEGFR, S6K1, MKNK2, AIMP2. BCL2L11, ENHA, KLK8, **DHX9**	**SF3B1, HNRNPK**, p53, p21, Cebpa, Cebpß, **U2AF1, SRSF2, ZRSR2, PRPF8**, SFPQ/PSF, **DDX41**,CD22, IKZF1, **WT1, SMC1A**

Red = Spliceosome genes (mutated/aberrantly expressed)

Importance of CLK



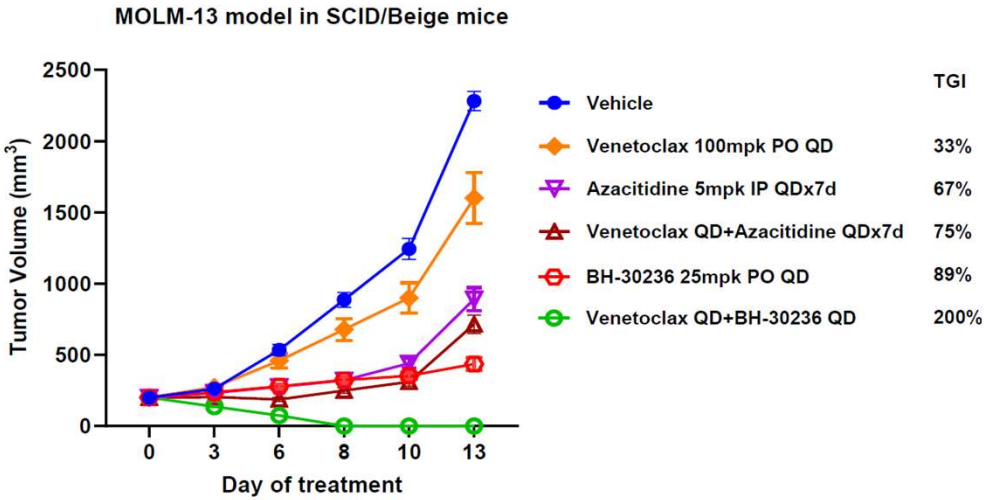
- CDC-like kinases (CLKs) can modulate aberrant splicing via phosphorylation of SRSF proteins
- Restoring normal splicing function is key to overcome off-target resistance in cancer
- Initial CLK inhibitors (eg. CTX-712) have demonstrated proof of concept

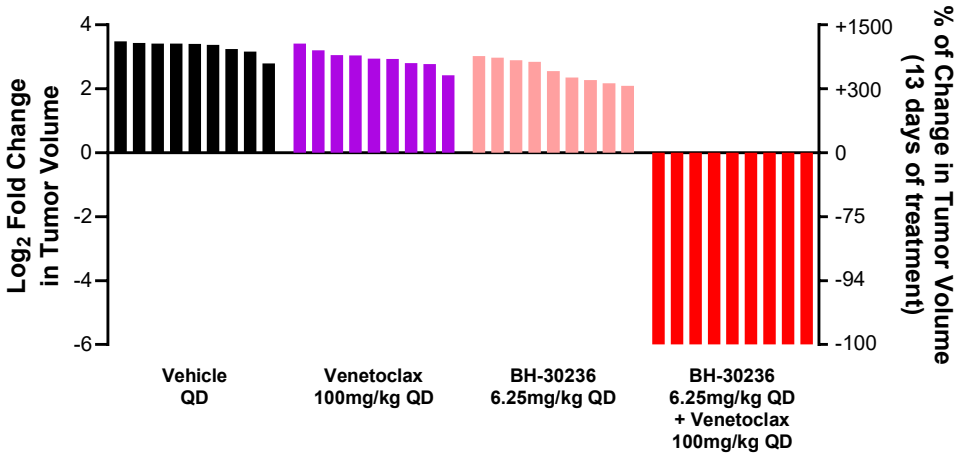
Expert Opin Ther Targets. 2018, 22(2): 107–121.

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

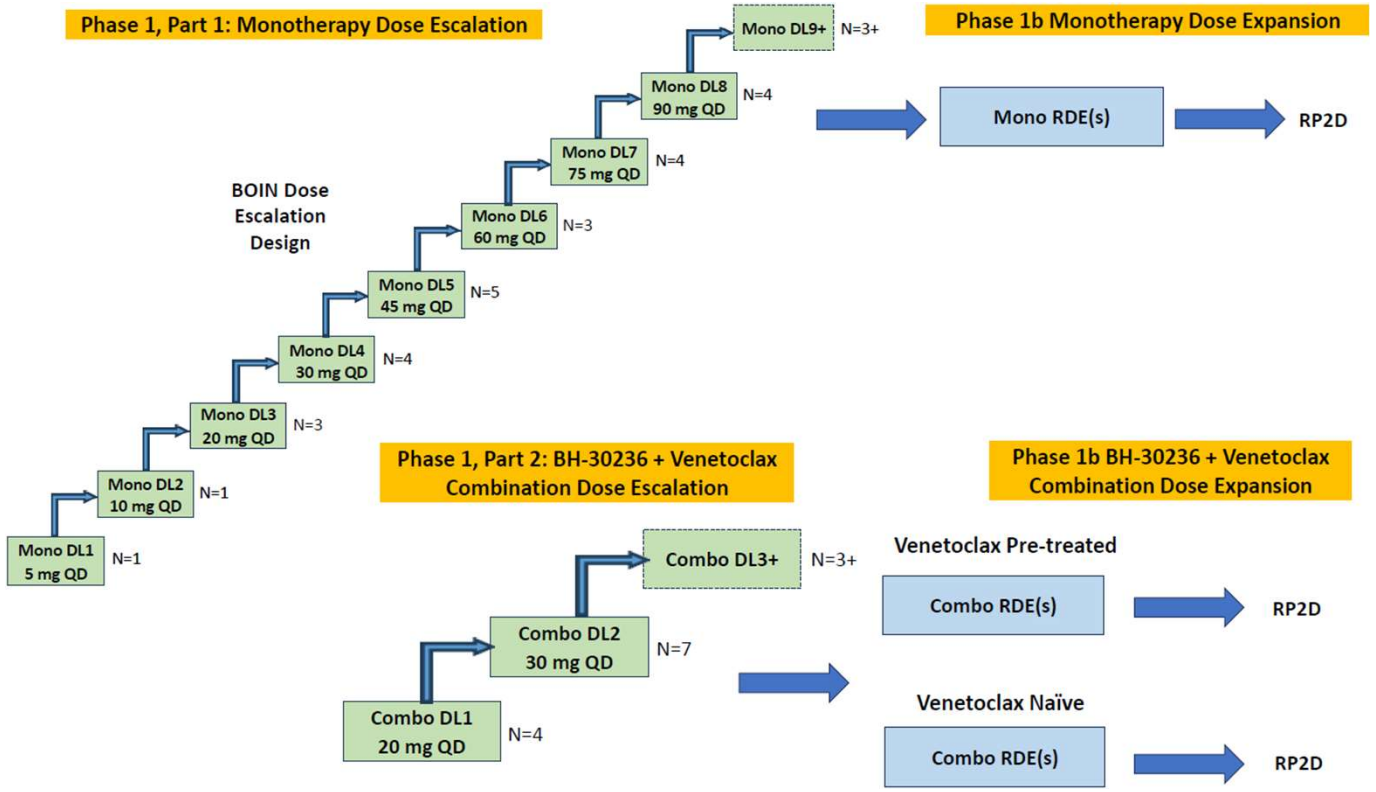




BH-30236: On-going Phase 1 FIH Study in AML/HR-MDS

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

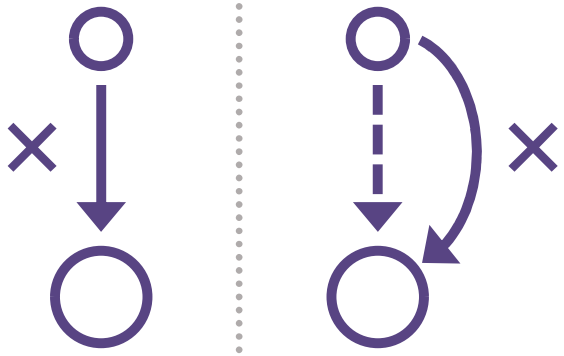


Making a Transformational Leap in Cancer Therapy

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