

# BlossomHill Therapeutics, Inc.

## Corporate Presentation

**October 2026**
San Diego, CA

BLOSSOMHILL
THERAPEUTICS

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BLOSSOMHILL THERAPEUTICS

# Intentionally designing novel medicines

## to address significant unmet medical needs in cancer treatment

**Strong leadership team** with proven track record of designing & developing FDA-approved cancer medicines

**Early launch opportunity targeting EGFR C797S** with a convenient oral monotherapy

**Broad EGFR development ongoing** including TKI naive cohorts, potentially offering substantial upside

**Differentiated wholly-owned pipeline** spanning novel mechanisms (CLK) and novel scaffolds (pan-KRAS)

## Pipeline Assets with Multiple Near-term Anticipated Milestones

### BH-30643 OMNI-EGFR™ Inhibitor

| | |
|---|---|
| **Q4 2026** | EOP1 Meeting: C797S potential accelerated approval pathway |
| **Q1 2027** | First Patient Dosed in anticipated pivotal Phase 2 trial |
| **1H 2027** | Phase 1 Update: C797S durability |
| **2H 2027** | Phase 1 Update: TKI-naive durability |
| **2H 2027** | Phase 1 Initial Data: chemo combo |

### BH-30236 Macrocyclic CLK Inhibitor

| | |
|---|---|
| **1H 2027** | Updated Phase 1 data on safety and anti-leukemic effect |

### BH-501284 Pseudo-irreversible Pan-KRAS Inhibitor

| | |
|---|---|
| **Q1 2027** | IND submission |

## Financial / Corporate Overview

| | |
|---|---|
| **Ticker** | BLSM |
| **Cash (end of Q2 2026)** | $95.4M |
| **IPO Net Proceeds (August 2026)** | $151.7M |
| **Shares Outstanding** | 31.8M |
| **Estimated Cash Runway** | Q2 2028 |

# Seasoned Management Team and Board

| Executive Team | Experience |
|---|---|
|  **J. Jean Cui, Ph.D.**<br>Scientific Founder, President & CEO<br>***Board of Directors*** | Turning Point Therapeutics, Pfizer |
|  **Y. Peter Li, Ph.D., M.B.A.**<br>Co-Founder, Executive Chairman<br>***Board of Directors*** | Turning Point Therapeutics |
|  **Geoffrey Oxnard, M.D.**<br>Chief Medical Officer and EVP | Lilly, Dana-Farber Cancer Institute, FOUNDATION MEDICINE |
|  **Jason Keyes, M.B.A.**<br>Chief Financial Officer and EVP | equillium, AMGEN, AMYLIN PHARMACEUTICALS, Baxter |
|  **Vincent P. Liptak, JD, Ph.D., M.B.A.**<br>General Counsel and EVP | Pfizer |

## Board of Directors



**Bihua Chen, M.B.A.**

CORMORANT ASSET MANAGEMENT



**Carl L. Gordon, Ph.D.**

orbimed



**John Schmid, M.B.A.**

Independent Board Member



**Sheila Gujrathi, M.D.**

Independent Board Member



**Sundeep Agrawal, M.D.**

BRAHMA CAPITAL

# Designing Cancer Medicines the BlossomHill Way



**Identify** unmet medical need for patients



**Structural analysis** of existing molecules and their limitations



**Precision drug design** based on deep understanding of target biology and protein structure dynamics



**Iterate** and optimize toward specified performance objectives

**Our goal is to develop orally available, potent precision medicines that maximize patient benefit**

# BlossomHill
# Product Candidate Pipeline

| Target | Candidate | Indication / Therapeutic Area | Design/ Discovery | IND Enabling | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|---|---|---|---|
| **EGFR** | **BH-30643** | EGFR-mutant NSCLC | | | | | |
| **CLK** | **BH-30236** *+/- venetoclax* | R/R AML and HR-MDS | | | | | |
| **Pan-KRAS** | **BH-501284** | Solid Tumors | | | | | |

**Our goal is to develop orally available, potent precision medicines that maximize patient benefit**

BLOSSOMHILL
THERAPEUTICS

# BH-30643: OMNI-EGFR™ Inhibitor

INVESTIGATIONAL, MACROCYCLIC, NON-COVALENT, BRAIN ACTIVE INHIBITOR
TARGETING MUTANT EGFR ACTIVE CONFORMATION



# Targeting *EGFR*-Mutant NSCLC: C797S Resistance And Beyond

**Total *EGFR*-mutant NSCLC incidence in 2025**
**USA, Europe, Japan, China**

**316,000**[1]

**209,000**
**Total Stage III-IV (advanced/metastatic)**
**USA, Europe, Japan, China**

**125,000**
**Treated with 3rd Gen TKI[2]: USA ~80%; ex-US ~50-60%**

**16,000**
**~13% develop C797S on target resistance mutation[3]**

## Substantial Market Opportunity in EGFR Mutant NSCLC

(2025 Tagrisso sales: ~$7.3B)[4]

### Early launch opportunity:

- ~5,400[5] C797S patients annually across planned accelerated approval markets (US: ~3,200, Japan: ~2,200)
- Osimertinib intolerance (~11-13%)[5] represents an additional near-term unmet medical need
- An effective TKI has potential for premium pricing and prolonged treatment duration compared to current SOC

### Growth opportunity:

- Unmet need for a novel TKI that offers prolonged effect in 1L with safety profile that allows combination development

1) GlobalData for EGFR-mutant NSCLC epidemiology estimates; 2) 3rd generation TKI treatment rates are management estimates; 3) C797S resistance frequency is based on Piotrowska 2026; 4) AstraZeneca Annual Report and Form 20-F Information 2025; 5) Management's estimates

# Why a Leap in *EGFR*-mutant NSCLC Is Attainable

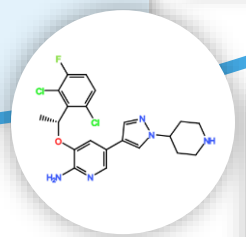
## ACHIEVING LONGER PFS AND PRE-EMPTION OF RESISTANCE WITH HIGH-POTENCY

### EML4-ALK Inhibitors in *ALK*+ NSCLC

Pfizer

1st Gen: Crizotinib
Cell Potency: 87 nM

**ORR: 74%**
**PFS: 10.9m**

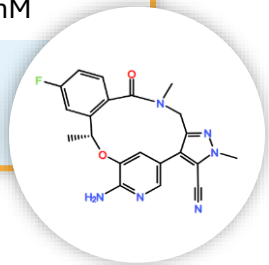


2nd Gen:
Alectinib, Brigatinib

Pfizer

3rd Gen:
Macrocyclic Lorlatinib
Cell Potency: 2.4 nM

**ORR: 76%**
**PFS: >84m**

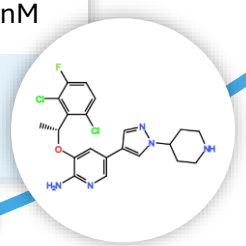


### ROS1 Inhibitor in *ROS1*+ NSCLC

Pfizer

1st Gen: Crizotinib
Cell Potency: 12 nM

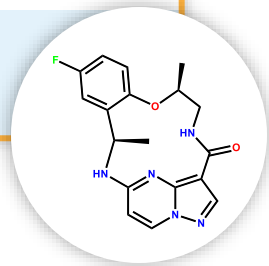
**ORR: 66%**
**PFS: 19.2m**



Turning Point Therapeutics

2nd Gen:
Macrocyclic Repotrectinib
Cell Potency: 0.2 nM

**ORR: 79%**
**PFS: 35.7m**

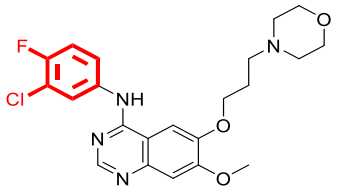


### Design & Development Approach

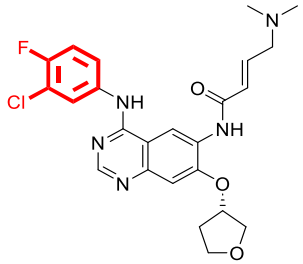
- Macrocyclic design for super-potency and reduced off-target toxicity
- Initial POC in resistant population, crafting a path to first-line development and adoption

# Existing EGFR Tyrosine Kinase Inhibitors Share Structural Families and Design Liabilities

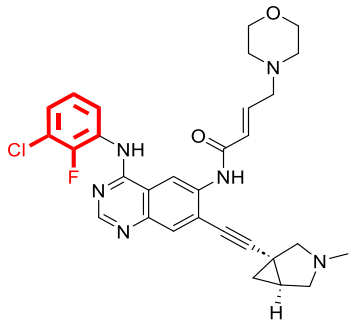
Many TKI designs use a **back-pocket motif** for potency, vulnerable to **T790M resistance**



**Gefitinib**

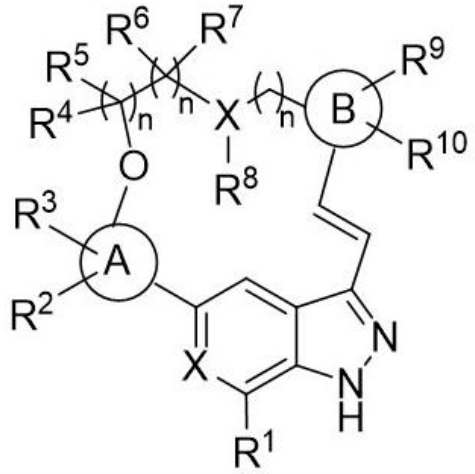


**Afatinib**



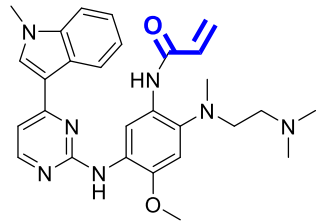
**BDTX-1535**

**BH-30643**

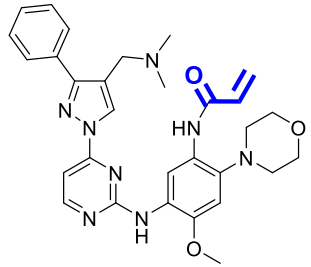


BH-30643 leverages an entirely novel macrocyclic scaffold to uniquely address both T790M and C797S resistance

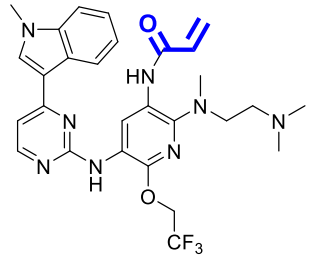
Other TKI designs use a **covalent bond** for potency, vulnerable to **C797S resistance**



**Osimertinib**



**Lazertinib**



**Firmonertinib**

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

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

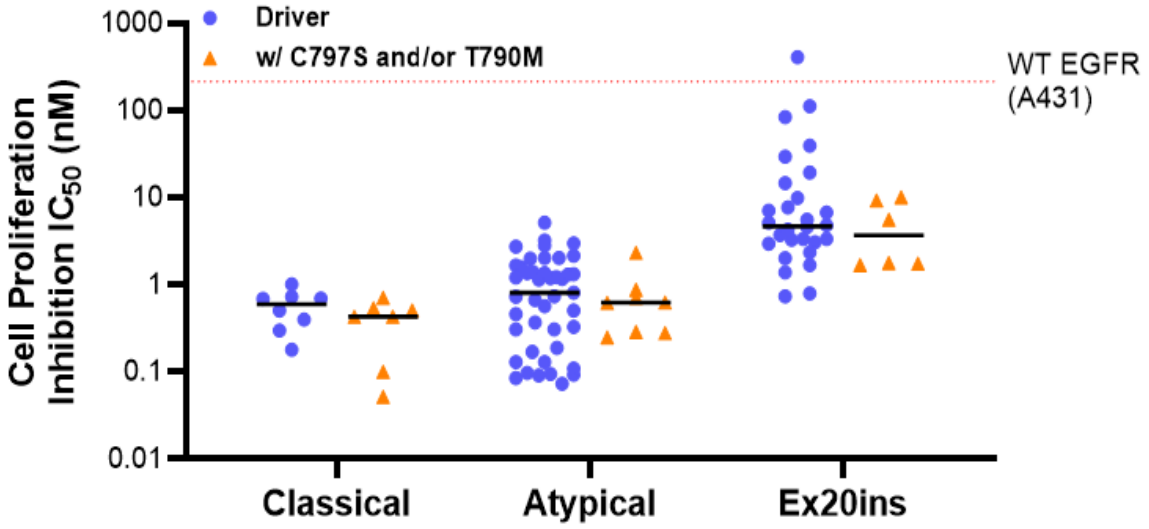
**Other TKIs covalently bind for potency**

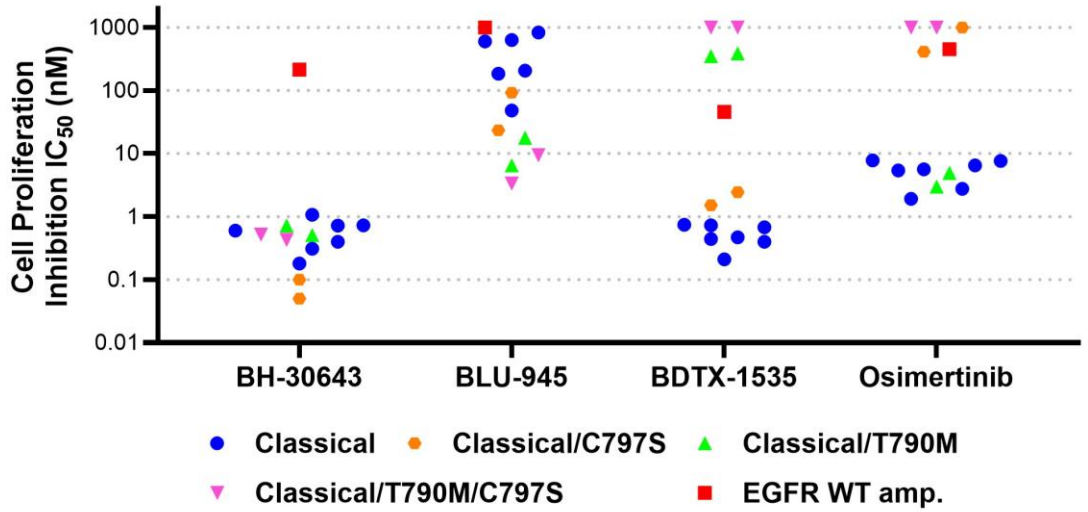
| | | |
|---|---|---|
| Osimertinib | Almonertinib | Mobocertinib |
| Rociletinib | Aumolertinib | Sunvozertinib |
| Lazertinib | Olmutinib | Firmonertinib |

# BH-30643: An Intentionally Designed Macrocyclic, Mutant-Selective OMNI-EGFR™ Inhibitor



- High cell potency against *EGFR* classical, atypical, and exon20ins
- Equipotent in the setting of on-target resistance mutations
- ~ 10 times more potent than osimertinib for L858R / 19del
- Avoided potency limitations of recent TKIs designed to target resistance




Note: Classical: L858R and ex19del; Any IC50 value > 1000 nM was plotted as 1000 nM.

1. AACR 2025
2. AACR 2026

# BH-30643 SOLARA Phase 1/2 Trial

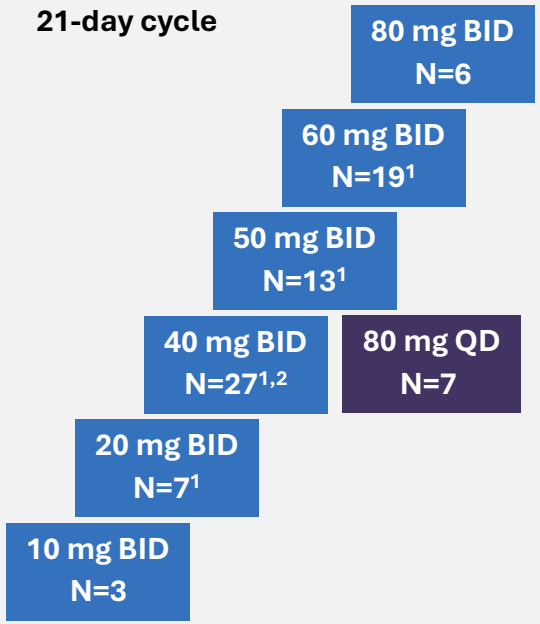
PRELIMINARY DOSE ESCALATION & EXPANSION EXPERIENCE

# SOLARA (NCT06706076):
# Study Design and Patient Characteristics for Dose Escalation

**Phase 1 escalation / backfill enrolled a heavily pretreated and heterogeneous patient population, with a median of 3 prior lines of therapy, 66% with history of brain metastases, and 71% ECOG=1**

## Phase 1 Part 1A (Escalation & backfill)

**BOIN design**
**21-day cycle**




**Patients enrolled at 29 sites across North America and APAC**

**Endpoints:**
- Primary: Selection of recommended doses for expansion (RDEs) and, if applicable, MTD
- Overall safety and tolerability
- PK characterization
- Preliminary antitumor activity

**Key eligibility:**
- Adults with advanced *EGFR* and/or *HER2* mutant NSCLC
- ECOG status 0-1
- Measurable disease by RECIST 1.1
- No limit on the number of prior therapy lines
- Untreated asymptomatic brain metastases allowed

| Patients Baseline Characteristics | N=82[3] |
|---|---|
| **Age (years), median (min, max)** | 61 (31, 81) |
| **ECOG = 1, n (%)** | 58 (71%) |
| **History of brain metastases, n (%)** | 54 (66%) |
| **Prior lines of therapy, median (min, max)** | 3 (1, 12) |
| Prior 3rd Gen EGFR TKI | 63 (79%) |
| Other prior targeted therapy | 17 (21%) |
| Prior chemotherapy and/or ADC | 58 (71%) |
| Prior immunotherapy | 14 (17%) |
| ***EGFR* or *HER2* driver mutation[4], n (%):** | |
| Classical *EGFR* (19del or indel, L858R) | 54 (66%) |
| *EGFR* exon 20 insertion | 16 (20%) |
| Atypical / other *EGFR* | 10 (12%) |
| *HER2* mutation | 2 (2%) |
| **Multiple *EGFR* mutations[4], n (%):** | 51 (62%) |

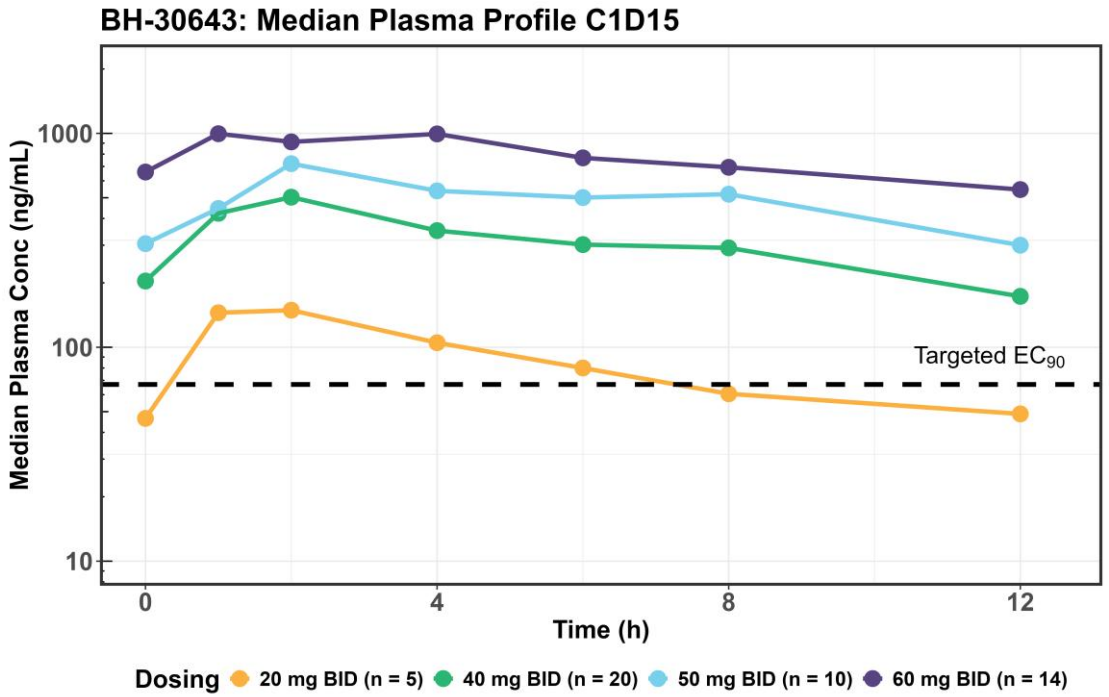
[1]Backfill cohorts enrolled at potentially efficacious doses based on PK and/or anti-tumor activity.
[2]Includes patients enrolled into pilot food effect sub study at 40mg BID

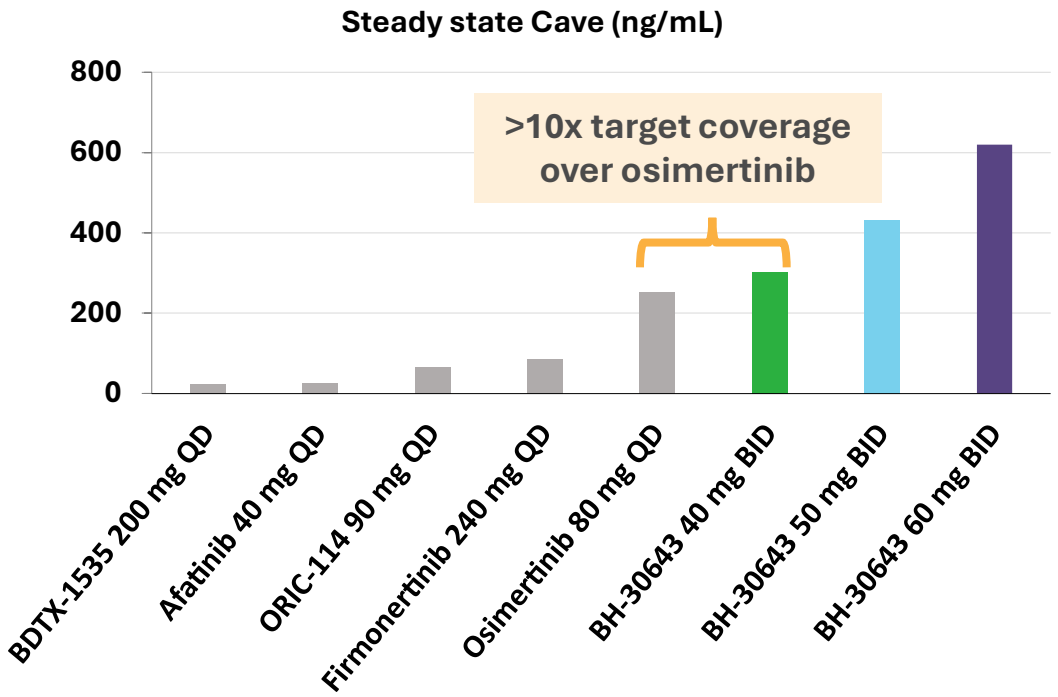
[3]All data as of 2 March 2026 data cut, with efficacy follow-up through 29 April 2026 data cut
[4]Includes historical and baseline molecular results

# High PK Exposures Observed in Escalation / Backfill Experience

Median preliminary steady state plasma exposures at ≥40mg BID achieved high coverage over target $EC_{90}$ and exceeded reported exposures of many contemporary EGFR TKIs

High exposure and high potency combined with $K_{p,uu}$ of 27% (CSF, primate) supports the observed preclinical and clinical CNS activity



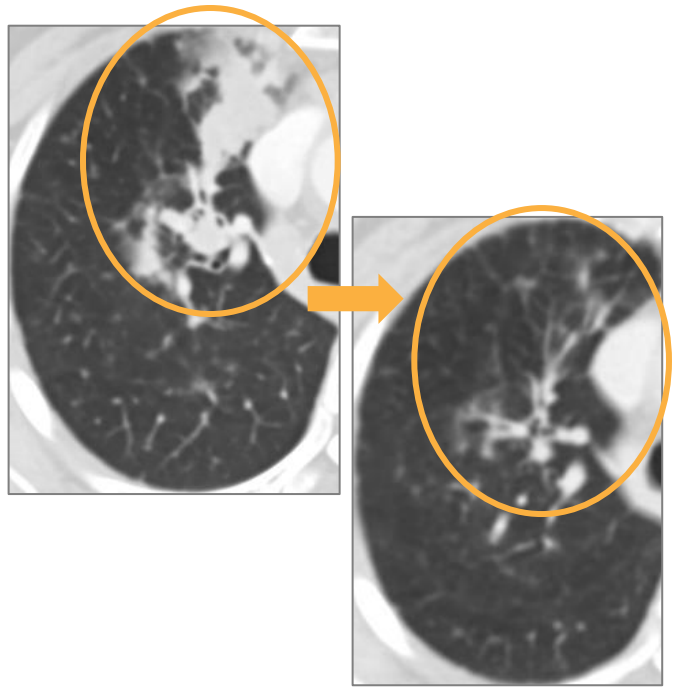




Note: The clinical data presented above are based on cross-study comparisons and are not based on any head-to-head clinical trials. Differences exist between trial designs, patient characteristics and other factors and caution should be exercised in drawing any conclusions from a comparison of the data across studies as cross study comparisons are inherently limited and such data may not be directly comparable.

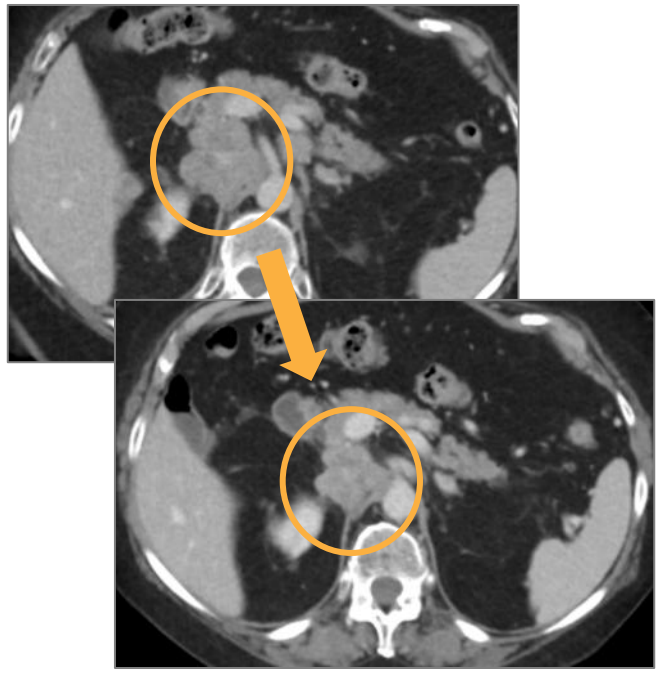
All data as of March 2, 2026 data cut, with efficacy follow-up through April 29, 2026 data cut

# Responses in Diverse *EGFR*-mutant Subtypes May Support Multiple Paths for Future Clinical Development

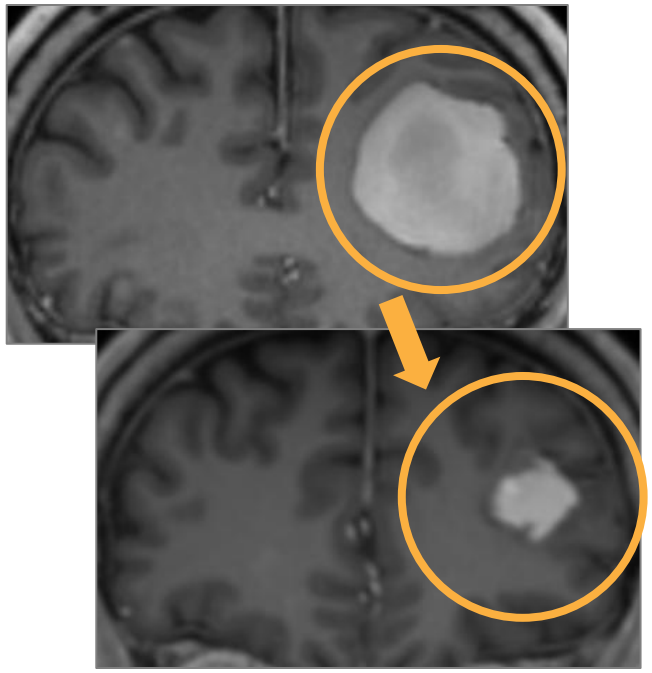
- 44 yo female, enrolled at 40mg BID
- EGFR **exon 19 deletion & C797S** detected after prior osimertinib, amivantamab and immunotherapy
- >11 months on treatment



- 68 yo female enrolled at 80mg QD
- EGFR **L861Q** previously treated with chemotherapy, erlotinib, osimertinib, mobocertinib
- 9 months on treatment



- 51 yo male enrolled at 80mg BID
- EGFR **exon 20 insertion** with 3 prior lines of chemotherapy; no brain radiation or steroids
- 8 months on treatment



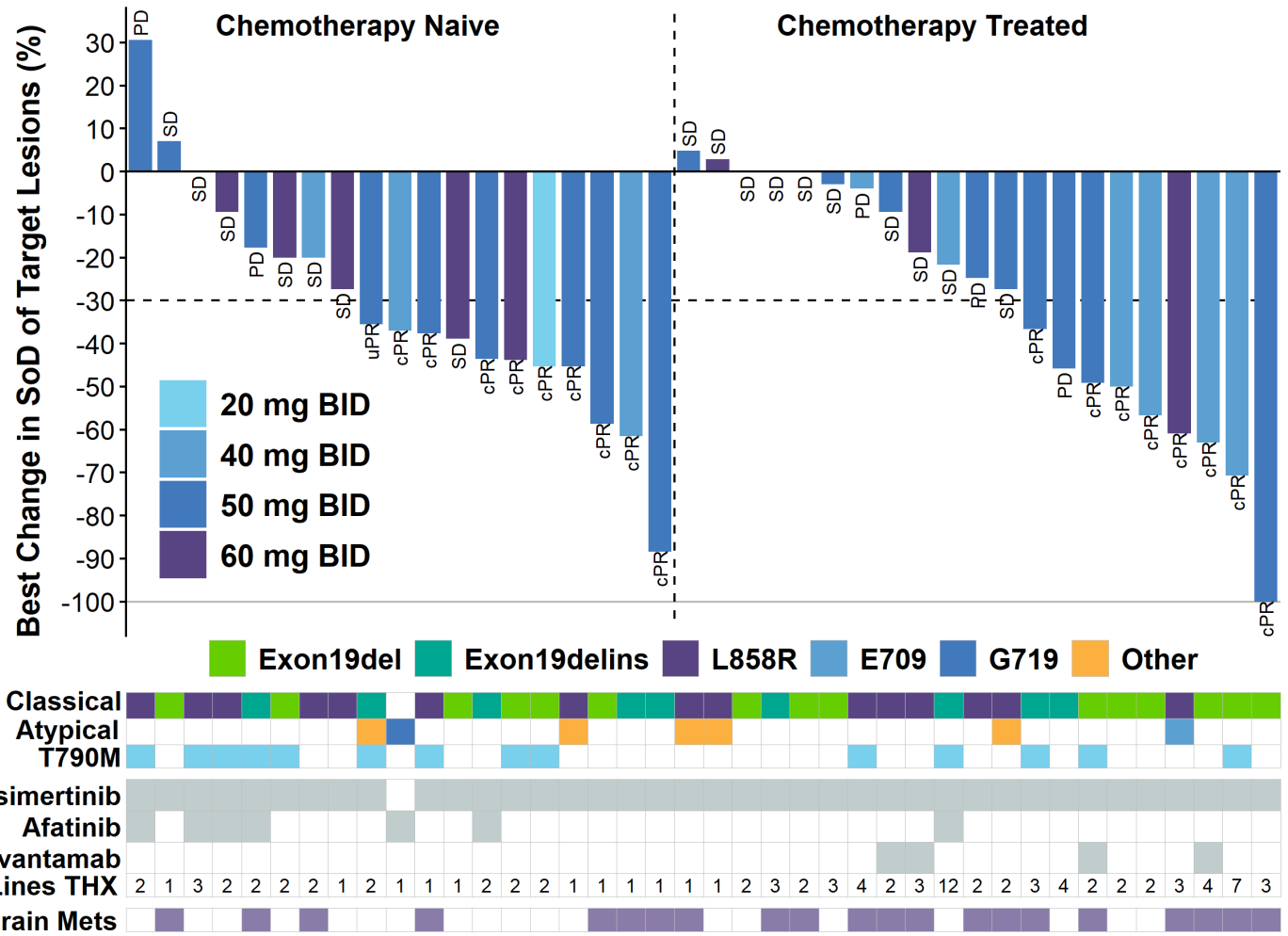
All data as of March 2, 2026 data cut, with efficacy follow-up through April 29, 2026 data cut

# BH-30643 Experience in C797S +/- T790M Resistance

PRELIMINARY DOSE ESCALATION / BACKFILL AND EARLY EXPANSION EXPERIENCE

# C797S Efficacy Results: Confirmed Responses Observed Across Dose Levels in Patients with C797S

- 40 patients from the target C797S population (19 chemo naïve and 21 chemo treated) were response evaluable across escalation and expansion cohorts
- Responses (45% ORR with 17 confirmed and 1 unconfirmed and ongoing) seen both without prior chemo (53% ORR) and with prior chemo (38% ORR)
- Responses observed with or without concurrent T790M and with or without prior history of brain metastases

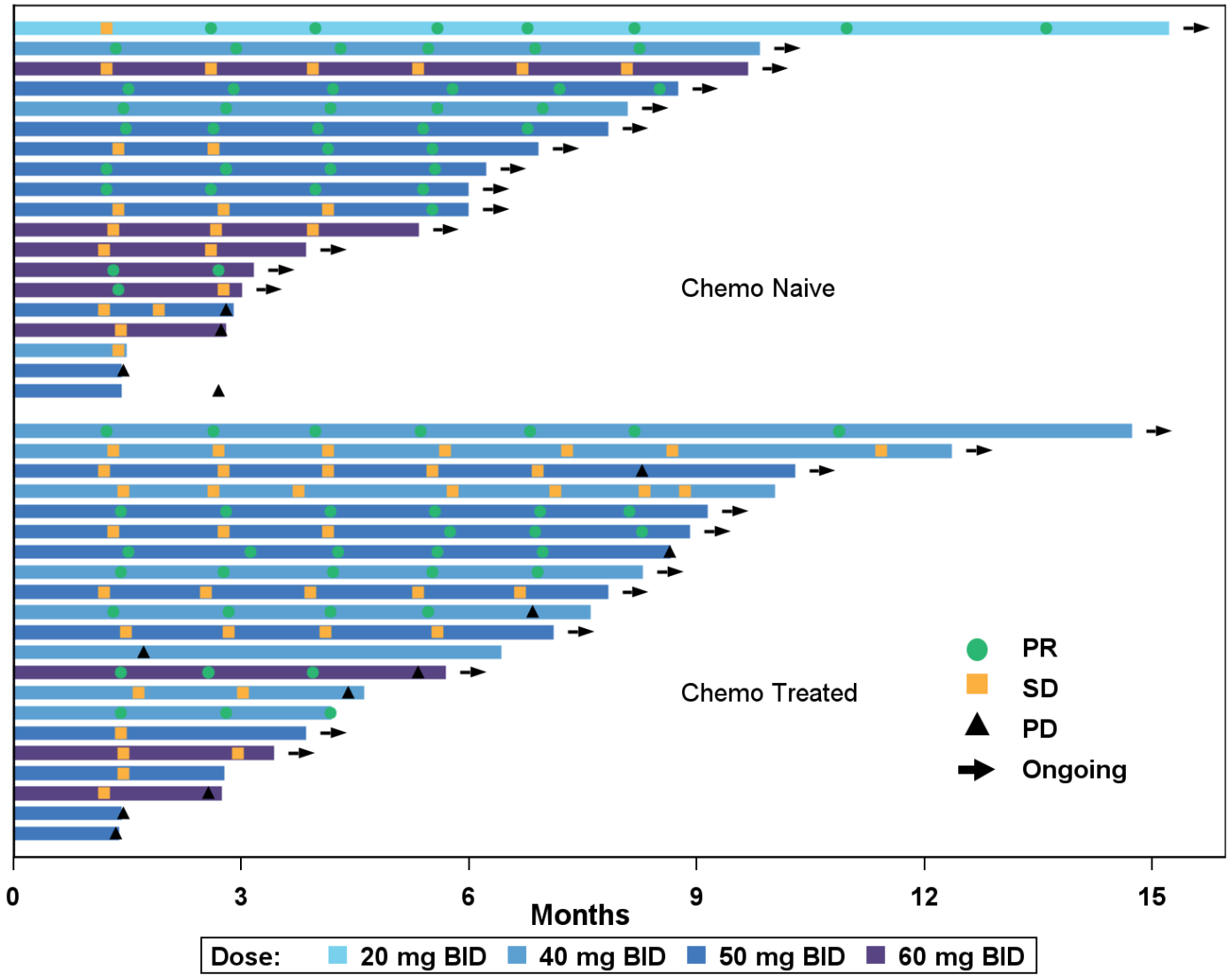



One patient enrolled at 20mg BID was escalated to 40mg BID after second cycle. Target C797S population excludes patients with concurrent driver alterations or who previously received EGFR TKI specifically targeting a known C797S. One patient discontinued treatment due to AE on day 6 and is not included in efficacy analysis set

All data as of 12 May 2026 data cut, with efficacy follow-up through 10 August 2026 data cut

# C797S Efficacy Results: Preliminary Durability

- Studied 40 patients in the target C797S population enrolled as of the data cutoff
  - ➢ Excludes patients with concurrent driver alterations or who previously received EGFR TKI specifically targeting a known C797S
- Median follow-up was 6.9 months
- 25 patients (63%) remain on therapy with 3 patients exceeding 12-month treatment and on-going




Updated analysis using 5/12/26 formal data cut obtained for regulatory purposes, with efficacy follow-up through 8/10/26. Compared to the 5/20/26 data snapshot, this excludes one patient who had not yet enrolled, one patient who discontinued treatment due to AE on day 6 and is not included in efficacy analysis set, and two patients found to have concurrent driver alterations.

# Maturing Safety Data Supports RP2D Selection

## Treatment-related adverse events (TRAE) in ≥ 10% patients[1]

| Preferred Term, N (%) | 40 mg, 50mg, 60 mg BID N=174 | | | |
|---|---|---|---|---|
| | All Grade | Grade 1 | Grade 2 | Grade 3/4[3] |
| **Any TRAEs** | **155 (89)** | **65 (37)** | **52 (30)** | **38 (22)** |
| **Bilirubin elevation[2]** | 78 (45) | 25 (14) | 40 (23) | 13 (7) |
| **Rash[2]** | 75 (43) | 60 (34) | 11 (6) | 4 (2) |
| **Diarrhea** | 67 (39) | 61 (35) | 4 (2) | 2 (1) |
| **Dry skin** | 38 (22) | 37 (21) | 1 (1) | 0 (0) |
| **Stomatitis[2]** | 37 (21) | 28 (16) | 6 (3) | 3 (2) |
| **ALT increased** | 30 (17) | 11 (6) | 6 (3) | 13 (7) |
| **AST increased** | 29 (17) | 11(6) | 10 (6) | 8 (5) |
| **Fatigue** | 25 (14) | 19 (11) | 6 (3) | 0 (0) |
| **Nausea** | 20 (11) | 13 (7) | 7 (4) | 0 (0) |
| **Paronychia** | 20 (11) | 8 (5) | 11 (6) | 1 (1) |

[1]12 May 2026 cut-off. Median duration of exposure of 3 months
[2]Grouped term
[3]No Grade 5 TRAE

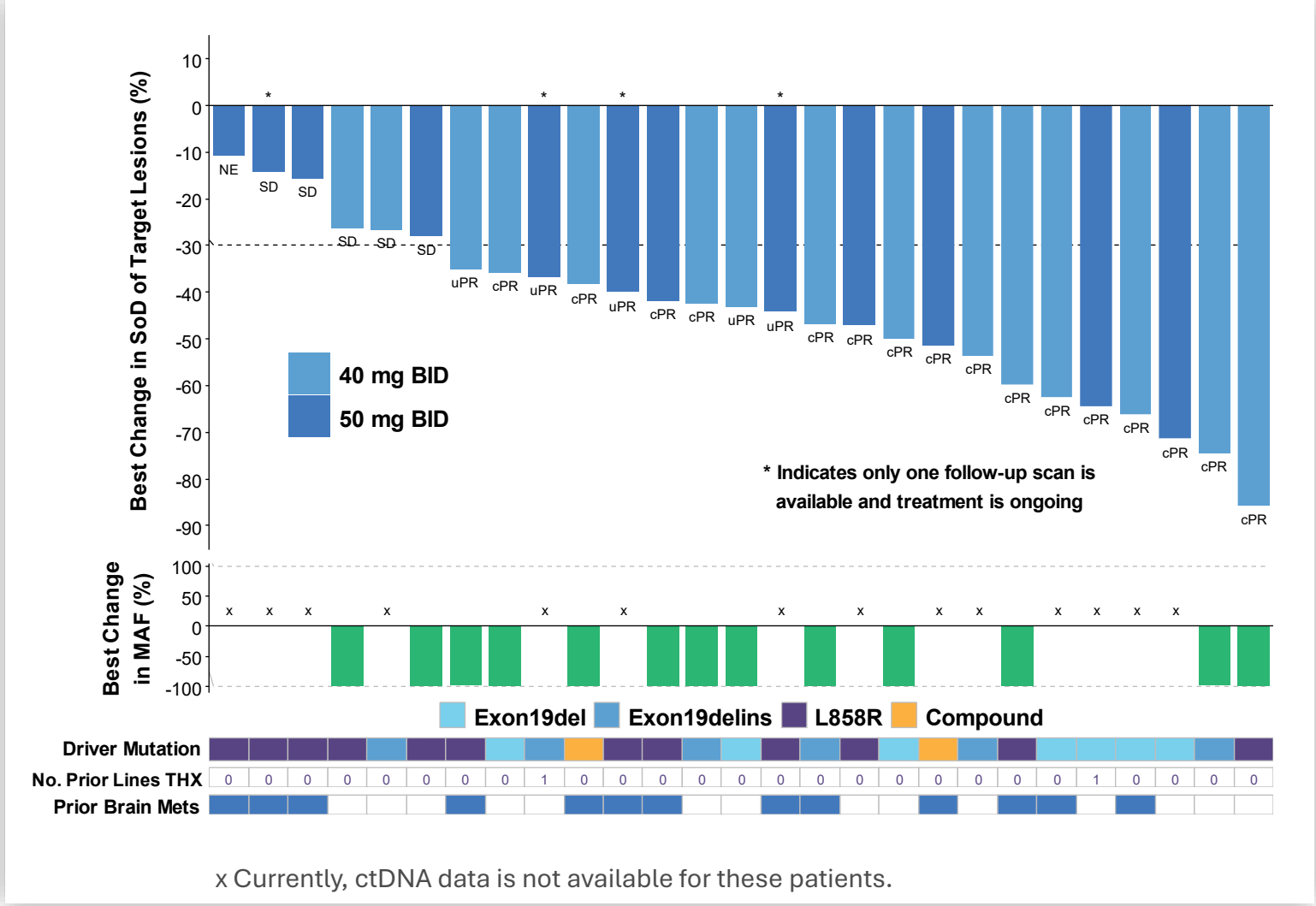
- Dose reduction (9%) and treatment discontinuation (3%) due to TRAE are uncommon
- EGFR-wildtype associated TRAEs are mostly Grade 1
- Most common TRAE is bilirubin elevation:
  - "Gilbert's-like" pattern: usually asymptomatic and predominately unconjugated due to UGT1A1 inhibition by BH-30643
  - Exposure dependent: Reversible with dose modification or often tolerated without dose adjustment
- TRAE of Grade 3+ ALT / AST increase in 7% / 5% of patients, respectively, with no cases of Hy's law
- Rare pneumonitis (~1%)
- No clinically significant treatment-related cardiac effects or QTc prolongation

# BH-30643 Experience in EGFR TKI Naive Classical Mutation

PRELIMINARY EARLY EXPANSION EXPERIENCE

# Compelling Early Activity Observed in the Classical TKI-naive Setting

- Response (confirmed or unconfirmed and ongoing) in 21 of 27 patients (78%) with on-treatment imaging; all had tumor reduction
- Enriched for brain mets (48%) and higher risk genotypes (30% exon19 indels or H870R)
- Median follow-up 4.2 months
- 11/13 pts (85%) showed 100% clearance of *EGFR* mutations in ctDNA and two had >98% reduction



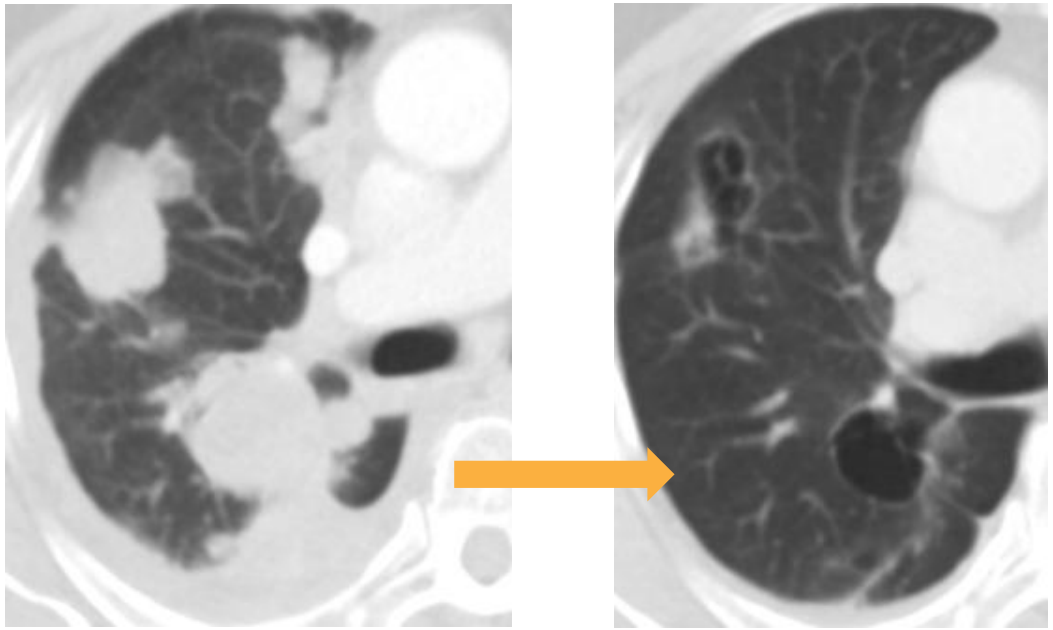

x Currently, ctDNA data is not available for these patients.

All data as of updated 20 May 2026 efficacy cutoff

# First-line Activity Against Challenging EGFR Mutations

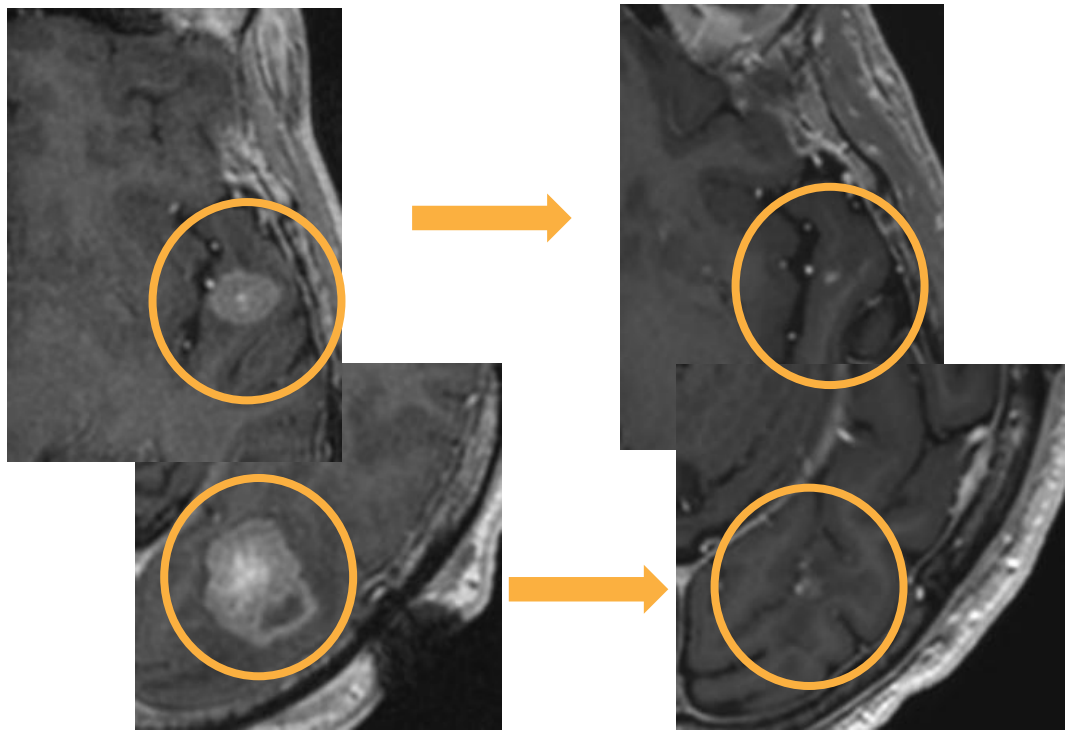
## L858R

- Treatment naive, treated at 40mg BID, with treatment ongoing
- Partial response confirmed on second scan (-86%)



## Exon19del & H870R

- TKI naive, presented with multiple brain mets
- Treated at 40mg BID with systemic and CNS PR, in the absence of radiation / steroids, with therapy ongoing

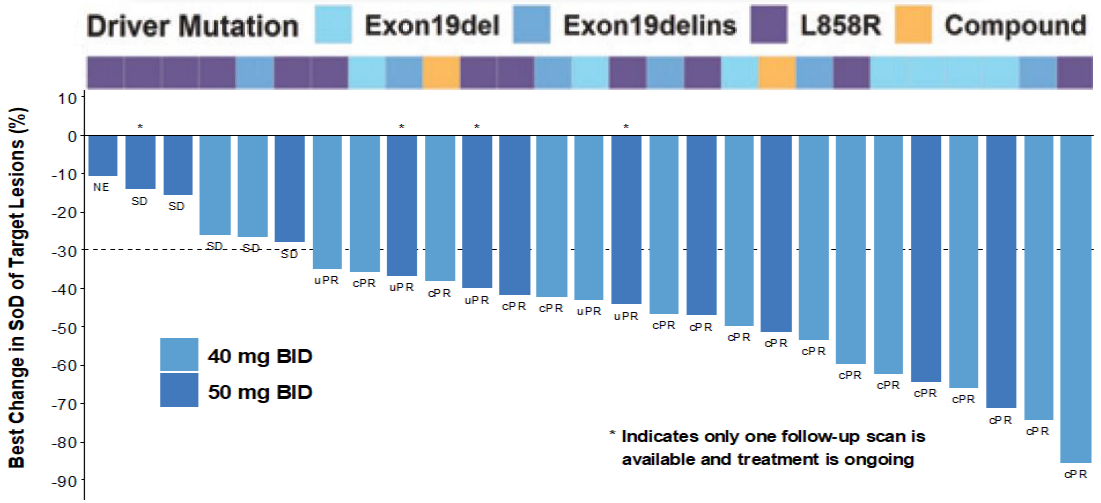


Interim data as of April 29, 2026

# Early Clinical Activity of BH-30643 in Classical TKI-naive Cohort

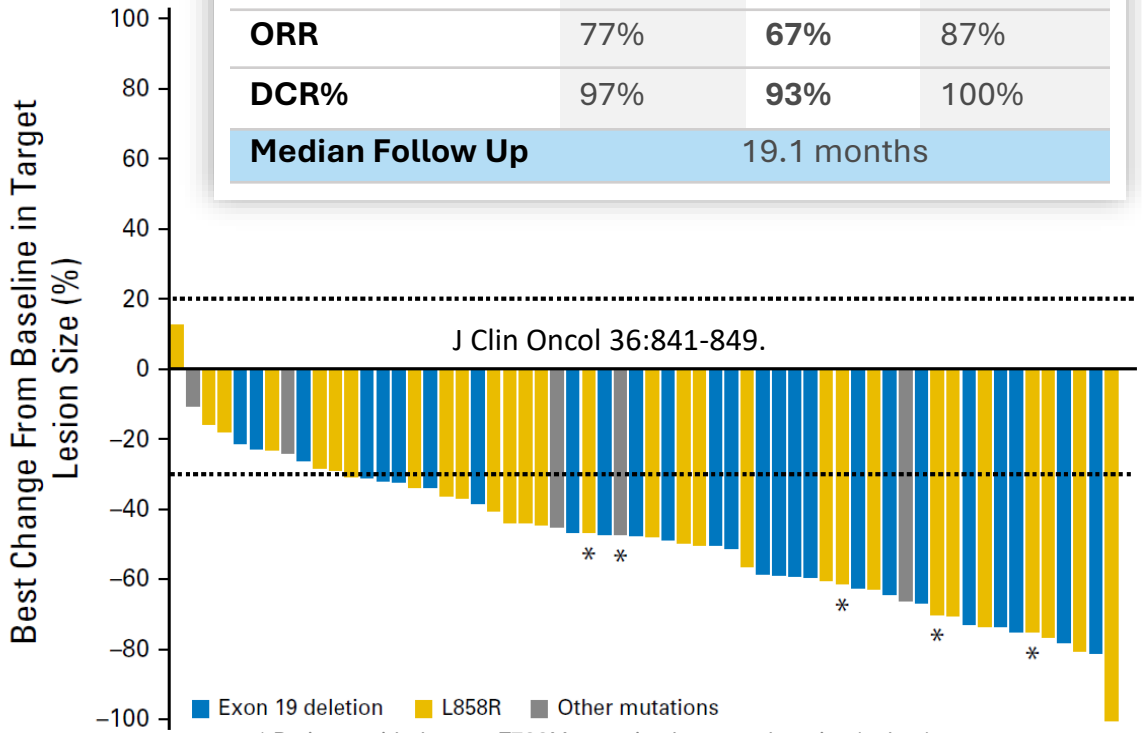
## BH-30643 TKI-naive

| | Total (40mg+50mg BID) |
|---|---|
| # Patients | 27 |
| Brain mets n (%) | 13 (48%) |
| ORR | 78% |
| DCR% | 96% |
| Median Follow Up | 4.2 months |




## Osimertinib Phase 1 Treatment-naive

| | Total | 80 mg | 160 mg |
|---|---|---|---|
| # Patients | 60 | **30** | 30 |
| Brain mets n (%) | 15 (25%) | **7 (23%)** | 8 (27%) |
| ORR | 77% | **67%** | 87% |
| DCR% | 97% | **93%** | 100% |
| Median Follow Up | 19.1 months | | |




All data as of updated May 20, 2026 efficacy cutoff

Note: The clinical data presented above are based on cross-study comparisons and are not based on any head-to-head clinical trials. Differences exist between trial designs, patient characteristics and other factors and caution should be exercised in drawing any conclusions from a comparison of the data across studies as cross study comparisons are inherently limited and such data may not be directly comparable.

# SOLARA Expansion Cohorts Now Enrolling Globally

## Expansion cohorts to inform Phase 2/3 development

**Escalation and backfill**

**TKI resistance**
- C797S detected after most recent therapy
- Atypical resistance mutations (L718X, G724X, etc.)

**Targeted therapy naive**
- Classical mutations
- Atypical mutations (G719X, L861Q, S768I)
- Exon 20 insertions

**Combination**
- With platinum/pemetrexed following progression on 3rd-gen EGFR TKI

**Potentially registrational Phase 2**

# BH-30643
# Key Takeaways

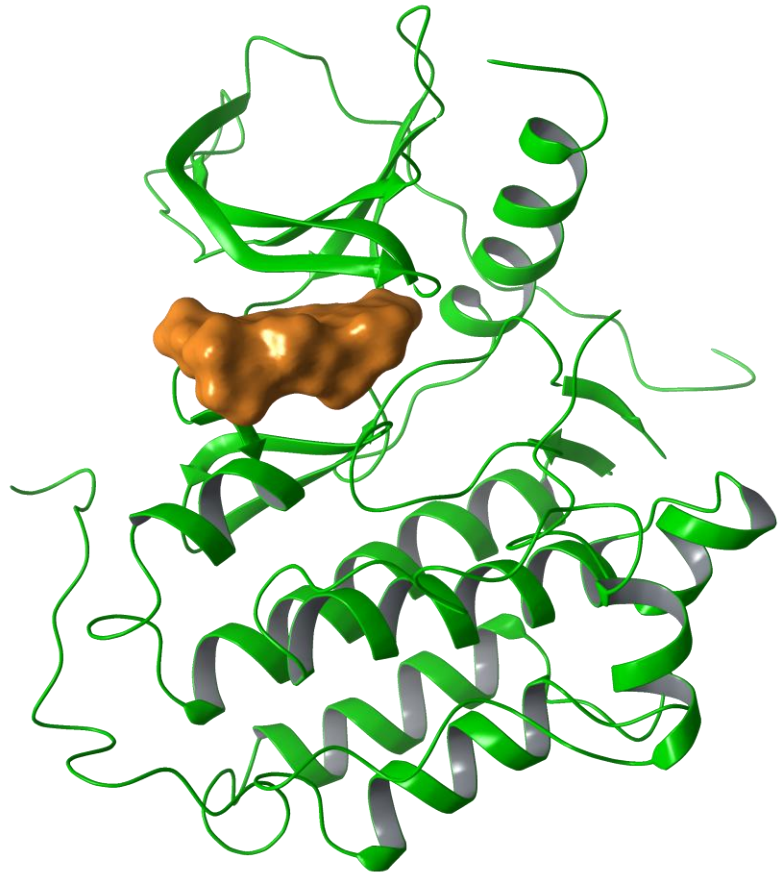
**Compelling activity in patients with C797S** with potential path to accelerated approval

**Early activity in TKI naive patients** with potential to expand 1L development

**Differentiated safety profile** mitigating many of the idiopathic toxicities seen with osimertinib

## EOP1 meeting planned for Q4 2026

to enable seamless transition to potentially registrational Phase 2 trial in C797S-positive resistance, with first patient expected to be dosed in Q1 2027



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THERAPEUTICS

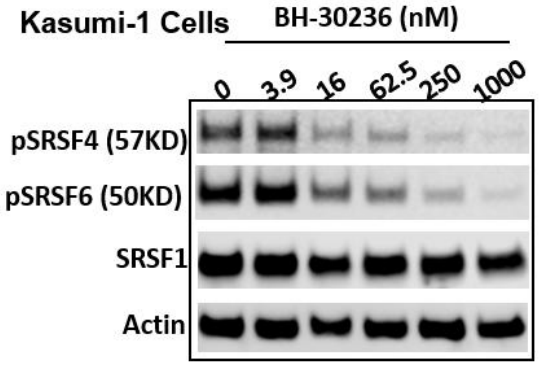
# BH-30236: CLK Inhibitor

INVESTIGATIONAL, MACROCYCLIC, NON-COVALENT INHIBITOR
TARGETING ABERRANT ALTERNATIVE SPLICING

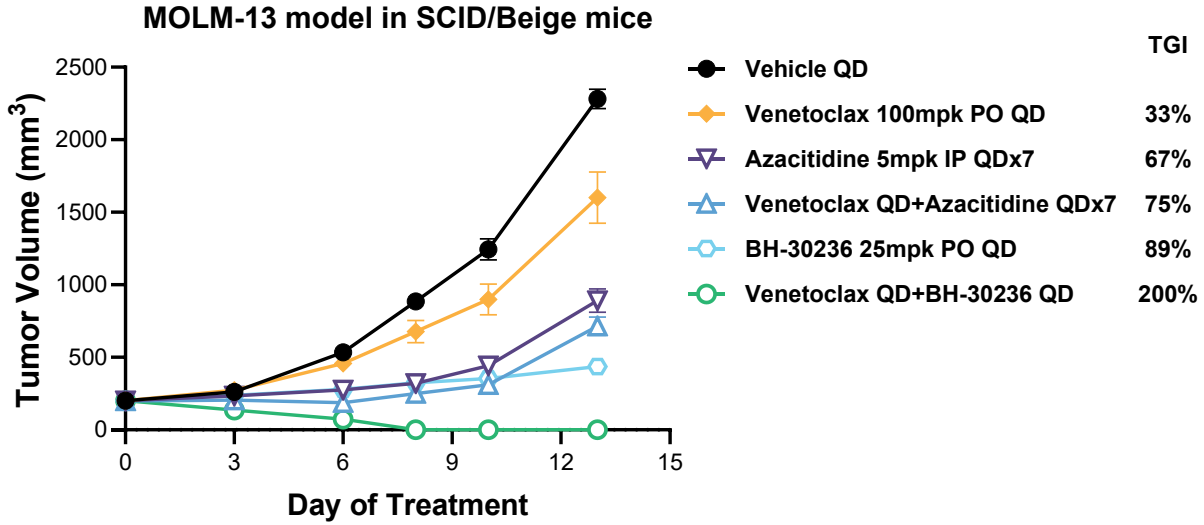


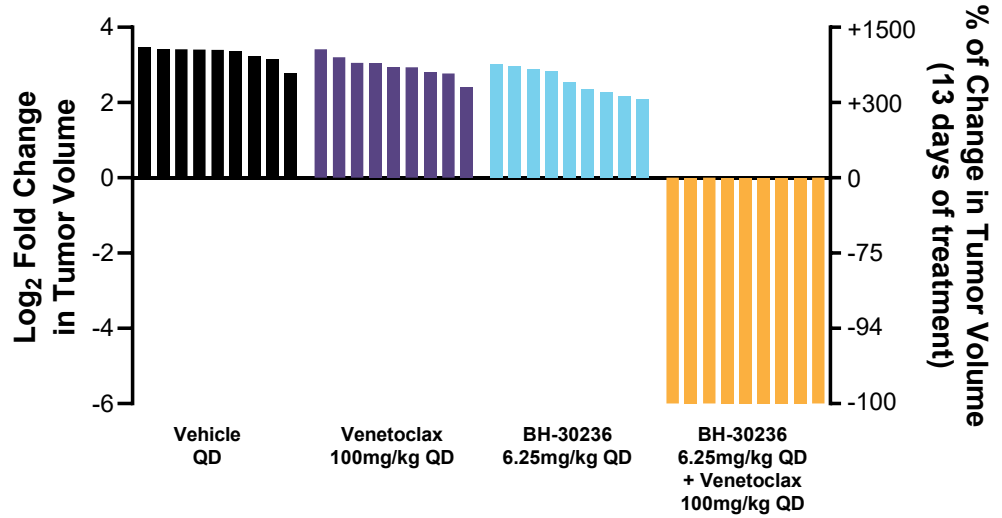
# BH-30236: Potent CLK inhibitor Modulating Aberrant Alternative Splicing

- Upregulation and mutations of serine/arginine rich splicing factors (SRSFs) have been reported in hematological malignancies and solid tumors
- CDC-like kinases (CLKs) can modulate aberrant splicing via phosphorylation of SRSF proteins
- BH-30236 is a potent CLK inhibitor of pSRSF leading to the modulation of aberrant alternative splicing and has demonstrated strong synergy with venetoclax in AML models




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

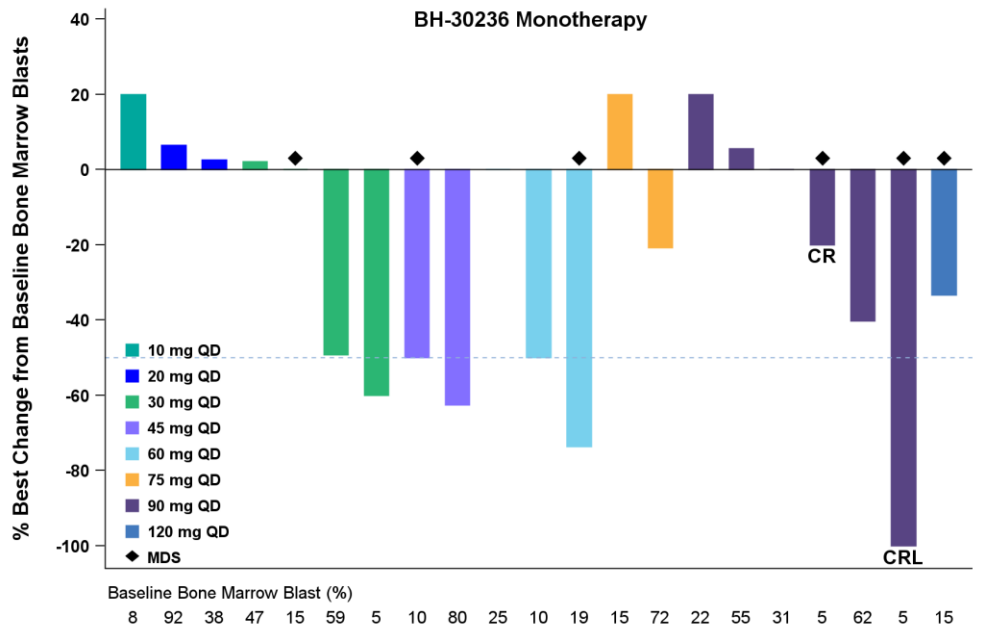


# BH-30236 Monotherapy Anti-leukemic Activity at ≥ 30mg QD

- 6/21 (28.6%) patients with post-baseline marrow assessment had ≥50% blast count reduction on therapy
- Of 6 evaluable patients with previously treated HR-MDS, 2 (33%) had a CR on monotherapy

## Best Change in Baseline Marrow Blast % (N=21)




## Anti-Leukemic Activity of BH-30236 Monotherapy in Relapsed HR-MDS

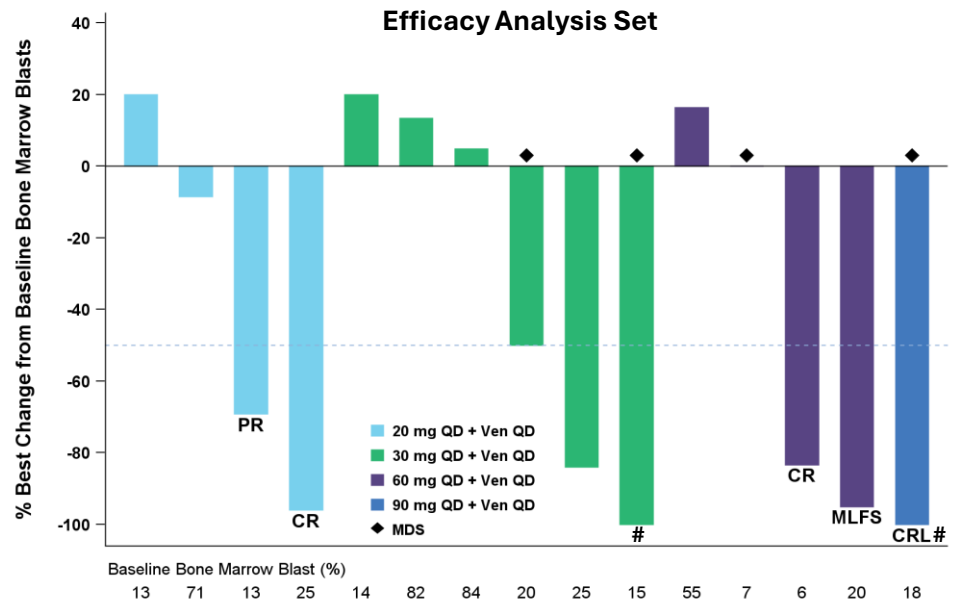
| Dose | Patient / Disease | Baseline Mutations | Prior Therapy | Key Blood and Marrow Parameters (pre → post) | Best Response / Outcome |
|---|---|---|---|---|---|
| 60 mg QD | 81 yo M Relapsed HR-MDS | ASXL1 DDX41 ETV6, SETBP1 SRSF2 PAX5 | 1. Aza + SL-172154/ Aza → CR | BM blasts: 19% → 5% ANC: 0.3 → 1.35 PLTs: 25 → 28 | NR* Continuing on treatment more than 1yr (Cycle 13+) |
| 90 mg QD | 66 yo M Relapsed HR-MDS | ASXL1 NF1 SETBP1 SRSF2 | 1. Aza + Ven → CR 2. allo-HSCT → CR | BM blasts: 5% → 0% ANC: 0.16 → 1.31 PLTs: 20 → 24 | $CR_L$ (MRD –) D/C for allogeneic HSCT |

Interim study data as of May 20, 2026

# Venetoclax Combo: Anti-leukemic Activity Observed in Ven Pre-treated Patients Across Dose Levels

- 13/15 patients with prior venetoclax exposure
- ≥ 50% blast count reduction in 8/15 (53%) patients with post-baseline marrow assessments
- In 11 evaluable patients with R/R AML, overall response rate was 36% (4/11)

## Best Change in Baseline Marrow Blast % (N=15)




## Clinical Responses to BH-30236 + Ven in AML patients Refractory to Venetoclax

| Dose | Patient / Disease | Baseline Mutations | Prior Therapy | Key Blood and Marrow Parameters (pre → post) | Best Response / Outcome |
|---|---|---|---|---|---|
| 20 mg QD | 60 yo M AML 2° to HR-MDS | DDX41 SETD2 | 1. AZA for MDS<br>2. 7+3 chemo→ NR<br>3. HiDAC →NR<br>4. FLAG-IDA + Ven →NR | BM blasts: 25% →1%<br>ANC: 0.86 → 5.86<br>PLTs: 59 → 158 | CR (MRD−)<br>D/C for allo-HSCT |
| 60 mg QD | 78 yo M R/R AML | DNMT3A<br>RAD21<br>RUNX1<br>SF3B1<br>TET2 | 1. Dec + Ven → CR (~12 mo)<br>2. Clad + LDAC + Ven → PR | BM blasts: 6% → 1%<br>ANC: 1.26 → 2.35<br>PLTs: 227 → 158 | CR<br>Treatment ongoing awaiting allo-HSCT<br>Loss of RUNX1 & SF3B1 mutations in BM |

Ongoing study data as of May 20, 2026

# BH-30236
# Key Takeaways

**Novel approach to target aberrant alternative splicing,** an emergent driver of cancer progression and resistance

**Tolerable with once daily dosing,** both as monotherapy and in combination with venetoclax

**Preliminary anti-leukemic effect**
motivating additional investigation in myeloid malignancies, with potential for future investigation in solid tumors



BLOSSOMHILL THERAPEUTICS

# BH-501284: pan-KRAS Inhibitor

DUAL-STATE, PSEUDO-IRREVERSIBLE, PAN-KRAS INHIBITOR



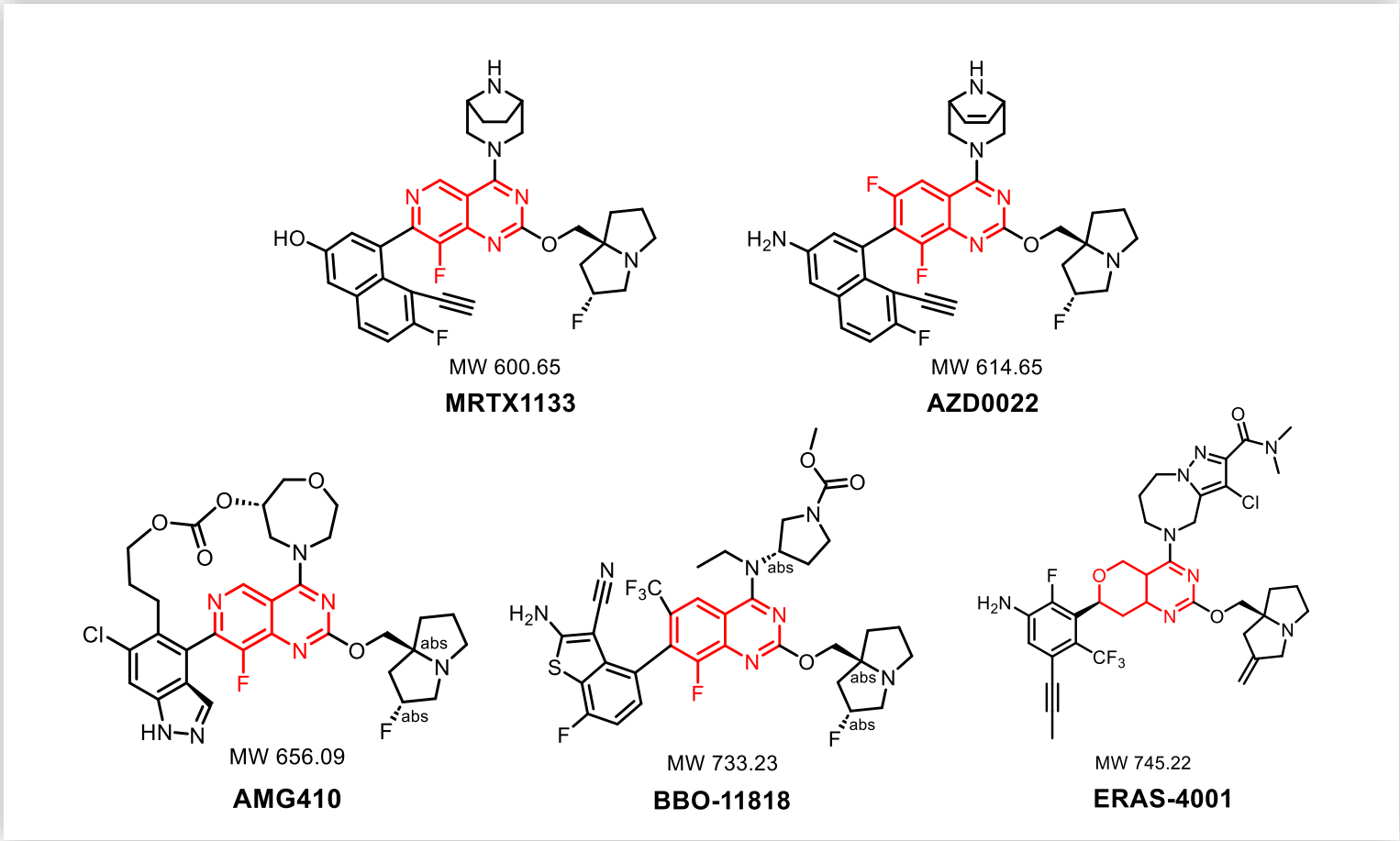
# A Fresh Approach to Pan-KRAS Inhibition

**Recent progress against KRAS comes with limitations:**

- Covalent KRAS inhibition is limited to G12C alleles
- Tricomplex pan-RAS inhibitors have burdensome toxicity that challenges combinations

**Non-covalent Switch-II KRAS inhibitors offer the potential for tolerability and broad activity:**

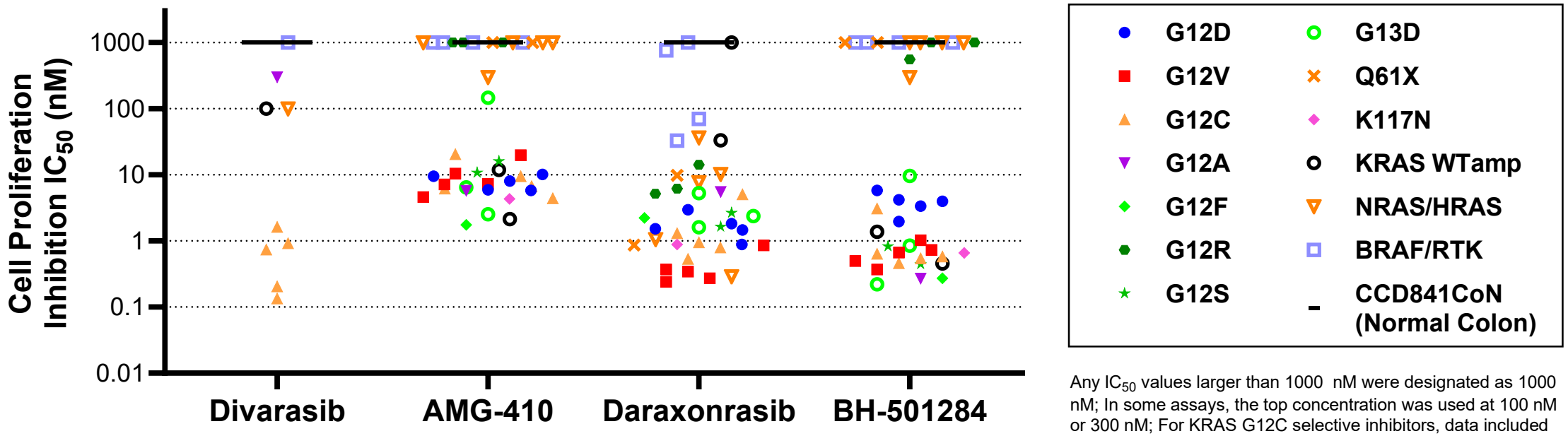
- Current clinical efforts are limited by low bioavailability leading to toxicity from high oral doses with limited efficacy




**We believe a fresh chemical scaffold will be needed to deliver a pan-KRAS Switch-II inhibitor which can achieve both high cell potency and marked oral efficacy in clinic**

# Cell Potency of BH-501284 Versus Clinical Stage KRAS Inhibitors

- Cellular potency mirrored divarasib in G12C with a non-covalent inhibitor and provided potency against diverse KRAS driver mutations and amplification that exceeded the potency of AMG-410
- Cellular potency matched daraxonrasib, but with a broader therapeutic window against HRAS/NRAS and other RTK-driven cancers

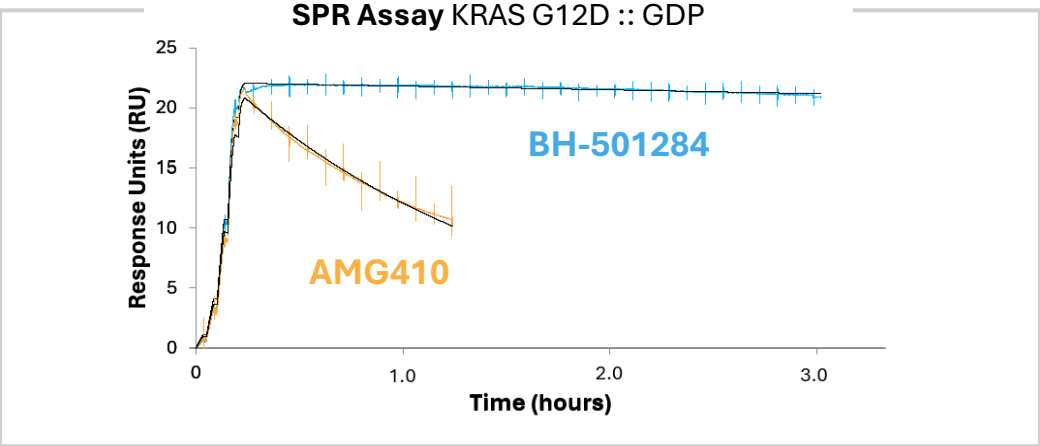



Any $IC_{50}$ values larger than 1000 nM were designated as 1000 nM; In some assays, the top concentration was used at 100 nM or 300 nM; For KRAS G12C selective inhibitors, data included was restricted to KRAS G12C mutated cells; Data cutoff: 04JUN2026

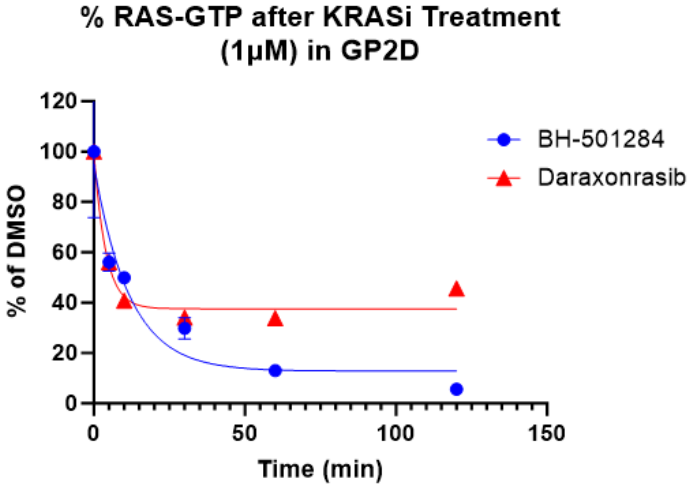
# BH-501284 Demonstrated Long Residence Time, Deep Blocking of RAS (GTP)-cRAF Interaction and Sustained Tumor Regression

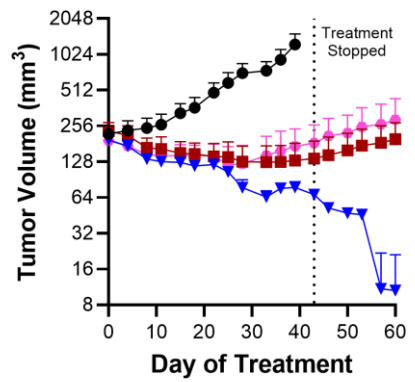
- BH-501284 showed pseudo-irreversible characteristics with long residence time
- BH-501284 showed greater max % KRAS inhibition than daraxonrasib, suggesting more complete elimination of GTP-bound RAS
- BH-501284 demonstrated greater efficacy with deeper and more sustained tumor regression in PANC04.03 CDX tumor model with KRAS G12D mutation than daraxonrasib and zoldonrasib

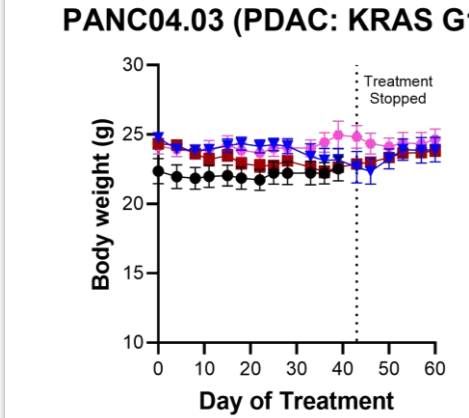
| | | BH-501284 | AMG410 |
|---|---|---|---|
| SPR Assay : "Off" state KRAS G12D :: GDP | $K_D$ (nM) | <0.0148 | 0.119 |
| | T_residence (hr) | >54.2 | 1.40 |




## Cellular Kinetic Profile



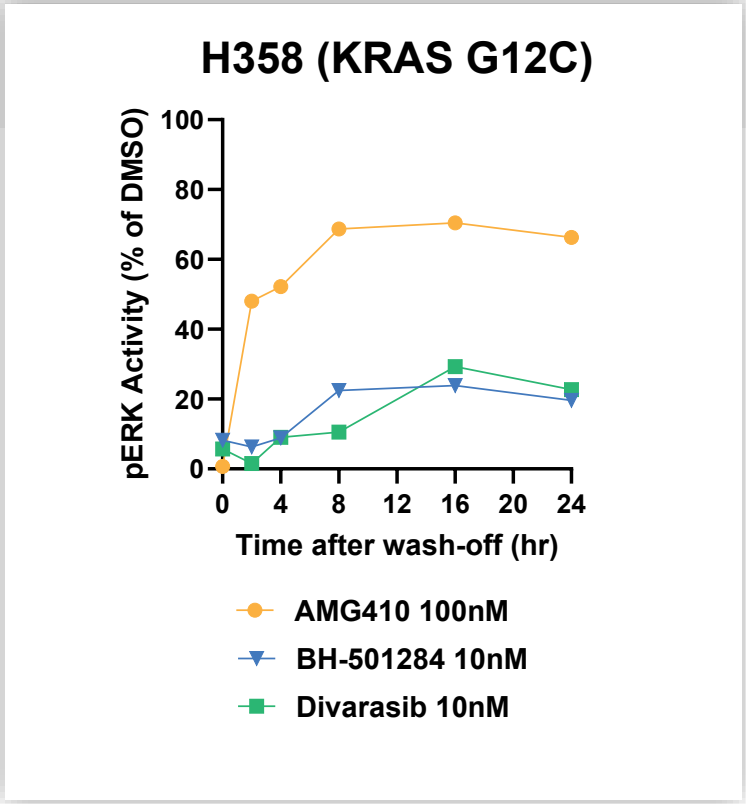



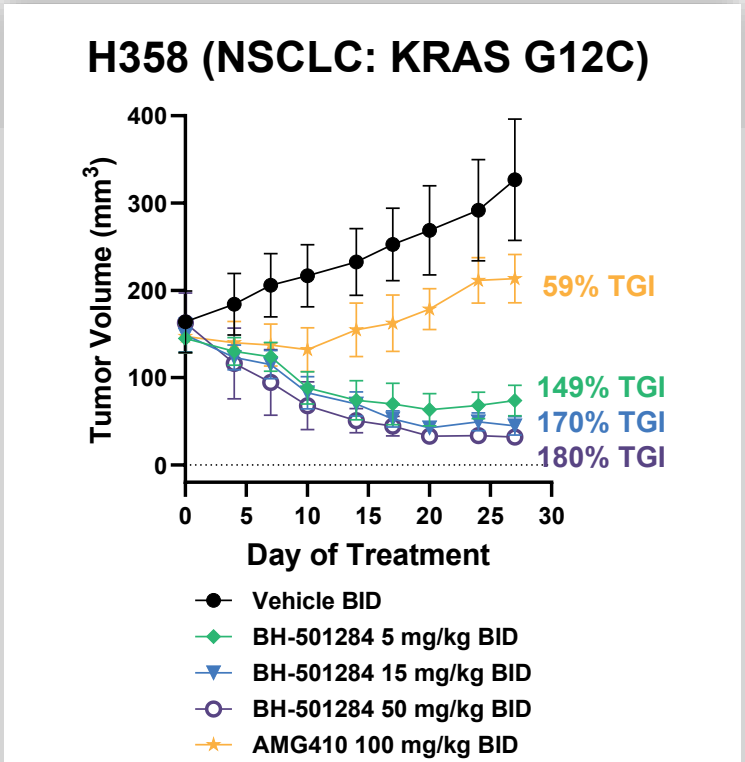



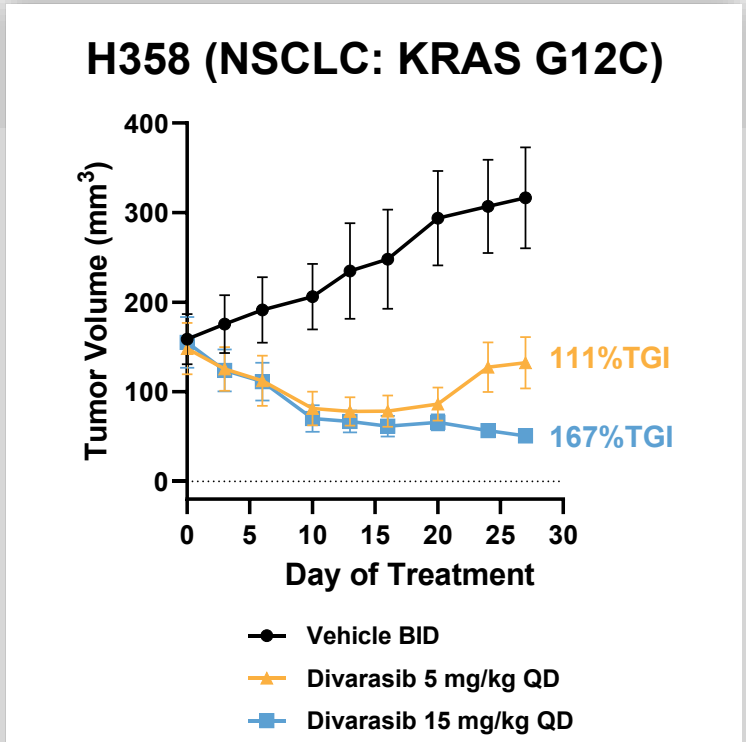

Note: SPR assay was performed at Reaction Biology

# BH-501284 Achieved Sustained Blocking of KRAS Signaling & Marked Efficacy, Comparable to Covalent KRAS G12Ci Divarasib

- In wash-off experiment, BH-501284 sustained pERK inhibition as effectively as divarasib, while AMG410 lost pERK inhibition
- In H358 KRAS G12C tumor model, BH-501284 induced tumor regression at a low dose level (5 mg/kg BID 149% TGI), comparable to divarasib, while AMG410 showed limited TGI at high dose



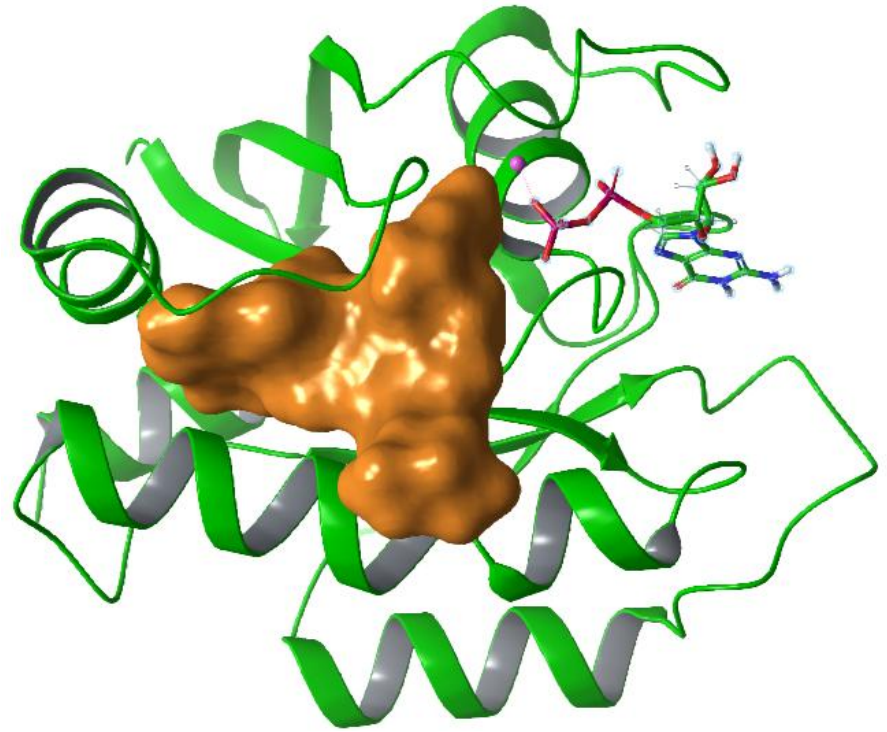
# BH-501284
# Key Takeaways

**Designed for potent pan-KRAS inhibition while sparing HRAS/NRAS**, to reduce toxicity seen with tricomplex inhibitors

**Unique pseudo-irreversible binding** (>54-hour residence time) through use of a novel non-covalent Switch–II chemical scaffold, can lead to prolonged blocking of KRAS signaling

**Marked *in vivo* pan-KRAS activity at low oral dose levels** across multiple *KRAS*-mutated mouse CDX tumor models

**Improved oral bioavailability across species** (mouse 30%; rat 27%; dog 13%; 12% bama miniature pig) positions the molecule for clinical impact, with IND-enabling studies ongoing





# Thank you

THE NEXT LEAP FORWARD IN PRECISION MEDICINE

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