

Corporate Presentation

December 2024

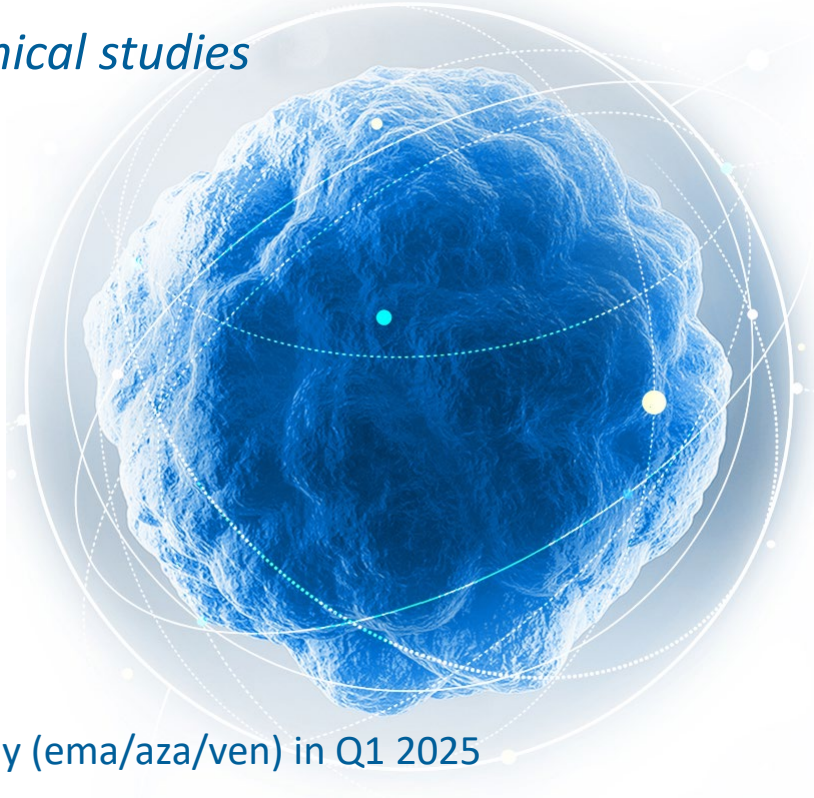
Cautionary note regarding forward looking statements and disclaimers

This presentation contains certain forward-looking statements about Curis, Inc. (“we,” “us,” or the “Company”) within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as “expect(s),” “believe(s),” “will,” “may,” “anticipate(s),” “focus(es),” “plans,” “mission,” “strategy,” “potential,” “estimate(s),” “opportunity,” “intend,” “project,” “seek,” “should,” “would” and similar expressions are intended to identify forward-looking statements. Forward-looking statements are statements that are not historical facts, reflect management’s expectations as of the date of this presentation, and involve important risks and uncertainties. Forward-looking statements herein include, but are not limited to, statements with respect to the timing and results of clinical milestones; ongoing and future clinical trials and the results of these trials; the clinical and therapeutic potential of emavusertib; our cash runway; the focus on emavusertib and management’s ability to successfully achieve its strategies and goals. These forward-looking statements are based on our current expectations and may differ materially from actual results due to a variety of important factors including, without limitation, risks relating to: whether and when the U.S. Food and Drug Administration (the “FDA”) may take further regulatory action with regard to our trials, whether emavusertib will advance further in the clinical development process and whether and when, if at all, it will receive approval from the FDA or equivalent foreign regulatory agencies; whether historical preclinical results will be predictive of future clinical trial results; whether historical clinical trial results will be predictive of future trial results; whether emavusertib development efforts will be successful; whether emavusertib will be successfully marketed if approved; our ability to achieve the benefits contemplated by our collaboration agreements; management’s ability to successfully achieve its strategies and goals; the sufficiency of our cash resources; our ability to raise additional capital to fund our operations on terms acceptable to us and the use of proceeds of any offering of securities or other financing; general economic conditions; competition; and the other risk factors contained in our periodic reports filed with the Securities and Exchange Commission, including the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 and the Company's Quarterly Reports on Form 10-Q for the quarters ended March 31, 2024, June 30, 2024 and September 2024 which are available on the SEC website at www.sec.gov. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events, except as required by law.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Emavusertib is a novel, first-in-class inhibitor of IRAK4

- *Being evaluated in Phase 1/2 clinical studies in NHL, AML, and Solid Tumors*
- *Cash runway into mid-2025*
 - *Sufficient to meet anticipated near term milestones*
- **Near-term milestones:**
 - ~20 pts in PCNSL study in Q1 2025
 - ~6 pts in AML frontline safety study (ema/aza/ven) in Q1 2025



Acceptable safety profile in monotherapy & combination

Demonstrated synergy with BTKi, HMA, BCL2i

Encouraging clinical data in NHL and AML

Broad Market Opportunity in NHL and AML

Current Programs

	PCNSL	FLT3m	AML
US Incidence per 100K	0.5¹	1.3²	4.2³
	<u>Newly Diagnosed Per Year</u>		
US	1,700 ¹	6,000 ²	20,000 ³
Big 5 Europe/Canada	1,800 ¹	5,200 ⁴	17,000 ⁴
Japan/China	<u>7,700¹</u>	<u>12,700⁴</u>	<u>41,200⁴</u>
Total	11,200	23,900	78,200

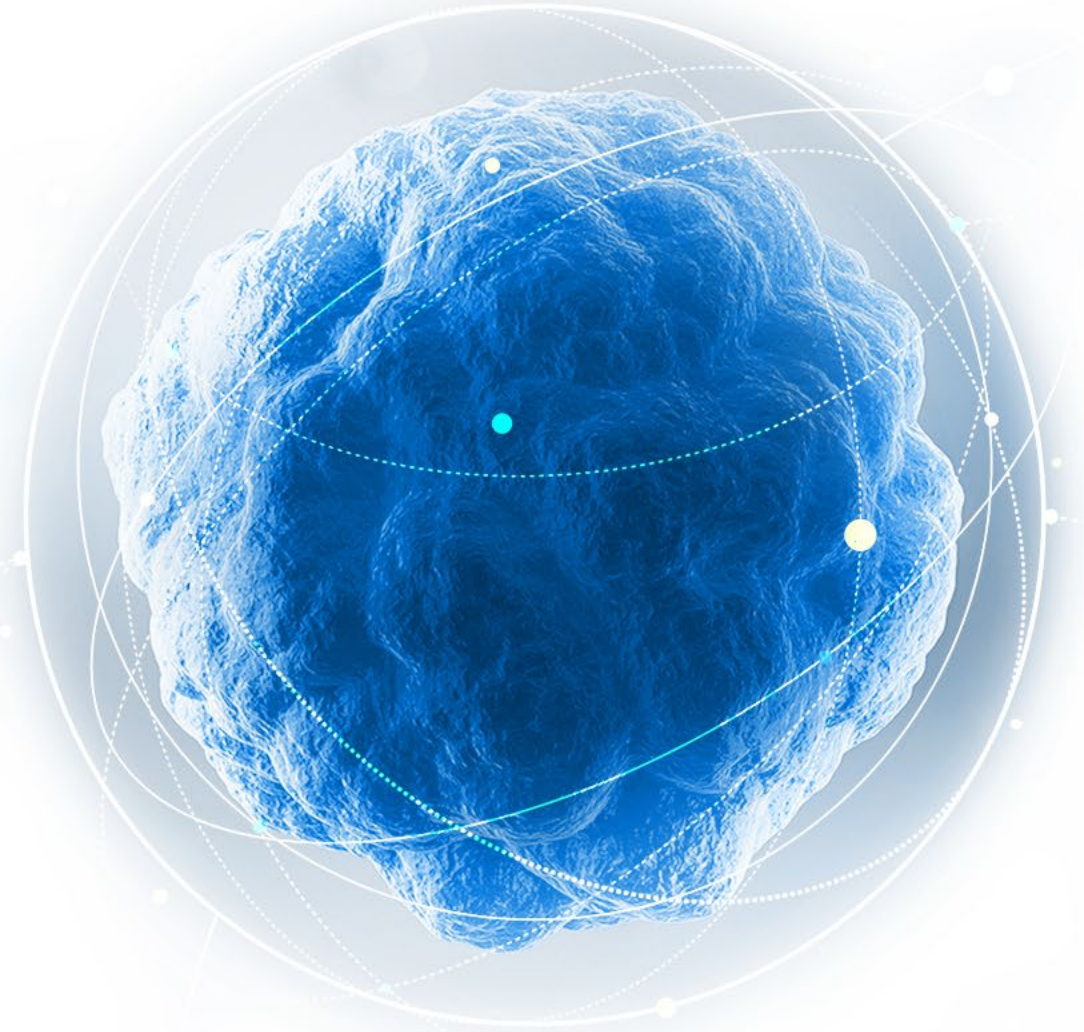
Potential Expansion Opportunities

WM	MCL	MZL	ABC-DLBCL	CLL/SLL
0.5⁵	0.5⁶	1.5⁷	2.0⁸	4.5⁹
	<u>Newly Diagnosed Per Year</u>			
1,700 ⁵	1,700 ⁶	5,000 ⁷	6,800 ⁸	15,000 ⁹
1,800 ⁵	1,800 ⁶	5,500 ⁷	7,500 ⁸	16,400 ⁹
<u>7,700⁵</u>	<u>7,700⁶</u>	<u>23,000⁷</u>	<u>31,400⁸</u>	<u>69,200⁹</u>
11,200	11,200	33,500	45,700	100,600

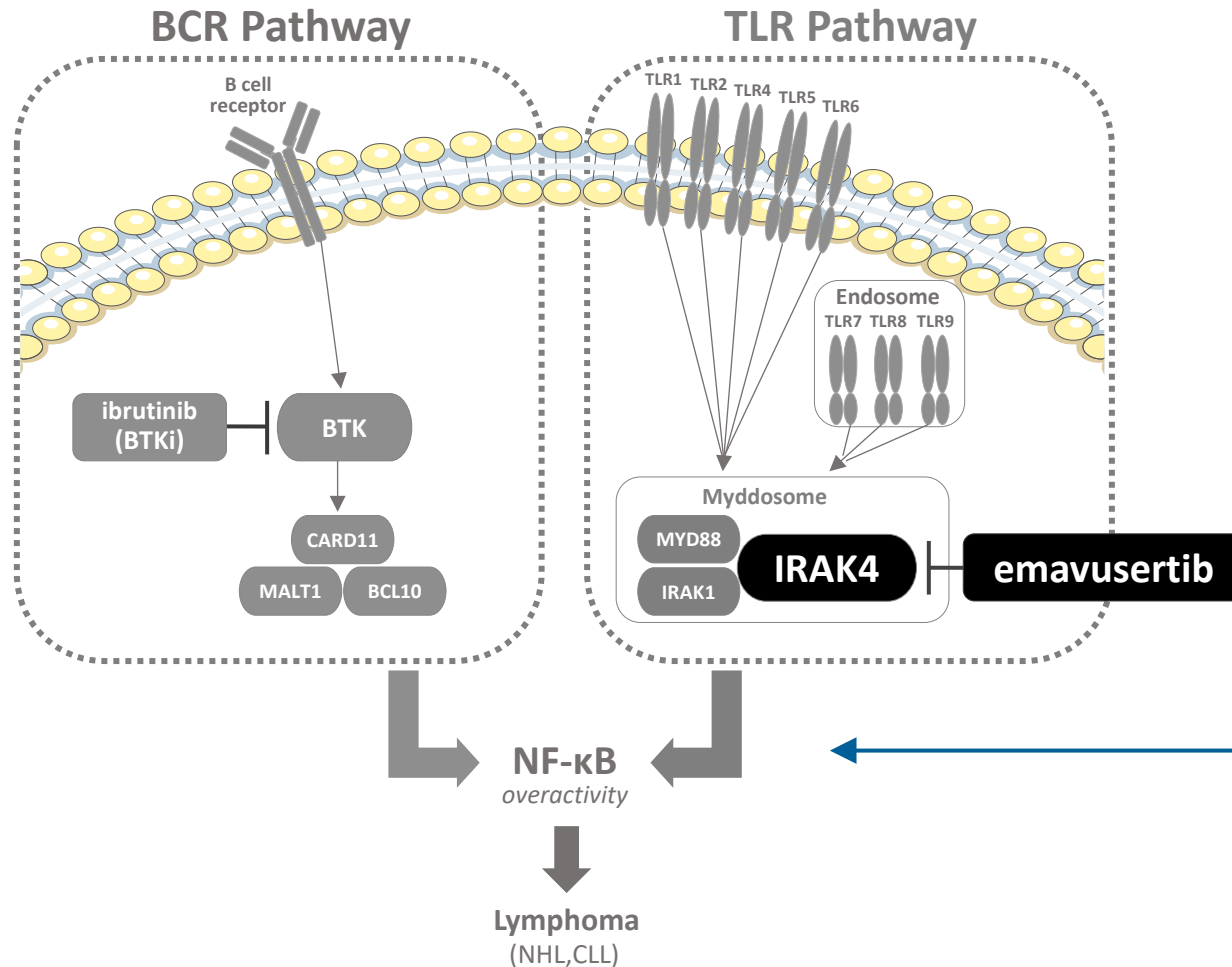
1 – Derived from incident rate in Lv Ther Adv Hematol 2022 and 2022 country population [data.worldbank.org]
 2 – Derived from total AML cases (see footnote 4); FLT3m represents 30% of newly diagnosed AML cases [Daver Leukemia 2019]
 3 – Vakiti Acute Myeloid Leukemia 2023 [www.ncbi.nlm.nih.gov]
 4 – Clarivate DRG, March 2024

5 – Derived from incident rate in <https://rarediseases.org/rare-diseases/waldenstroms-macroglobulinemia/#affected> and 2022 country population [data.worldbank.org].
 6 – Derived from incident rate in <https://www.ncbi.nlm.nih.gov/books/NBK536985/> and 2022 country population [data.worldbank.org].
 7 – Derived from incident rate in Kalashnikov, Blood Cancer Journal, April 2023 and 2022 country population [data.worldbank.org].
 8 – Derived from incident rates in NHL incident rate of 18.6 per 100,000 (seer.cancer.gov) with DLBCL representing 25% of NHL per <https://www.ncbi.nlm.nih.gov/books/NBK557796/>. ABC represents 44% Mareschal, Haematologica, 2011, 96(11) and 2022 country population [data.worldbank.org].
 9 – Derived from incident rate in <https://seer.cancer.gov/statfacts/html/cllsl.html> and 2022 country population [data.worldbank.org].

Emavusertib in NHL



Emavusertib's Mechanism in NHL



*2 pathways drive NF-κB
(which drives NHL)*

*blocking both pathways
(block BCR with BTKi – block TLR with emavusertib)*

enables dual blockade of NF-κB

Emavusertib synergy with BTKi demonstrated in NHL

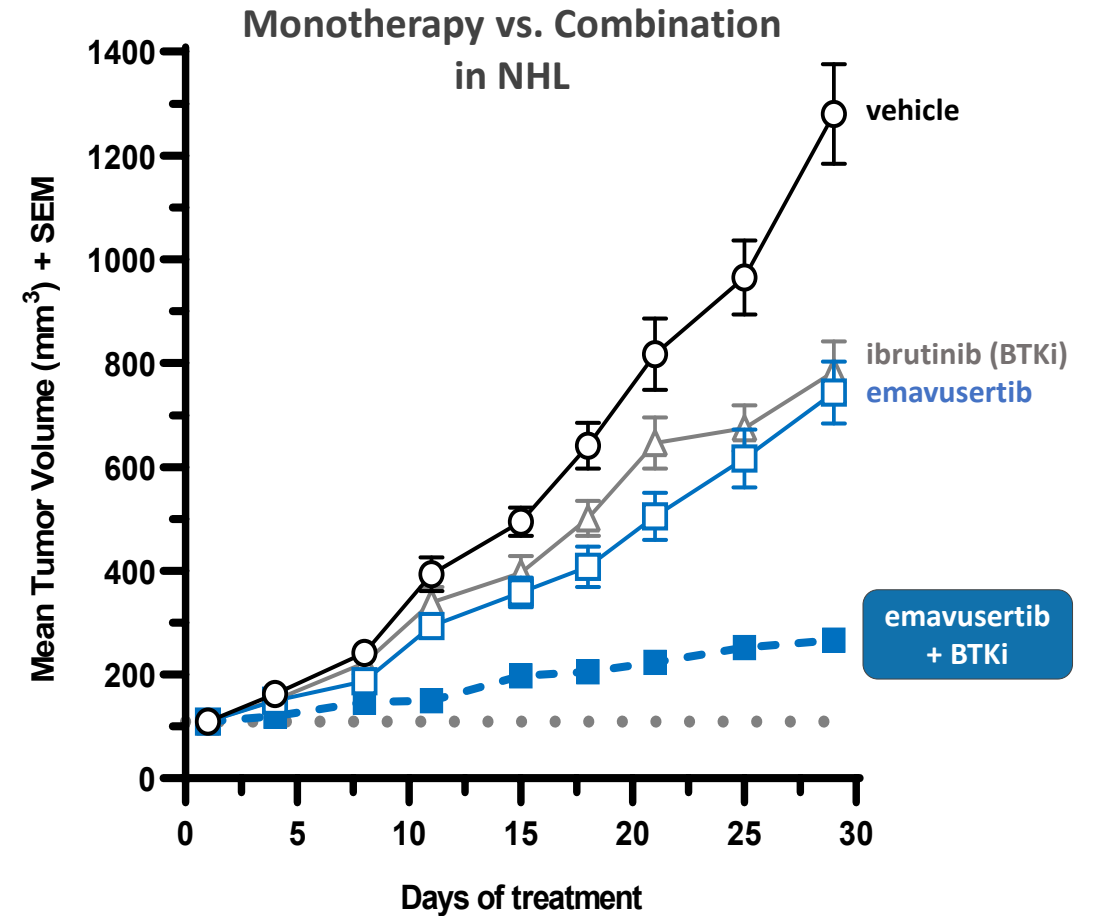
emavusertib + BTKi

dual blockade of the TLR and BCR pathways was demonstrated to be more effective than blocking either one alone

emavusertib: blocks the TLR pathway
BTKi: blocks the BCR pathway

Utility in Multiple NHL Subtypes

- IRAK4i synergizes with BTKi to promote killing of **ABC-DLBCL**¹
- Concurrent treatment with IRAKi and BTKi was significantly more potent in patient **CLL** cells than either drug alone²
- Data suggest IRAK4 as a novel treatment target for **CLL**; inhibition of IRAK4 blocks survival and proliferation of CLL cells³



Preclinical data for emavusertib and ibrutinib in OCI-Ly10 model (Booher et al., IWWM 2018)

¹ Kelly J Exp Med 2015, ² Dadashian Ca Res 2019, ³ Giménez Leukemia 2020

Strategy in NHL

1**Demonstrate safety**

31 patients¹ treated in TakeAim Lymphoma Ph 1b study, acceptable safety profile established, no overlapping dose-limiting toxicity with ibrutinib

2**Demonstrate single-agent activity**

Single-agent activity demonstrated, with patients remaining on study up to 4 years

3**Pursue fastest path to 1st label in R/R patients**

Identify orphan indication with clear unmet need that is addressable with emavusertib's novel mechanism of action

4**Pursue partnership to expand across NHL**

Significant resources will be required to execute clinical studies across multiple NHL subtypes and prepare for potential commercial launch

Emavusertib safety profile in NHL¹

- 31 patients treated with emavusertib in combination with ibrutinib in multiple NHL subtypes
- Shown to be well tolerated with an acceptable safety profile
 - No DLTs observed at 100mg or 200mg
 - 2 reversible DLTs observed at 300mg (stomatitis and syncope)
- Emavusertib crosses the BBB and no dose-limiting CNS toxicities have been observed
- No dose-limiting myelosuppression has been observed

Grade 3+ TRAE in > 1 Patient	100 mg BID ema +ibr (n=6)	200 mg BID ema +ibr (n=18)	300 mg BID ema +ibr (n=7)	Total (n=31)
	n (%)	n (%)	n (%)	n (%)
# patients having gr 3+ TRAEs	4 (67)	8 (44)	6 (86)	18 (58)
Lipase increased	2 (33)	1 (6)		3 (10)
Neutropenia	2 (33)	1 (6)		3 (10)
Platelet count decreased		2 (11)	1 (14)	3 (10)
Alanine aminotransferase increased		1 (6)	1 (14)	2 (6.5)
Amylase increased	2 (33)			2 (6.5)
Aspartate aminotransferase increased		1 (6)	1 (14)	2 (6.5)
Fatigue		1 (6)	1 (14)	2 (6.5)
Hyponatraemia		2 (11)		2 (6.5)

1 – As of July 10, 2024

Abbreviation: Treatment Related Adverse Event (TRAE), ibrutinib (IBR), Dose Limiting Toxicity (DLT), Blood Brain Barrier (BBB), Central Nervous System (CNS), twice daily (BID)

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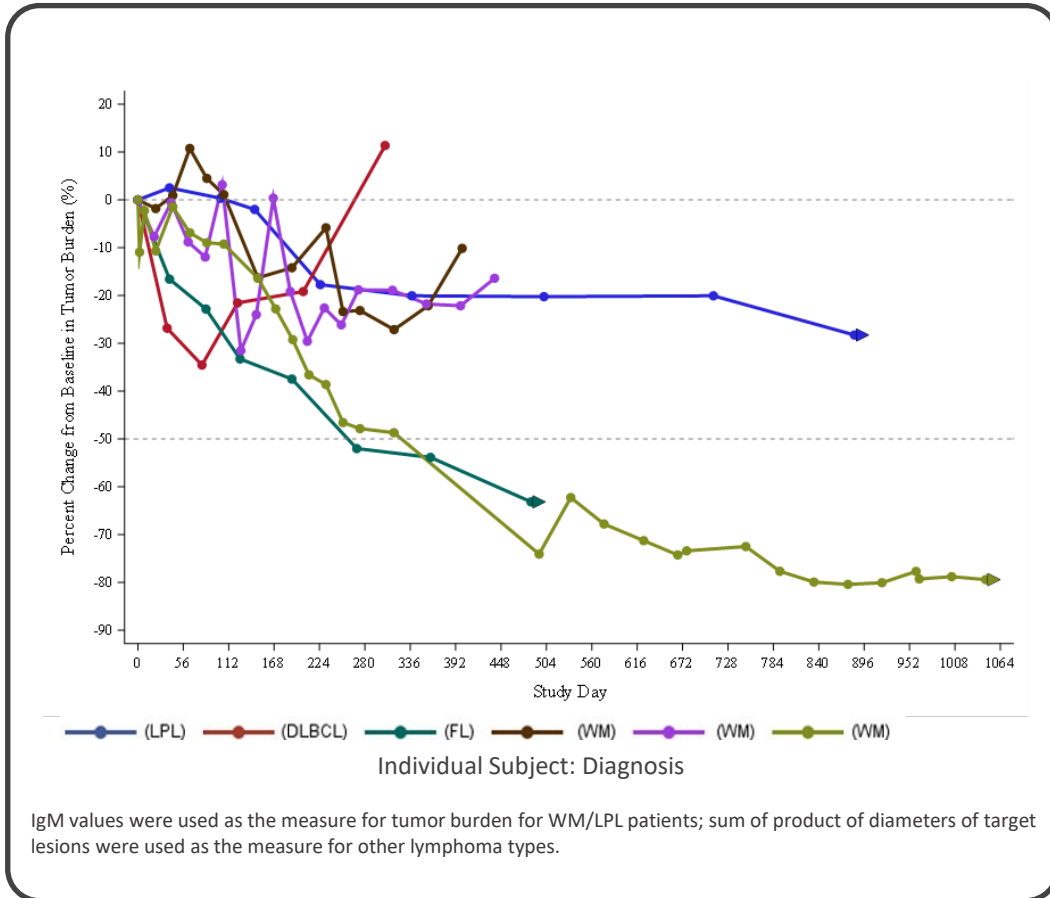
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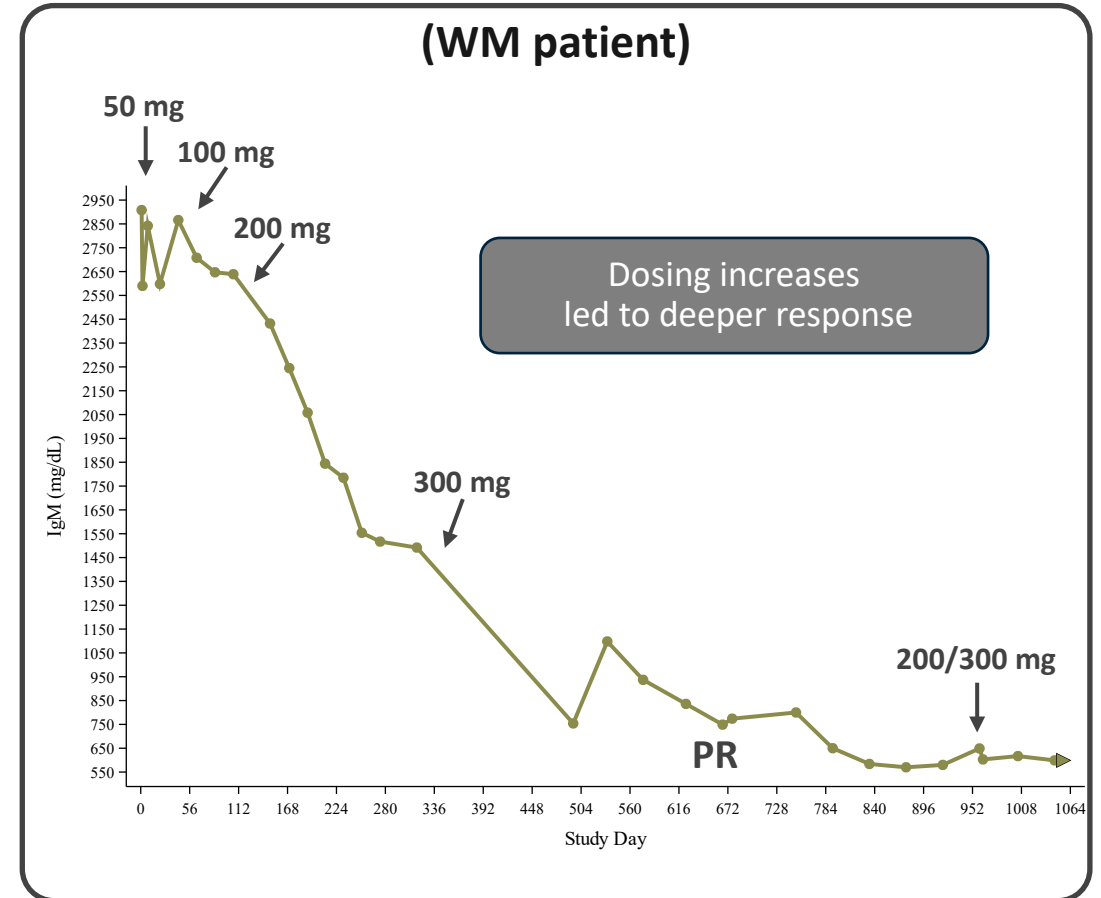
Significant resources will be required to execute clinical studies across multiple NHL subtypes and prepare for potential commercial launch

Single-agent activity demonstrated in NHL

Tumor Reduction Sustained up to 3+ years



Case Study in Dose Response (WM patient)



2022 IWWM Conference Presentation

Abbreviations: Lymphoplasmacytic Lymphoma (LPL), Follicular Lymphoma (FL), Partial Response (PR)

Strategy in NHL

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BTKi is currently used in 6 NHL subtypes

PCNSL was selected as our first NHL indication for pursuing FDA approval

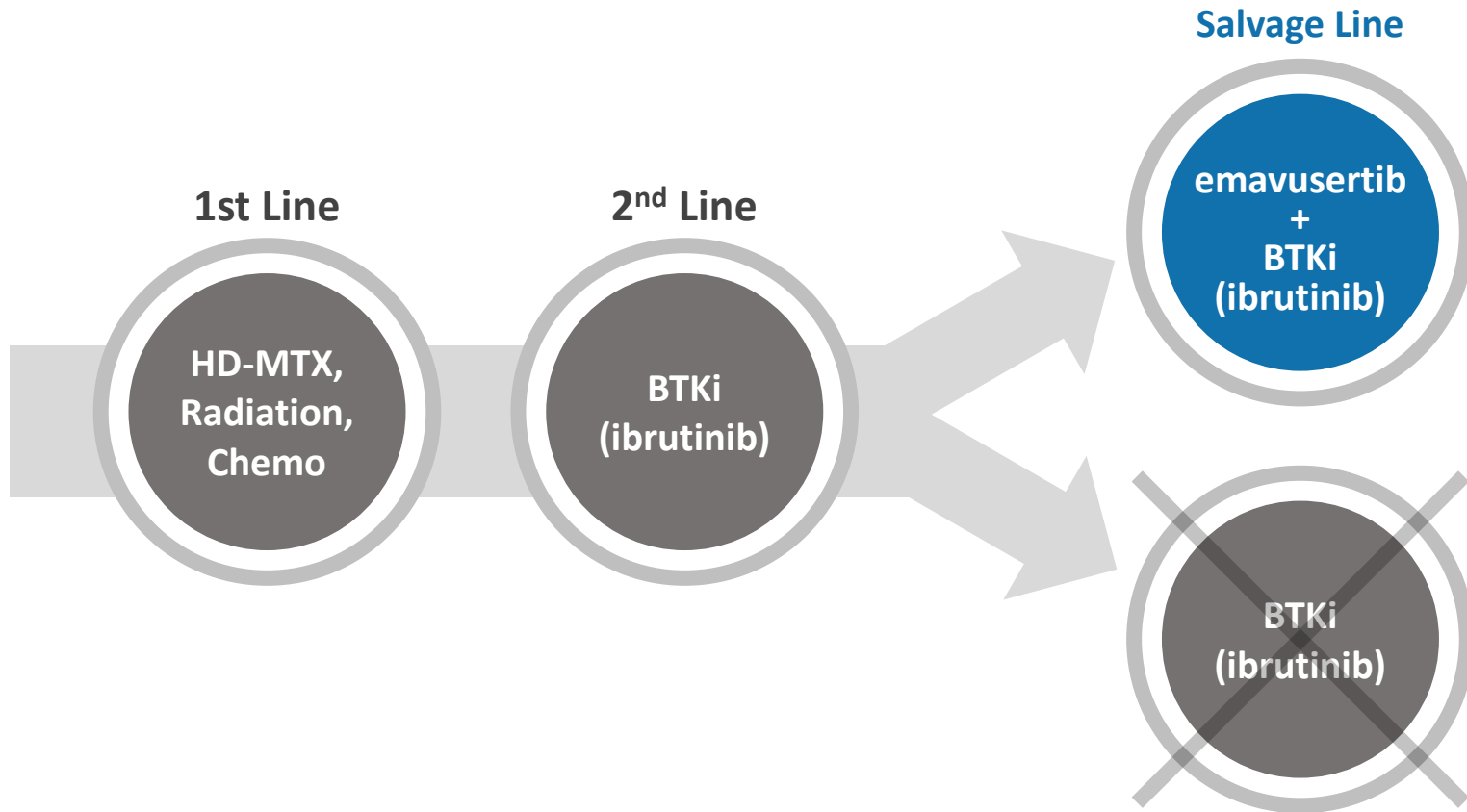
Tumor	Incidence in U.S.	Key Targets of Interest	Therapies Used
ABC-DLBCL	2 per 100,000 ~ 6,800 patients	IRAK4, MYD88, CD79, NF-kB	R-CHOP, BTKi
PCNSL	0.5 per 100,000 ~ 1,700 patients	IRAK4, MYD88, CD79, NF-kB	MTX, Chemo, RT, BTKi
WM	0.5 per 100,000 ~ 1,700 patients	IRAK4, MYD88, CD79, NF-kB	Chemo, BTKi
MCL	0.5 per 100,000 ~ 1,700 patients	BCR and TLR pathway activation	Chemo, αCD20, BTKi
MZL	1.5 per 100,000 ~ 5,000 patients	IRAK4, MYD88, CARD11, NF-kB	Chemo, αCD20, RT, BTKi
CLL	4.5 per 100,000 ~ 15,000 patients	NF-kB	αCD20, BTKi

Abbreviations: NF-kB, Nuclear factor-kB, proteasome inhibitors (PI)

Sources: 1. Vermaat, J. S., et al. (2019). MYD88 mutations identify a molecular subgroup of diffuse large B-cell lymphoma with an unfavorable prognosis. *Haematologica*, 105(2), 424–434 ([Link](#)); 2. Zhou, Y., et al (2018). Analysis of genomic alteration in primary central nervous system lymphoma and the expression of some related genes. *Neoplasia*, 20(10), 1059–1069 ([Link](#)); 3. Alcoceba, M., et al (2022). MYD88 mutations: Transforming the landscape of IGM monoclonal gammopathies. *International Journal of Molecular Sciences*, 23(10), 5570. ([Link](#)); 4. Shekhar, R., et al. (2021). Frequency of MYD88 L265P mutation and its correlation with clinico-hematological profile in mature B-cell neoplasm. *Hematology/Oncology and Stem Cell Therapy*, 14(3), 231–239 ([Link](#)); 5. Insuasti-Beltran, G., et al. (2015). Significance of MYD88 L265P mutation status in the subclassification of Low-Grade B-Cell Lymphoma/Leukemia. *Archives of Pathology & Laboratory Medicine*, 139(8), 1035–1041 ([Link](#)); 6. Shuai, W., et al. (2020). Clinicopathological characterization of chronic lymphocytic leukemia with MYD88 mutations: L265P and non-L265P mutations are associated with different features. *Blood Cancer Journal*, 10(8) ([Link](#));

R/R PCNSL selected for 1st NHL indication

Critical unmet need – patients often proceed to hospice after 2 lines of treatment

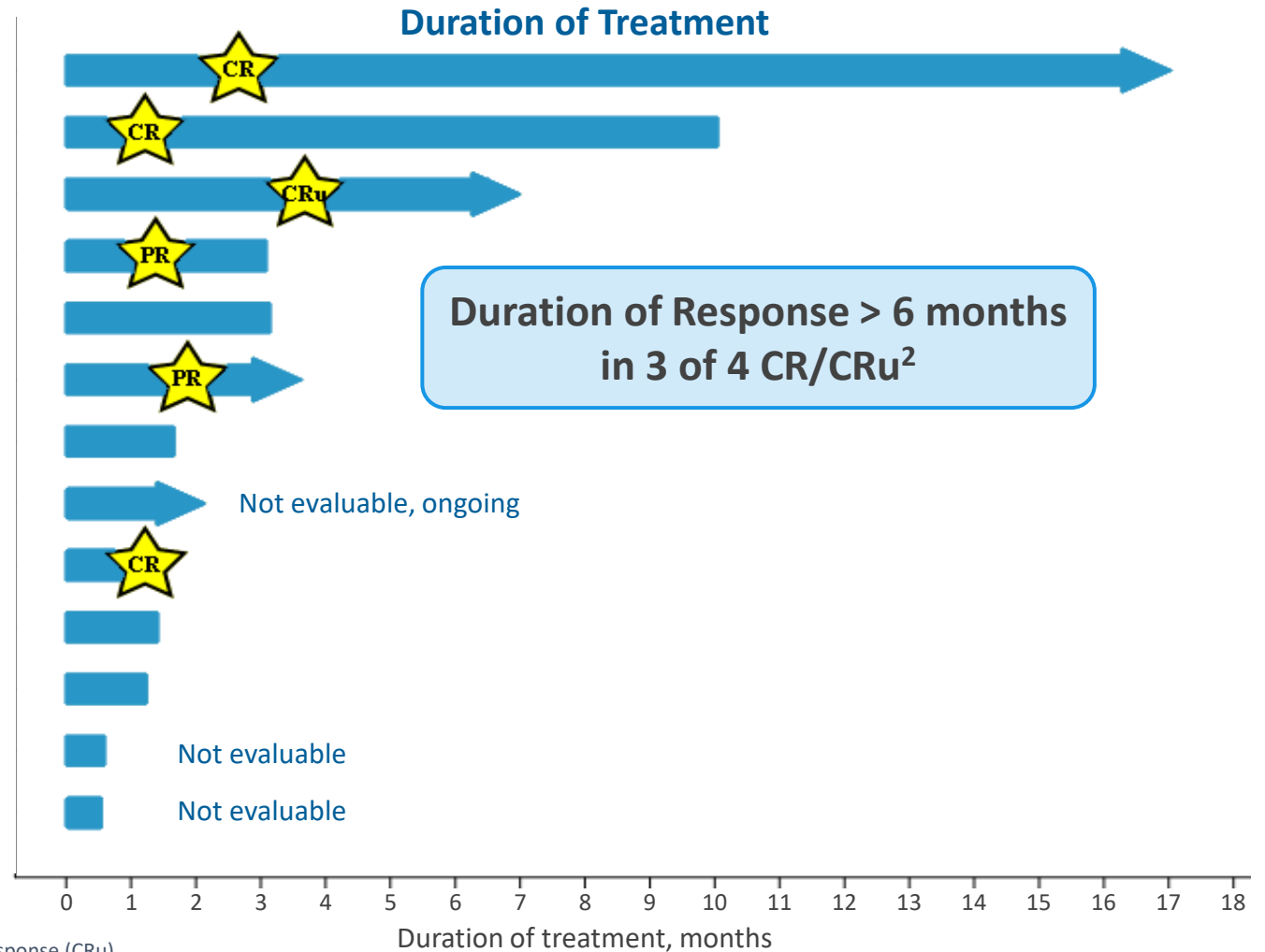
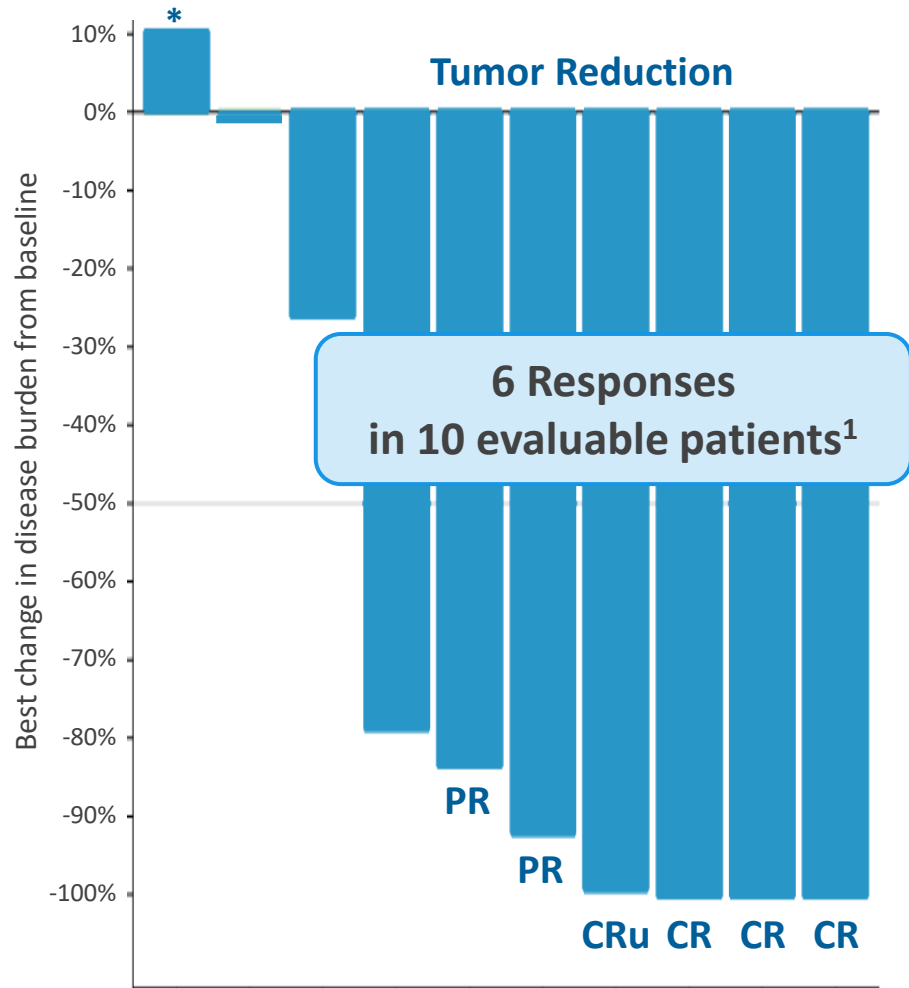


Stay on BTKi – add emavusertib
*blocking both the TLR and BCR pathways
 maximizes downregulation of NF-κB and
 may lead to tumor reduction*

Re-treating with BTKi is ineffective
*Physicians do not repeat BTKi treatment,
 if a patient’s disease progressed while on it*

Encouraging clinical data in R/R PCNSL

Results for patients treated with emavusertib + ibrutinib, after they have progressed on prior BTKi



As of July 10, 2024

*Indicates best percent change > 10%. Abbreviations: Complete Remission (CR), Unconfirmed Complete Response (CRu)

¹Evaluable patients are those who have completed at least one cycle of treatment and received at least one post-treatment assessment. ²As of August 27, 2024

PCNSL Case Study

Patient with R/R PCNSL treated with emavusertib + ibrutinib

Male patient, 53 yrs

Diagnosis: PCNSL diagnosed on 30 Jun 2020

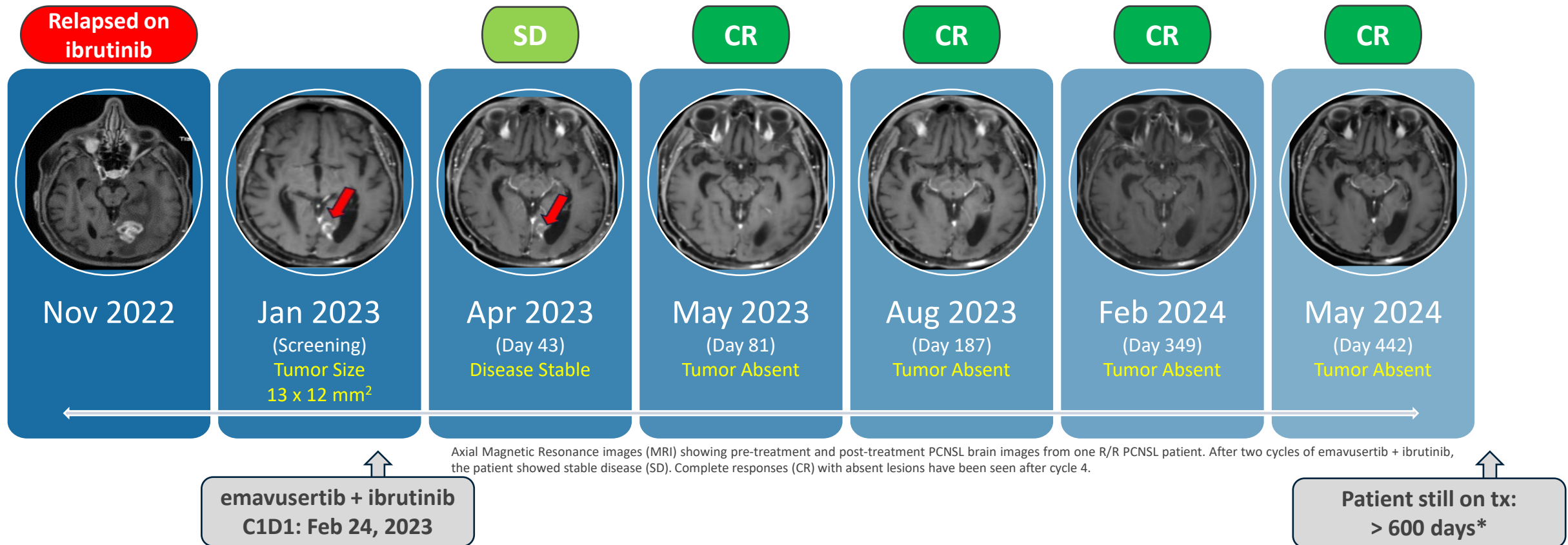
Baseline: Depression, elevated LFTs, loss of appetite, cerebral edema, mixed IBS, hiatal hernia, GERD, essential hypertension, and obstructive sleep apnea

Prior Tx: Line 1: MTX, high-dose BCNU, Ara-C, thiotepa, WBRT, rituximab, and ASCT (PR)
Line 2: ibrutinib (CR)

Relapse: Disease progressed on treatment with ibrutinib on 29 Nov 2022, primary lesion measured 13 x 12 mm

PCNSL Case Study

Patient with R/R PCNSL who achieved CR on emavusertib + ibrutinib



Axial Magnetic Resonance images (MRI) showing pre-treatment and post-treatment PCNSL brain images from one R/R PCNSL patient. After two cycles of emavusertib + ibrutinib, the patient showed stable disease (SD). Complete responses (CR) with absent lesions have been seen after cycle 4.

Consistent with previous findings, these data support the hypothesis that emavusertib can re-sensitize patients to BTKi therapy, and demonstrates its potential to significantly advance R/R PCNSL treatment

* as of Nov 2024

Strategy in NHL

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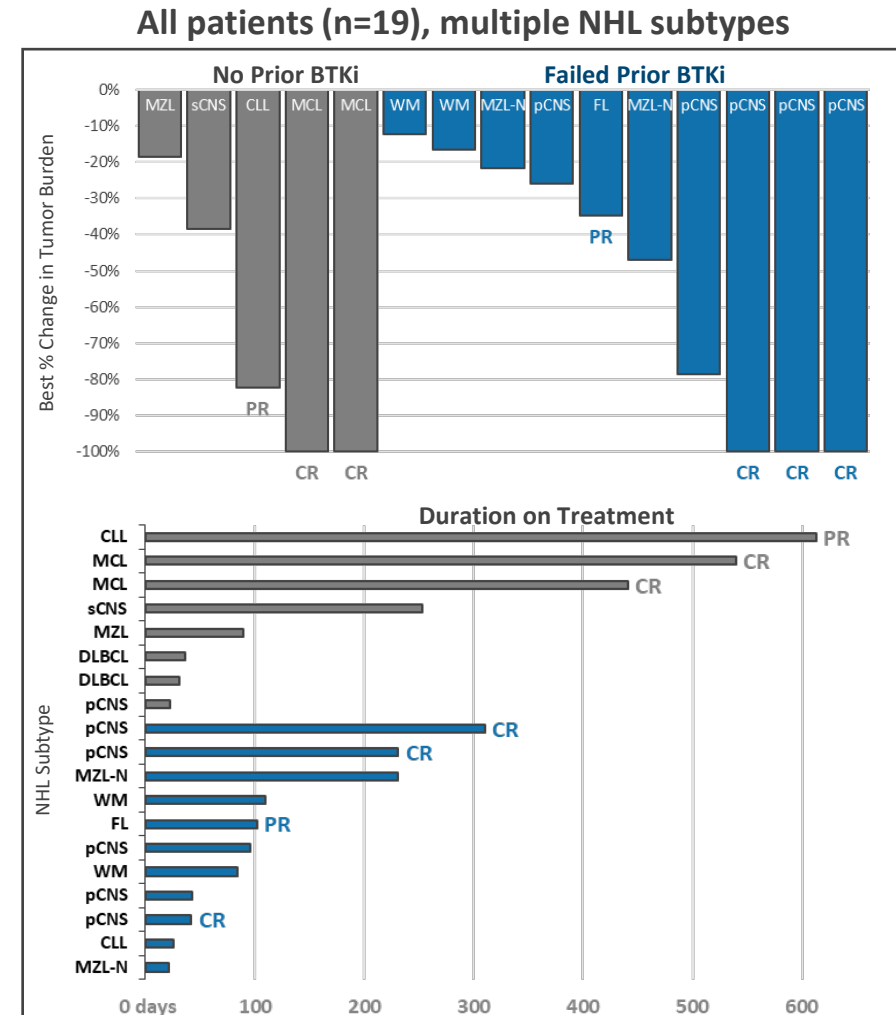
4**Pursue partnership to expand across NHL**

Significant resources will be required to execute clinical studies across multiple NHL subtypes and prepare for potential commercial launch

Anti-cancer activity shown across multiple NHL subtypes

Data presented at ASH 2023 supports emavusertib + BTKi combination in additional NHL subtypes

- Heavily pre-treated patients (1-10 prior lines)
- Ongoing study with median treatment of 96 days (range 21-613 days)
- 7 of 19 patients achieved objective responses, **including patients who failed prior BTKi**
- 15 of 19 patients saw a reduction in tumor burden

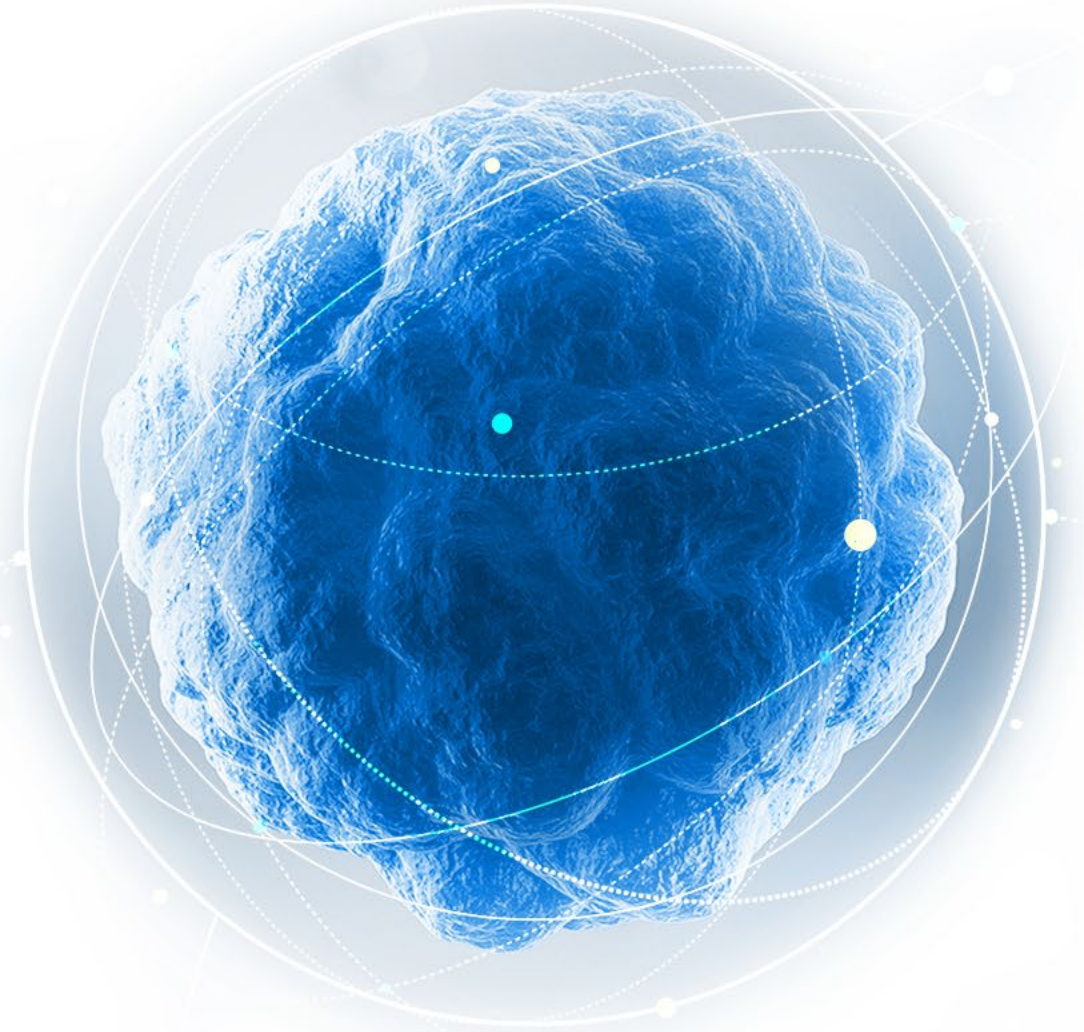


Summary in NHL



- Emavusertib has demonstrated anti-cancer activity in R/R PCNSL
- Received Orphan Drug designation in EMA
- Next steps:
 - Work with FDA and EMA to align on a registrational path in R/R PCNSL
 - Prioritize additional NHL indications (after PCNSL) that could benefit from the dual-blockade of NF- κ B

Emavusertib in AML



Emavusertib binds to IRAK4 and FLT3, blocking both the TLR and FLT3 pathways

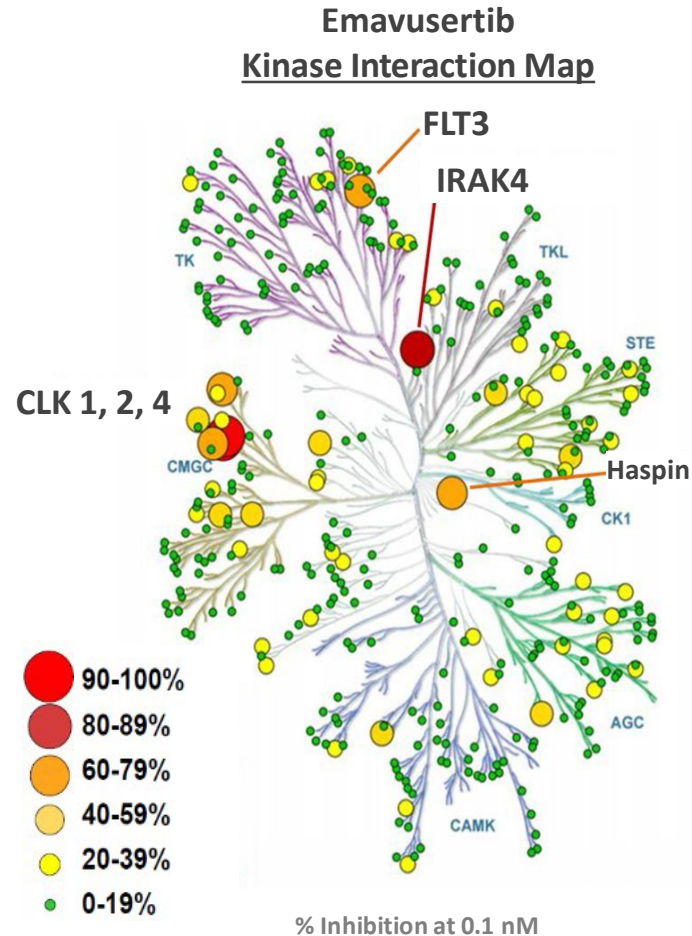


Illustration reproduced courtesy of Cell Signaling Technology

Emavusertib Binding Affinity

Target	K _d nM
IRAK1	12,000
IRAK2	>20,000
IRAK3	8,500
IRAK4	23
DYRK1A	25
FLT3 WT	31
FLT3 (D835H)	5
FLT3 (D835V)	44
FLT3 (D835Y)	3
FLT3 (ITD)	8
FLT3 (K663Q)	47
FLT3 (N841I)	16
Haspin (GSG2)	32
CLK1	10
CLK2	20
CLK3	>20,000
CLK4	14
TrkA	130

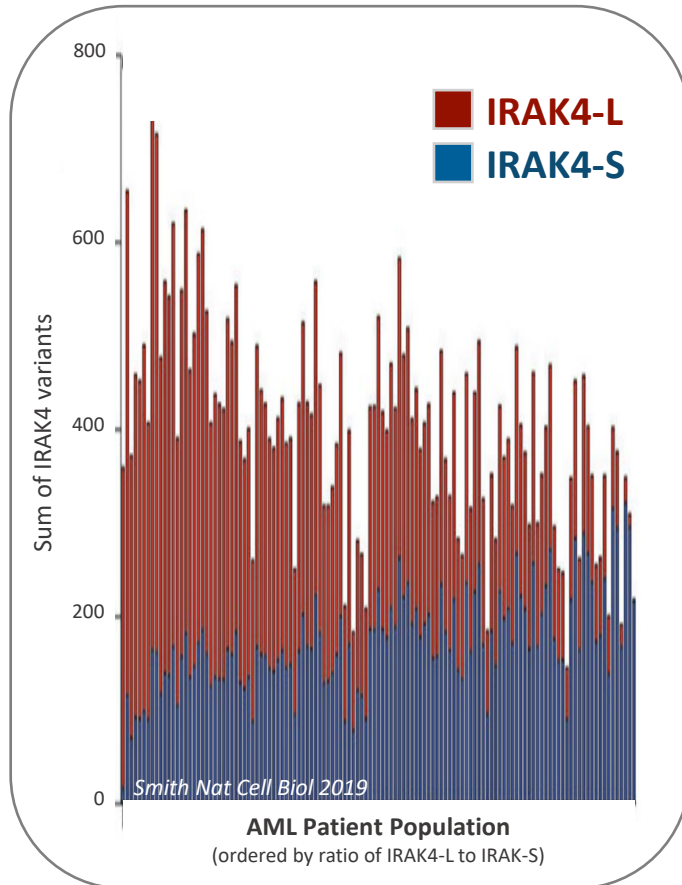
DiscoverX Kinase Panel
(378 kinases screened)

Binds tightly to IRAK4

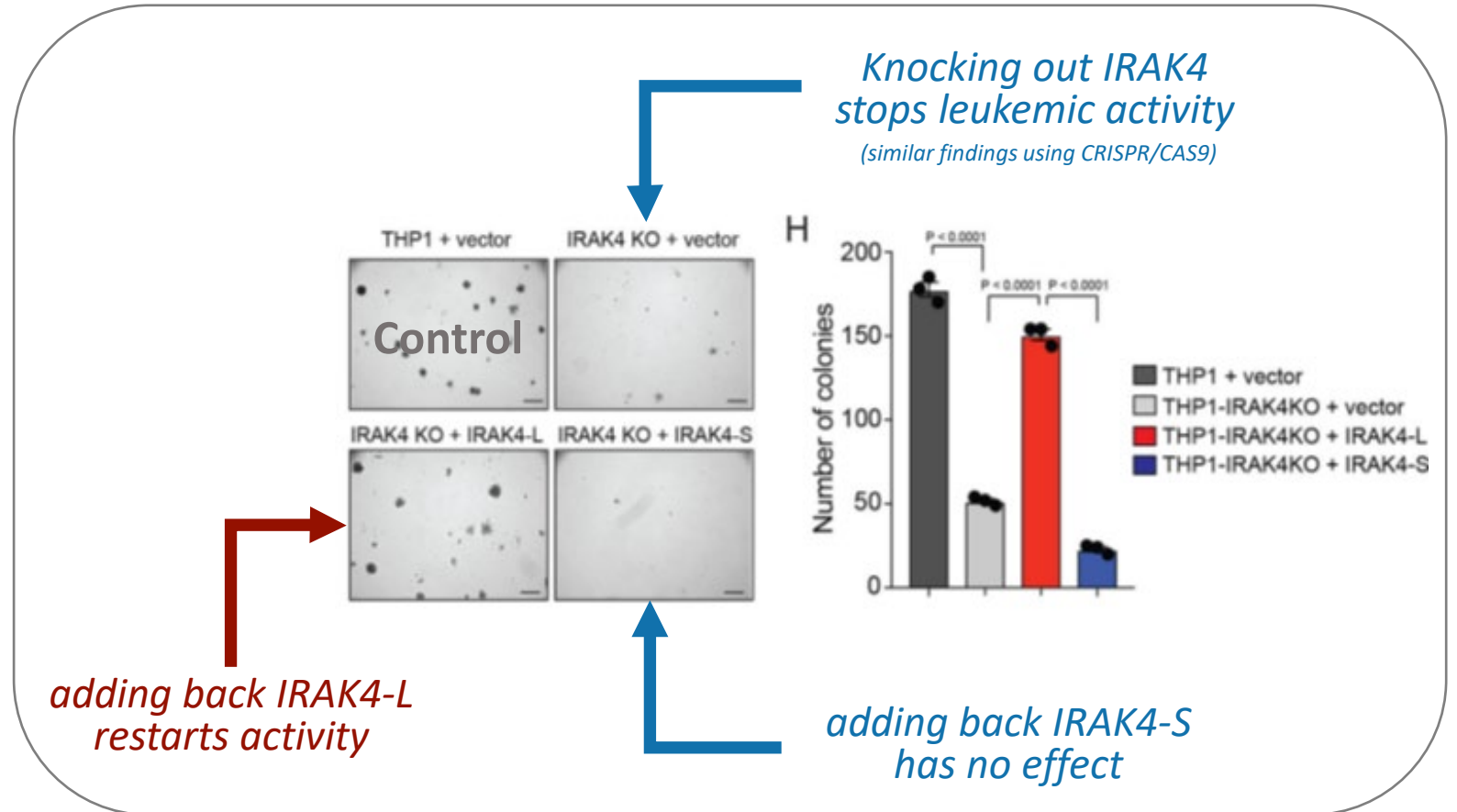
Engineered to hit multiple targets of interest in oncology, including FLT3

IRAK4-L is an independent and powerful driver of disease in AML

IRAK4-L is expressed in nearly all AML patients



IRAK4-L is oncogenic in AML



Strategy in AML

1

Demonstrate safety

102 AML patients¹ treated in TakeAim Leukemia Ph 1/2 study, acceptable safety profile established

2

Demonstrate single-agent activity

Single-agent activity observed; next step is to confirm these initial findings in a larger number of patients

3

Pursue fastest path to 1st label in R/R patients

Address genetically-defined AML population with emavusertib's novel mechanism of action

4

Explore frontline opportunity with combination

IRAK4-L is expressed in nearly all AML patients; preclinical "all comer" models suggest emavusertib is synergistic with azacitidine and venetoclax

5

Pursue partnership to maximize potential commercial opportunity

Significant resources will be required to execute a large clinical study and prepare for potential commercial launch

Grade ≥ 3 Treatment-Related Adverse Events (TRAEs) in All Treated R/R AML Patients

Emavusertib has an acceptable and manageable safety profile in R/R AML patients

Grade 3+ Treatment-Related Adverse Event Reported in > 1 patients, n (%)	200 mg BID (n = 17)	300 mg BID (n = 75)	400 mg BID (n = 8)	500 mg BID (n = 2)	All AML Patients (n = 102)
# of patients having grade 3+ TRAEs	1 (5.9)	29 (38.7)	3 (37.5)	1 (50.0)	34 (33.3)
Blood creatine phosphokinase increased	0	6 (8.0)	0	0	6 (5.9)
Neutropenia	0	5 (6.7)	1 (12.5)	0	6 (5.9)
Anaemia	0	5 (6.7)	0	0	5 (4.9)
Platelet count decreased	0	3 (4.0)	0	0	3 (2.9)
Rhabdomyolysis*	0	2 (2.7)	1 (12.5)	0	3 (2.9)
Syncope	0	1 (1.3)	1 (12.5)	1 (50.0)	3 (2.9)
Aspartate aminotransferase increased	0	2 (2.7)	0	0	2 (2.0)
Febrile neutropenia	0	1 (1.3)	1 (12.5)	0	2 (2.0)
Leukopenia	0	2 (2.7)	0	0	2 (2.0)
Orthostatic hypotension	0	2 (2.7)	0	0	2 (2.0)
Thrombocytopenia	0	2 (2.7)	0	0	2 (2.0)

Source: TakeAim Leukemia FLT3 Clinical Presentation ASH 2024. Data as of October 31, 2024

* Three events of rhabdomyolysis were investigator-reported, 1/3 met laboratory defined criteria for rhabdomyolysis (CPK >10 x ULN and SCr \geq 1.5 x ULN).

Abbreviation: Treatment Related Adverse Event (TRAE), Upper Limit Normal (ULN)

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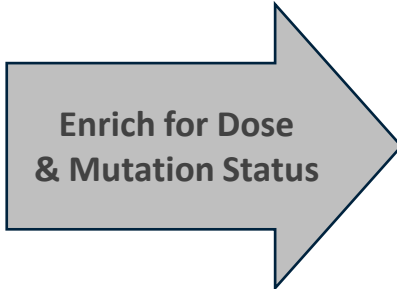
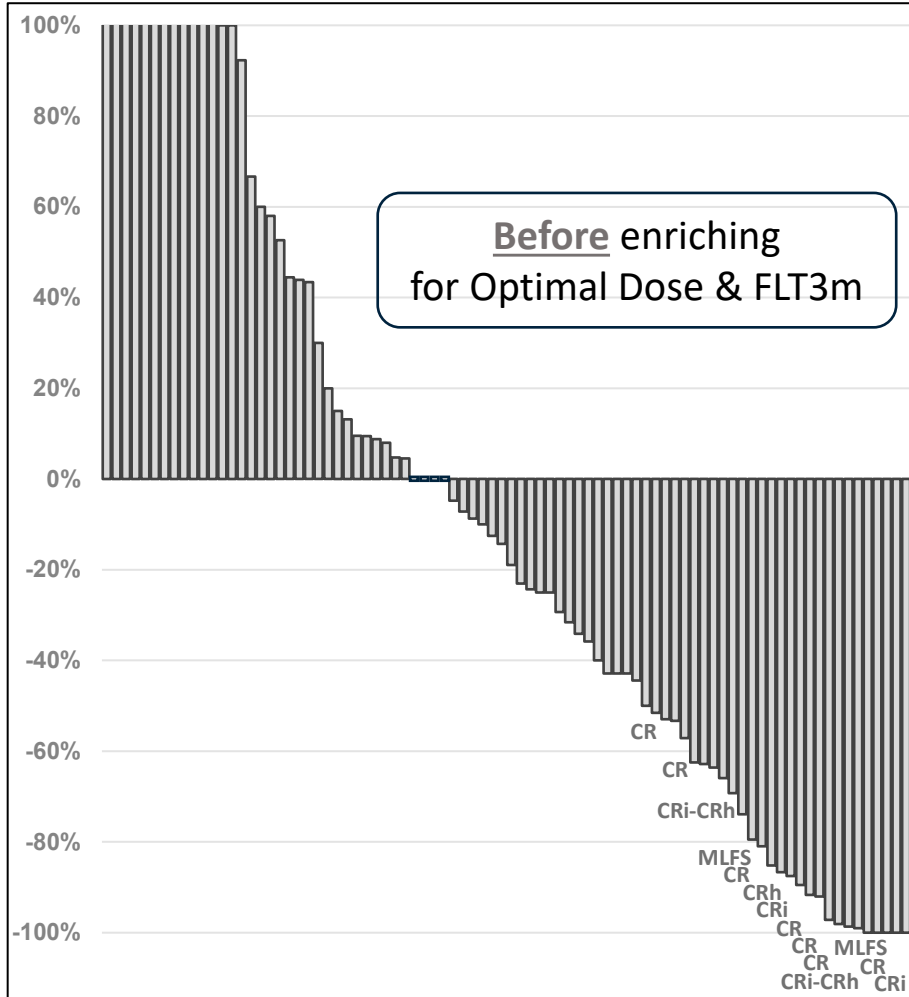
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Pursue partnership to maximize potential commercial opportunity

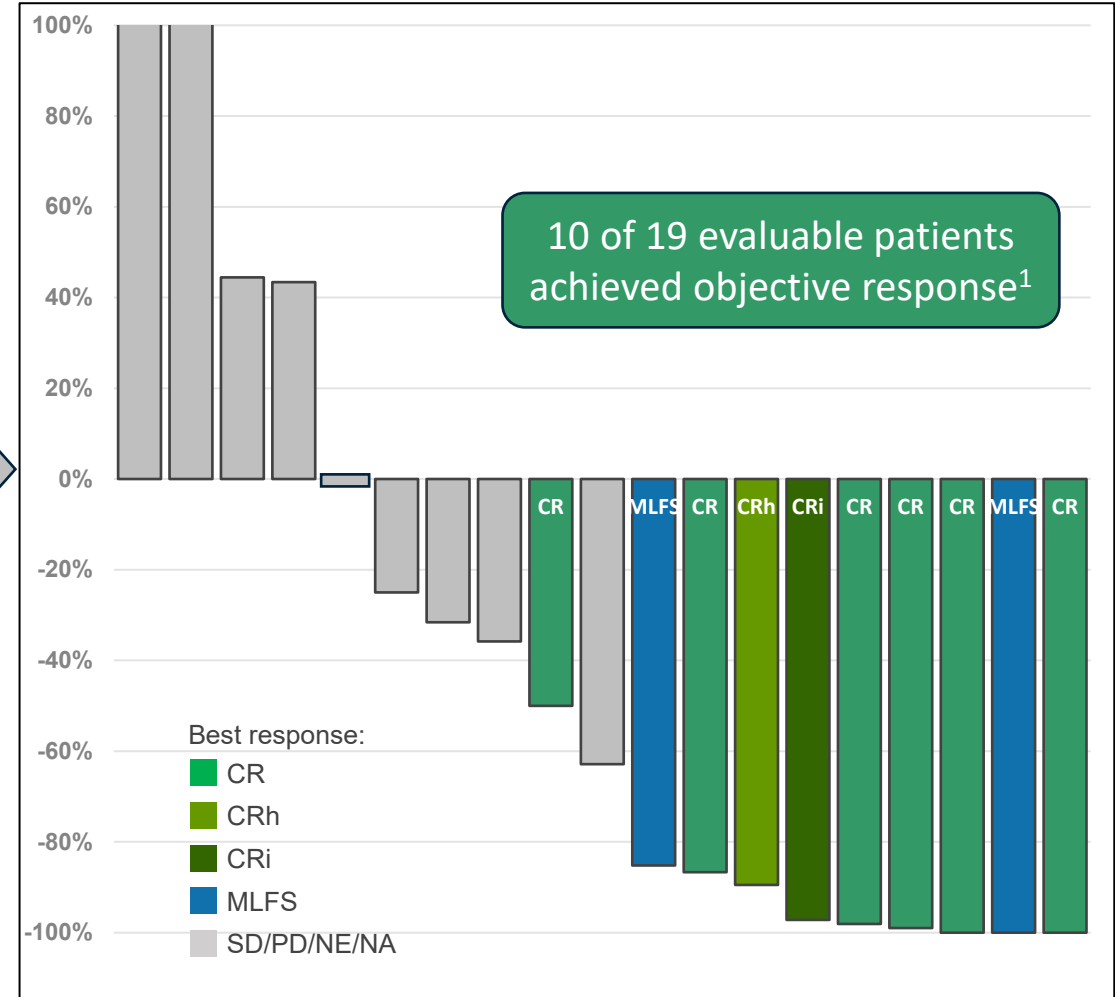
Significant resources will be required to execute a large clinical study and prepare for potential commercial launch

Single-agent activity demonstrated in AML

All Patients, All Dose Levels



Patients with < 3 lines of prior therapy with FLT3 mutation and treated at 300mg BID



Data include all R/R AML patients determined to be evaluable for objective response using baseline and post-treatment marrow assessments as of October 31, 2024. Abbreviations: complete remission with partial hematological recovery (CRh); Complete remission with partial hematological recovery (CR); morphologic leukemia-free state (MLFS)

Source: TakeAim Leukemia FLT3 Clinical Presentation ASH 2024. Data as of October 31, 2024
 1 - 2 of 21 patients were treated, but discontinued treatment prior to first disease response assessment (death occurred at Day 8 and Day 13, respectively), and were not included as evaluable.

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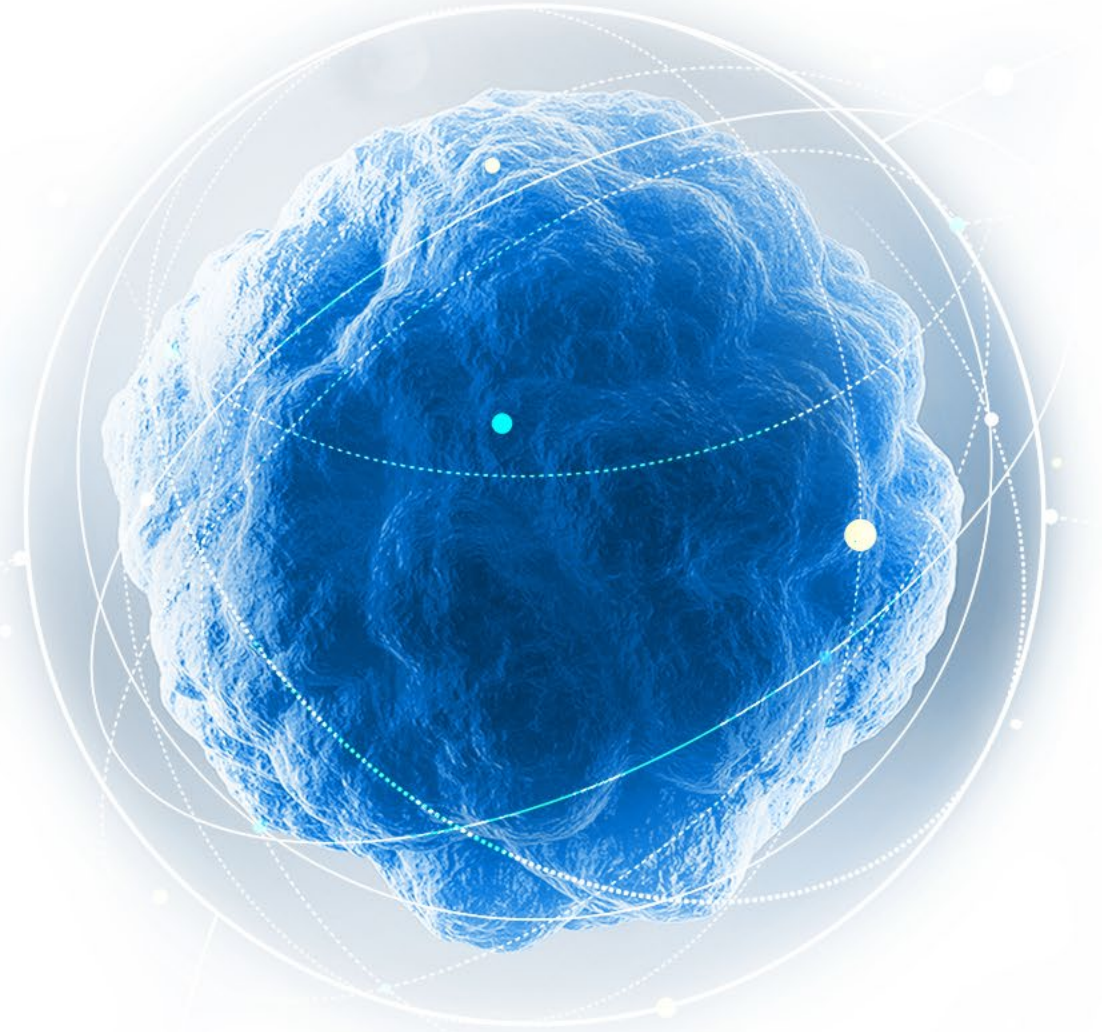
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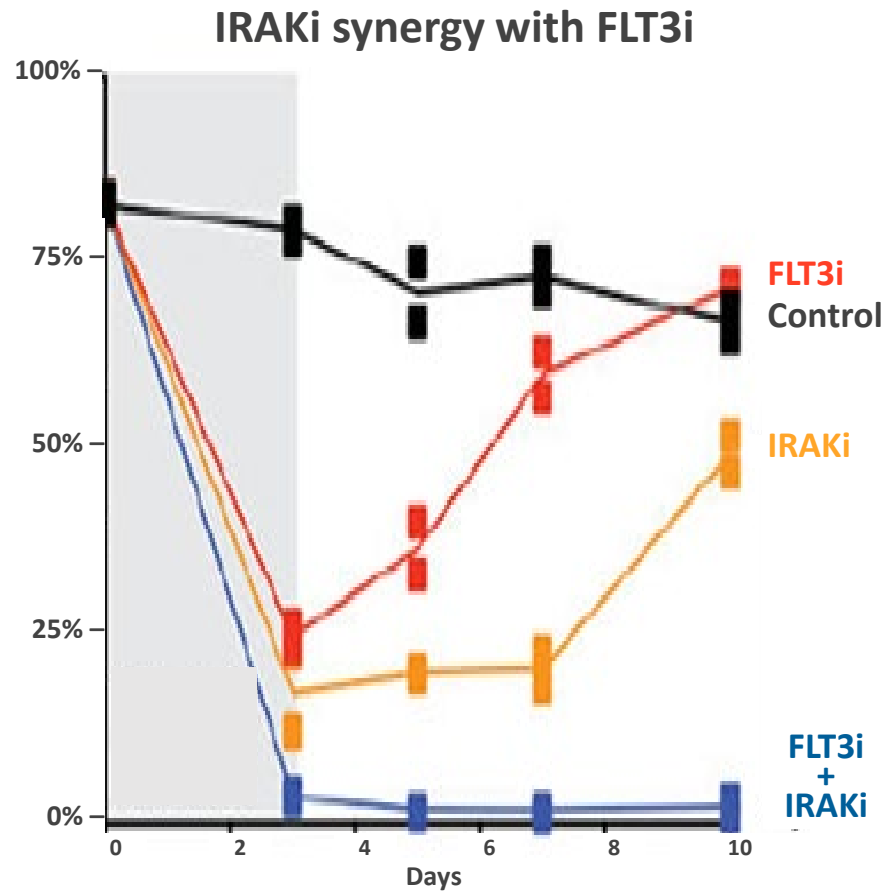
Pursue partnership to maximize potential commercial opportunity

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Emavusertib in FLT3m AML



Emavusertib's dual-targeting of IRAK4 and FLT3 enables monotherapy opportunity in FLT3m AML

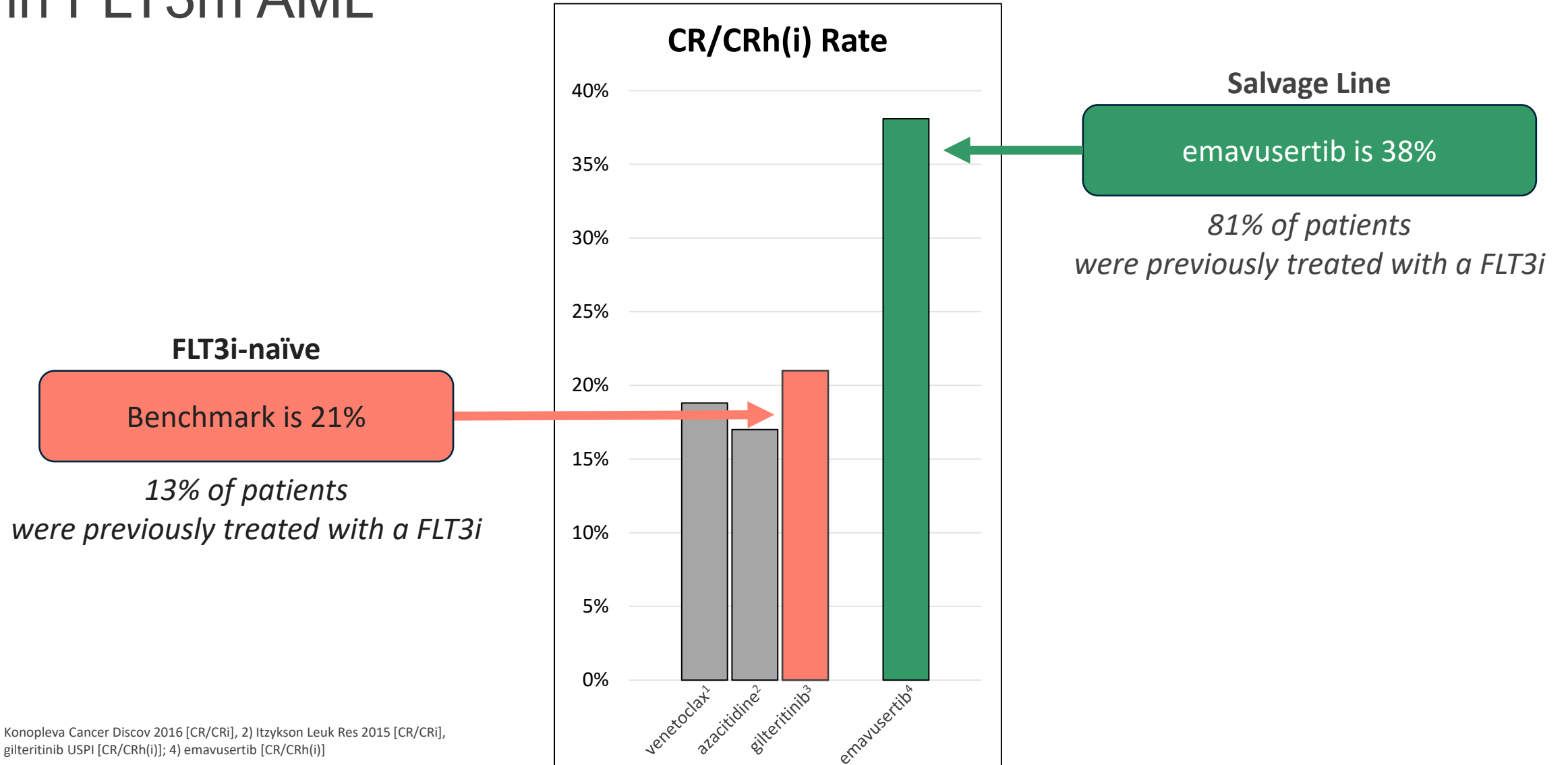


**IRAK4 inhibition
overcomes adaptive resistance
to FLT3i**

Concomitant targeting of IRAK1 or IRAK4, alongside FLT3, is the most effective means to overcome the adaptive resistance incurred when targeting FLT3¹

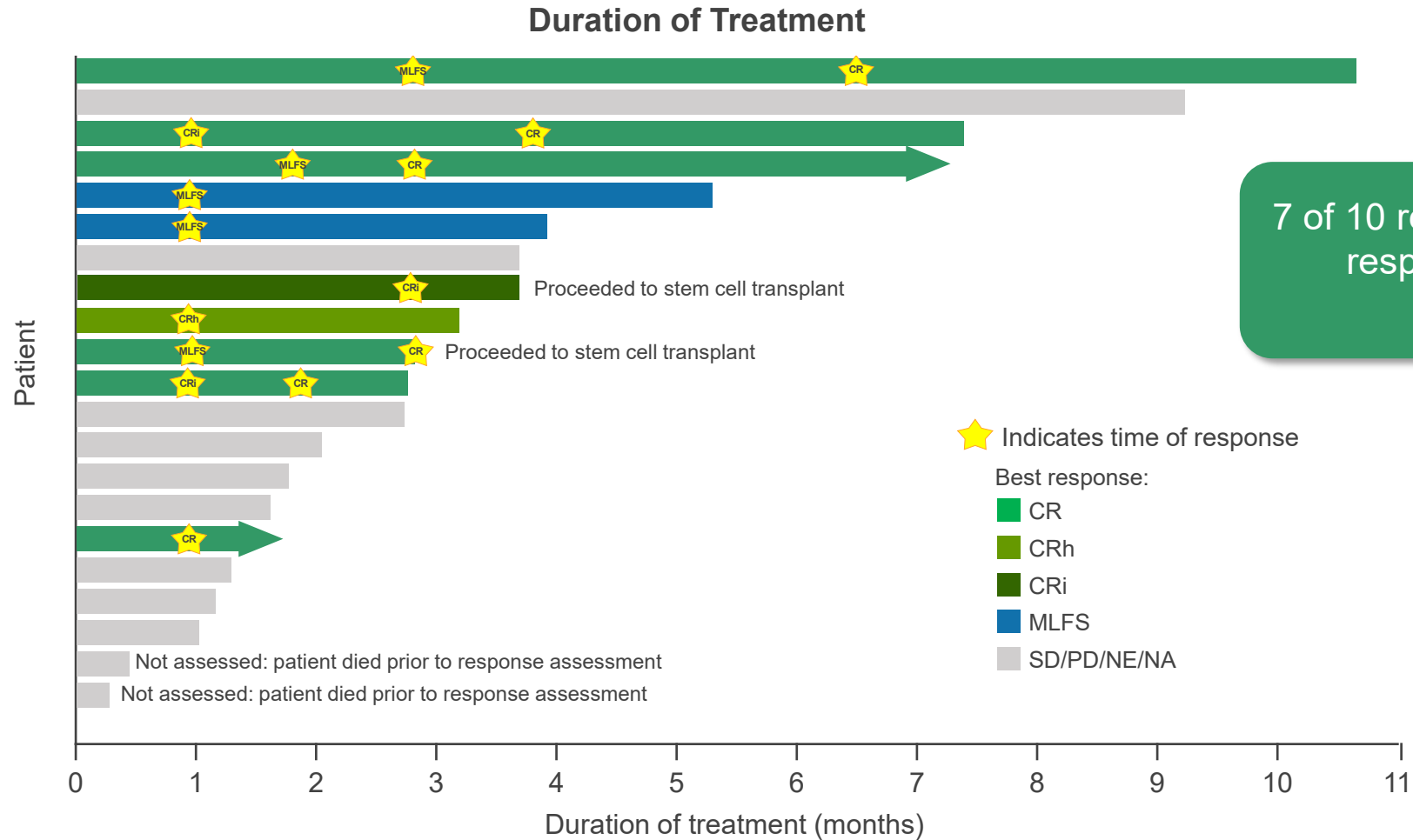
Percent viable cells in preclinical AML cell lines (FLT3-ITD) treated for 72 hrs
¹ Melgar Sci Transl Med 2019

Emavusertib is a potential best-in-class therapy in FLT3m AML



1) Konopleva Cancer Discov 2016 [CR/CRi], 2) Itzykson Leuk Res 2015 [CR/CRi], 3) gilteritinib USPI [CR/CRh(i)]; 4) emavusertib [CR/CRh(i)]

Encouraging updated data in FLT3m AML presented at ASH 2024



7 of 10 responders achieved their first response at first assessment (Cycle 2 Day 1)

Presented at ASH 2024, data as of October 31, 2024
 Includes 21 patients < 3 lines of prior therapy treated with emavusertib monotherapy at 300mg BID

Strategy in AML

1

Demonstrate safety

102 AML patients¹ treated in TakeAim Leukemia Ph 1/2 study, acceptable safety profile established

2

Demonstrate single-agent activity

Single-agent activity observed; next step is to confirm these initial findings in a larger number of patients

3

Pursue fastest path to 1st label in R/R patients

Address genetically-defined AML population with emavusertib's novel mechanism of action

4

Explore frontline opportunity with combination

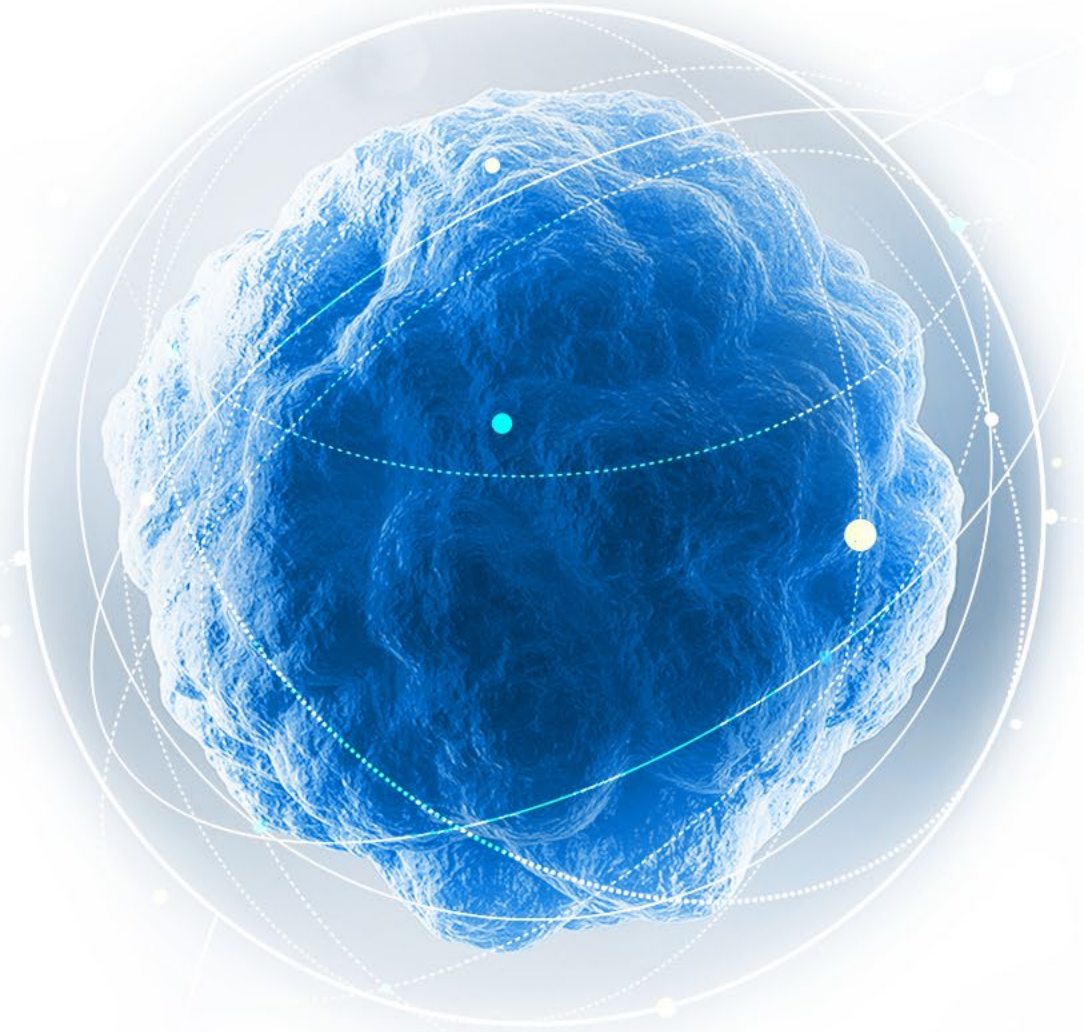
IRAK4-L is expressed in nearly all AML patients; preclinical "all comer" models suggest emavusertib is synergistic with azacitidine and venetoclax

5

Pursue partnership to maximize potential commercial opportunity

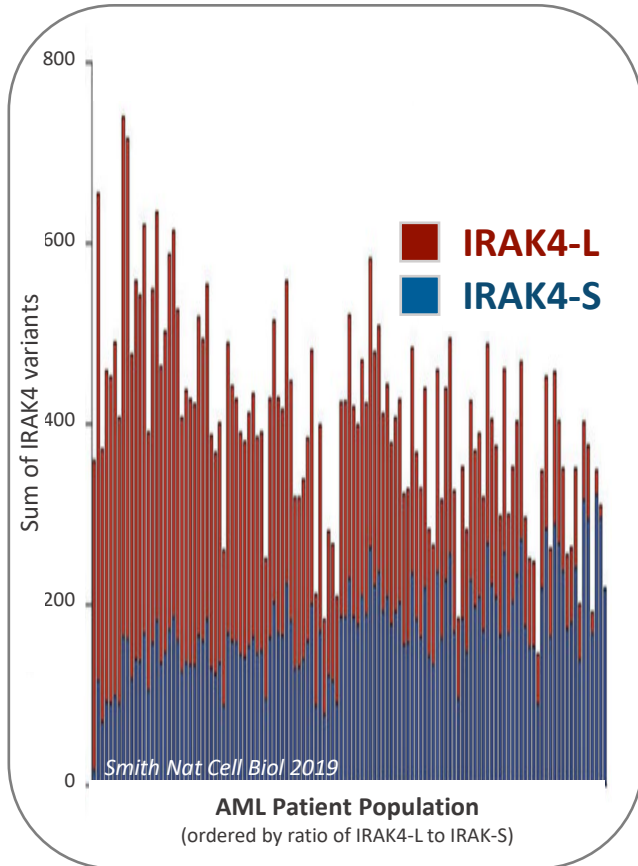
Significant resources will be required to execute a large clinical study and prepare for potential commercial launch

Emavusertib in All Comers

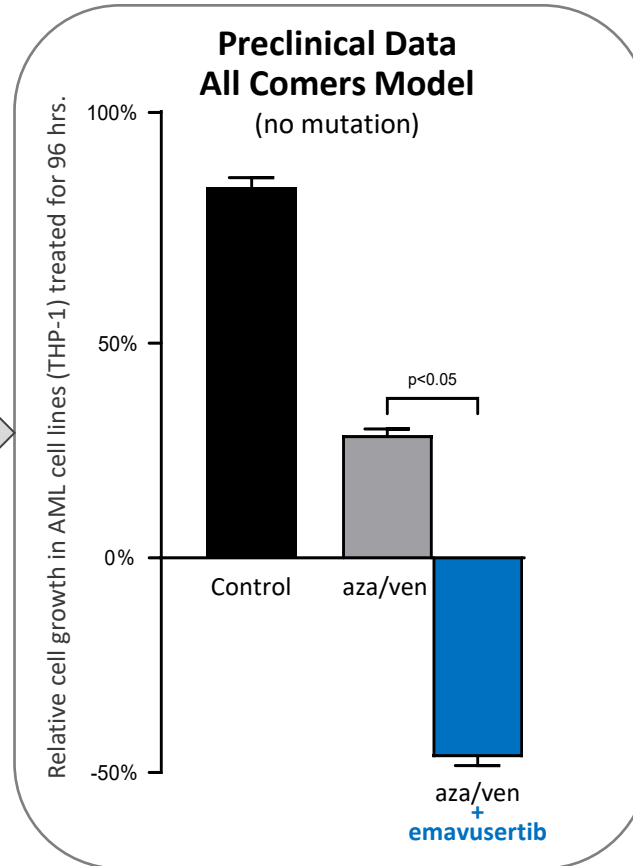


Emavusertib combination with aza/ven targets all comers in frontline AML

oncogenic IRAK4-L is expressed in nearly all AML patients



emavusertib synergy with aza/ven in preclinical studies



ema/aza/ven triplet combination

Ph 1 study initiated 1H2024

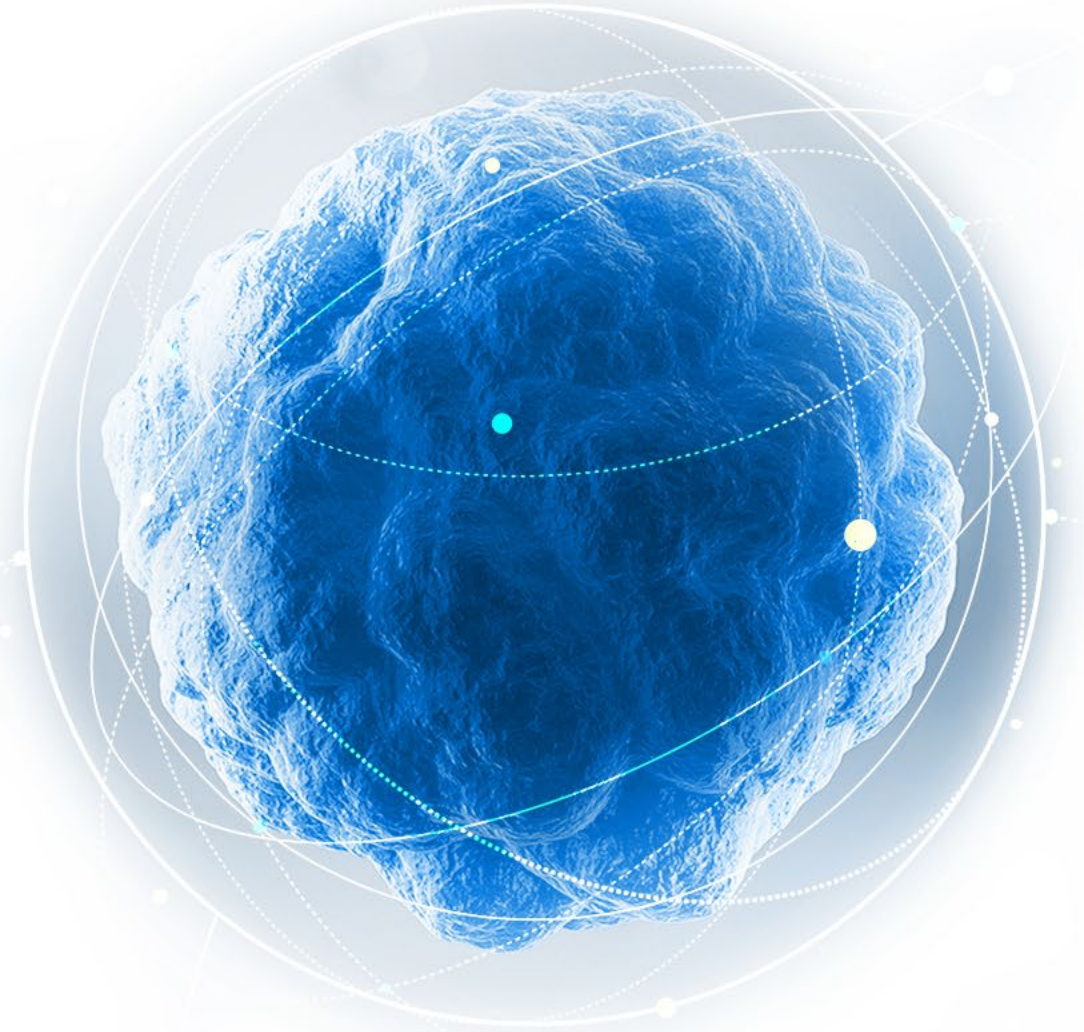
initial safety data expected Q1 2025

Summary in AML



- Emavusertib targets both FLT3 and IRAK4
- Emavusertib offers potential for best-in-class therapeutic in FLT3m AML (a genetically-defined population)
- Oncogenic IRAK4 is expressed in nearly all AML patients and is not addressed by current standard-of-care (azacitidine and venetoclax)
- Emavusertib, in combination with azacitidine and venetoclax, offers the potential for broad commercial opportunity in frontline AML

Solid Tumors

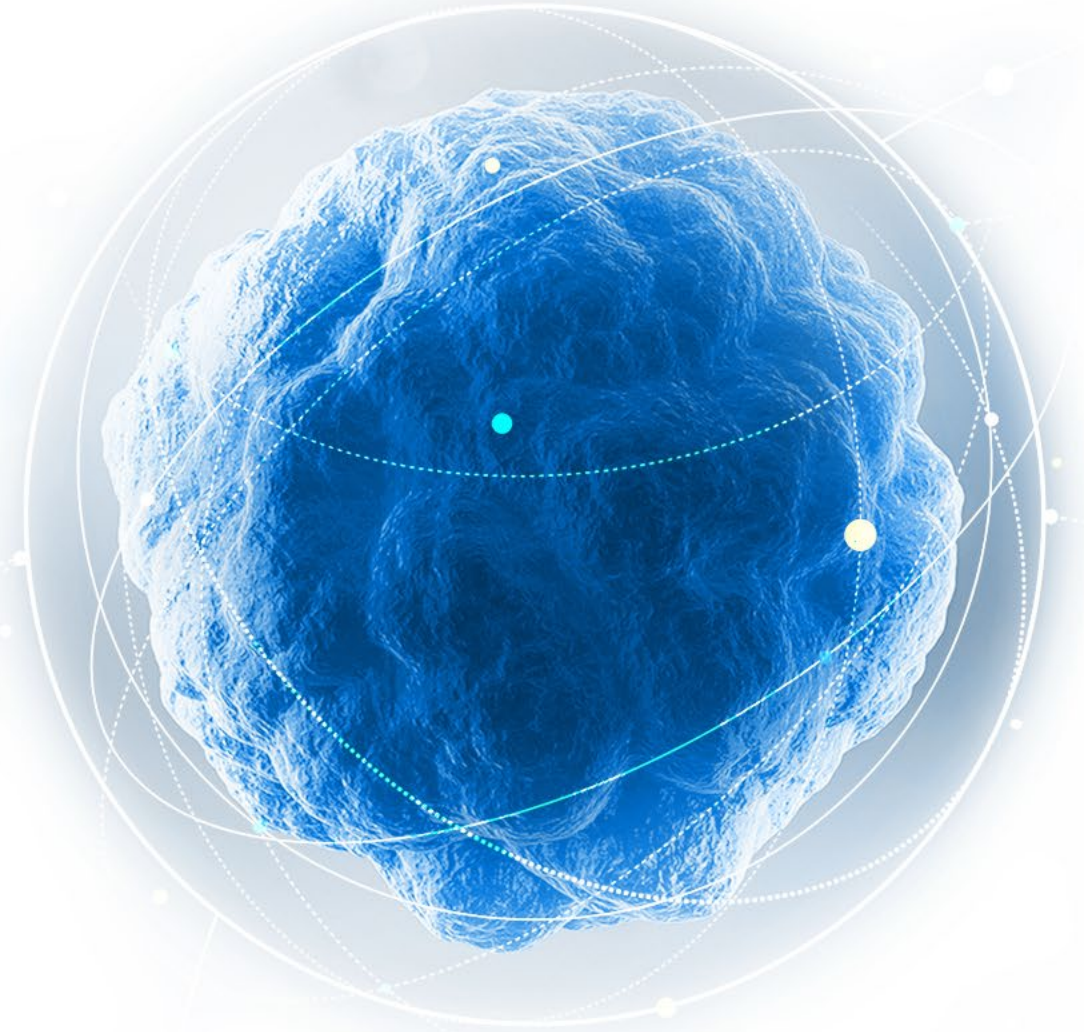


Ongoing studies (ISTs) of emavusertib in Solid Tumors

Tumor Type	Institution (Investigator)	Emavusertib Combination Partner
Pancreatic	CRADA Washington University (Grierson, Lim)	gemcitabine, nab-paclitaxel
Colorectal	CRADA Oklahoma University (Ulahannan) Washington University (Lim)	FOLFOX, bevacizumab
Gastro/Esophageal	Washington University (Grierson)	FOLFOX, PD1 +/- trastuzumab
Melanoma	University of Florida (Doonan)	pembrolizumab
Urothelial	CRADA Mount Sinai (Galsky)	pembrolizumab

Abbreviation: Investigator Sponsored Trial (IST)

Other Information



Financials and IP

As of September 30, 2024¹

\$31.6M Cash and Investments
 ~8.5M Shares Outstanding
 ~12.0M Shares Fully Diluted

2035 Composition of Matter IP on emavusertib
 (before potential extension)

We believe cash is sufficient to achieve anticipated near-term milestones

- *Updated PCNSL data in ~20 patients (1Q25)*
- *AML triplet initial safety data (1Q25)*

¹ includes the impact of the October 2024 Offerings, extends cash runway to mid-2025.

End of Presentation

