



Corporate Presentation

NASDAQ: CRIS

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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.

Corporate Overview

Leader of IRAK4 Inhibition in Oncology; Developing Emavusertib with Broad Hematological Applications

Investment Thesis

Emavusertib is a highly-active inhibitor with potential to be the cornerstone agent in hematologic malignancies

Clinical Path

- Potential fast path to NDA in genetically-defined populations (R/R AML with FLT3 or Spliceosome mutation)
- Potential for front-line position in combination

Current Trials

TakeAim Leukemia: IRAK4 and FLT3 are the two most prevalent drivers of disease in AML/MDS^{1,2}

TakeAim Lymphoma: emavusertib/ibrutinib enables blockade of both pathways driving NF-κB in NHL

Market Opportunity

There are no drugs approved for IRAK4 inhibition in oncology

- AML/MDS: **333K patients³** (*current standard of care is HMA*)
- NHL/CLL: **1.9M patients³** (*current standard of care is BTKi*)

Upcoming Milestones

- Clarify monotherapy registrational study design in Leukemia with the FDA
- Updated data in R/R Leukemia (monotherapy and combination)
- Updated data in R/R Lymphoma (combination)
- Cash runway into 2025 – Proforma cash of \$77.4M as of June 30, 2023

1) Smith et al. Nat Cell Biol 2019; 2) Saygin, et al. J Hematol Oncol. 2017 Apr 18; 3) 2022 Prevalence Data DRG Clarivate

A circular inset image showing a microscopic view of cells, likely leukemia cells, with a white horizontal bar overlaid across the center. The cells are blue and have a textured, irregular appearance.

Emavusertib in Leukemia
(AML/MDS)

Emavusertib has A Unique Molecular Fingerprint

Targeted design is specifically engineered to be best-in-class

The NCI selected emavusertib for NCI-sponsored research and clinical studies of IRAK4

Emavusertib Kinase Interaction Map

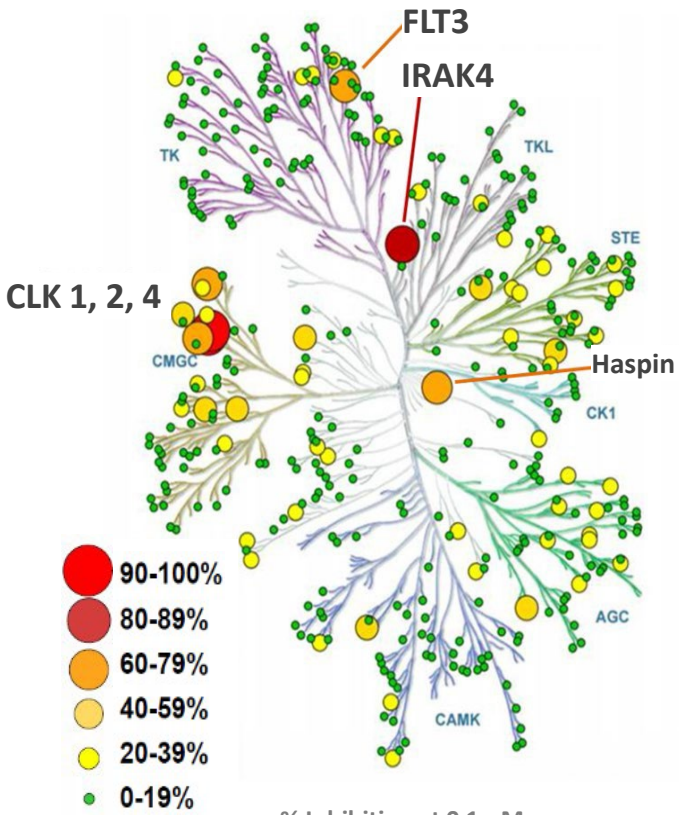


Illustration reproduced courtesy of Cell Signaling Technology

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)

*high binding affinity to IRAK4
(>97% inhibition achieved at clinical dose concentrations)*

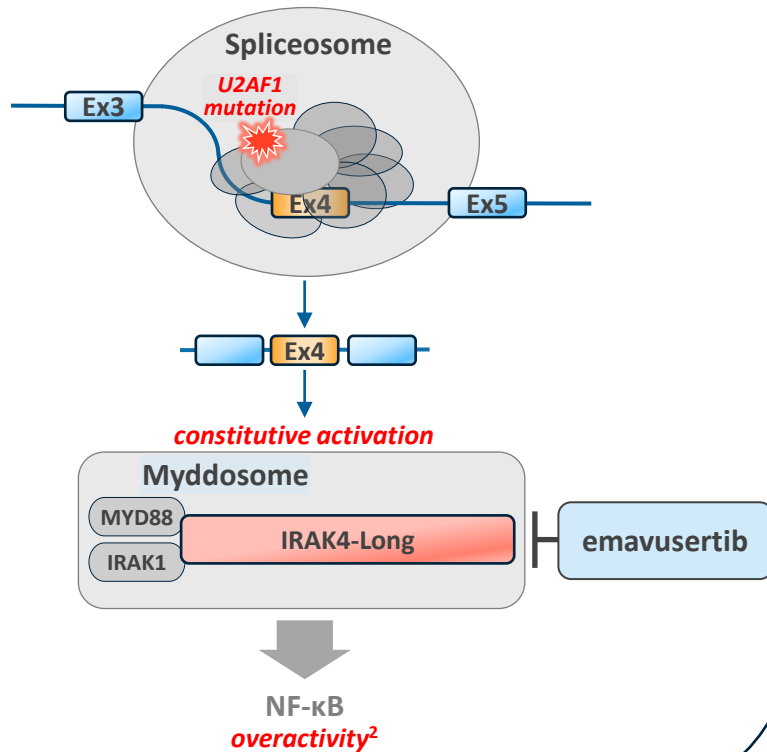
*high binding affinity to FLT3
contributes additional anti-cancer activity, differentiating emavusertib from other IRAK4-directed therapies*

Emavusertib Has a Unique Mechanism of Action

The two primary targets of emavusertib are independent drivers of cancer

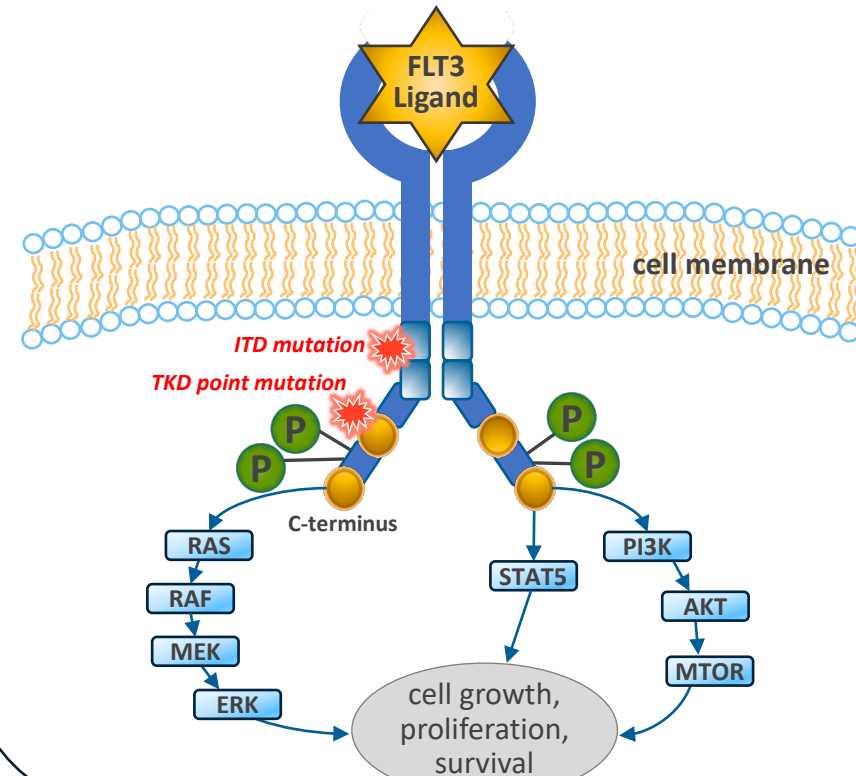
IRAK4

spliceosome mutations drive overexpression of IRAK4-Long, which constitutively activates the myddosome, driving NF-κB overactivity



FLT3

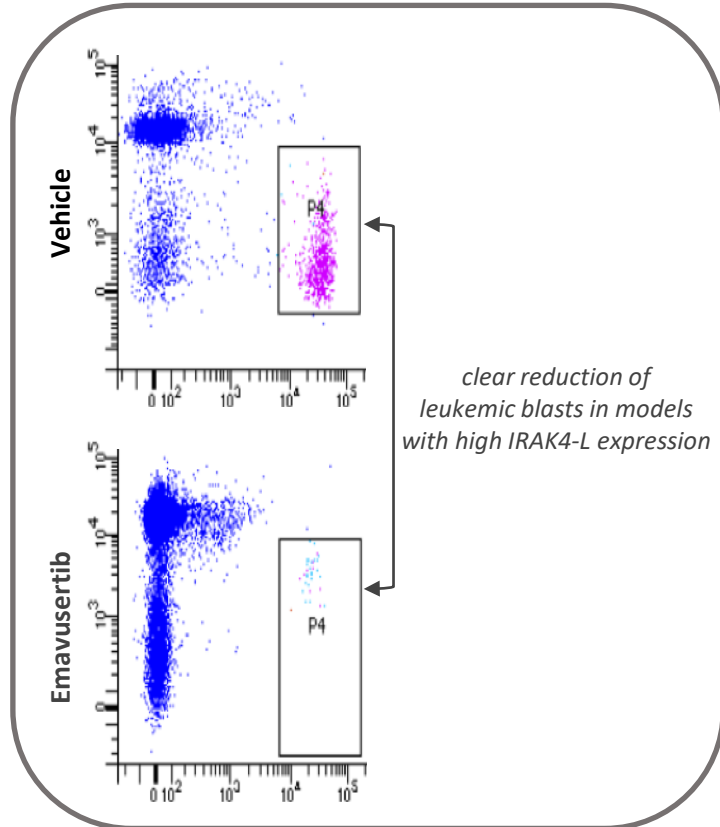
genetic mutations cause constitutive activation of FLT3 and downstream cell growth, proliferation, and survival pathways



Emavusertib Preclinical Data

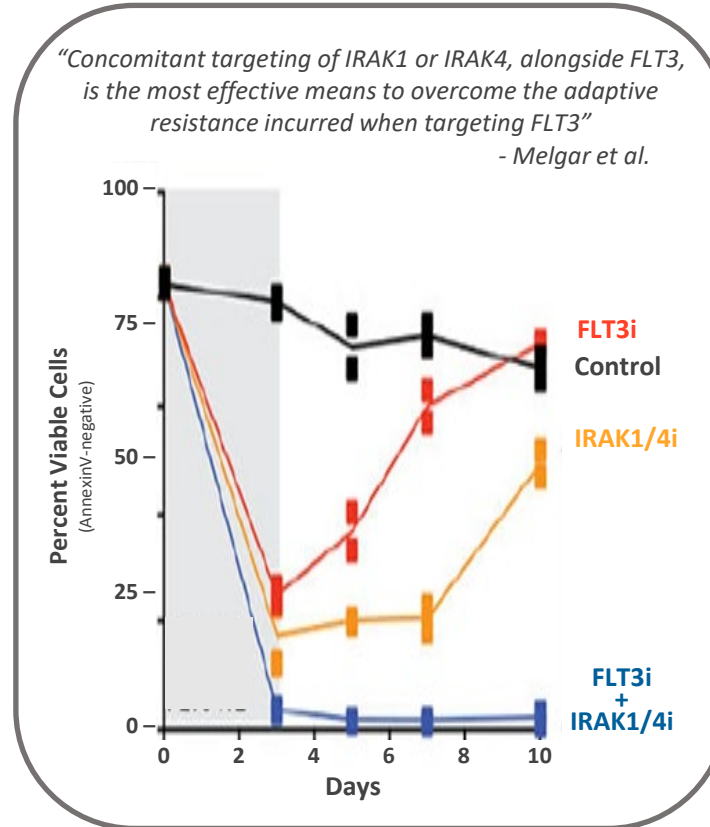
Rationale for monotherapy and combination with azacitidine/venetoclax

Monotherapy in IRAK4



emavusertib demonstrates monotherapy activity in patient-derived xenografts¹

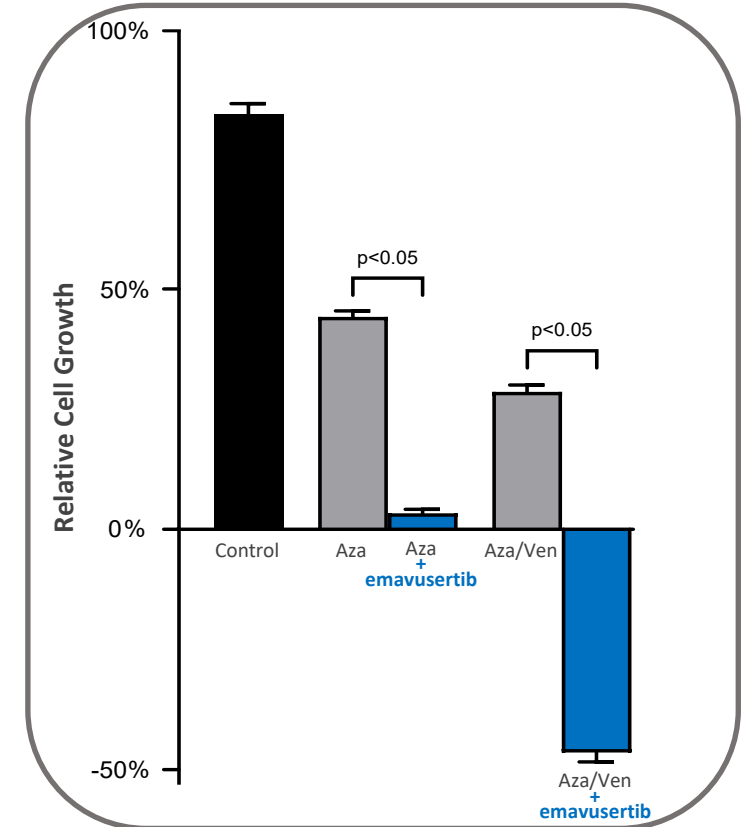
Monotherapy in FLT3



IRAK/FLT3 combination demonstrates synergy in pre-clinical studies²

FLT3-ITD cells treated for 3 days with DMSO (control), quizartinib (0.5 μM), IRAKi (10 μM), and quizartinib + IRAKi

Combination with Aza/Ven



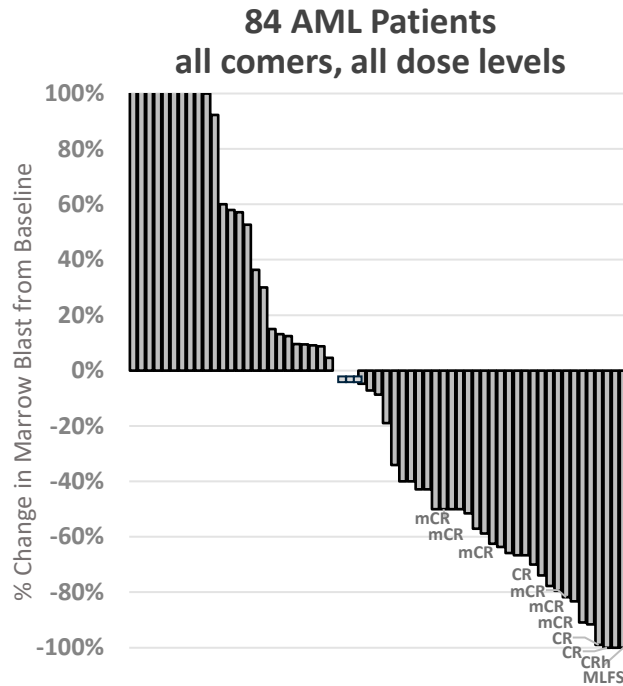
emavusertib demonstrates synergy with both azacitidine and venetoclax in THP-1 model³

AML cell lines treated for 96 hrs (values presented as mean ± SE)

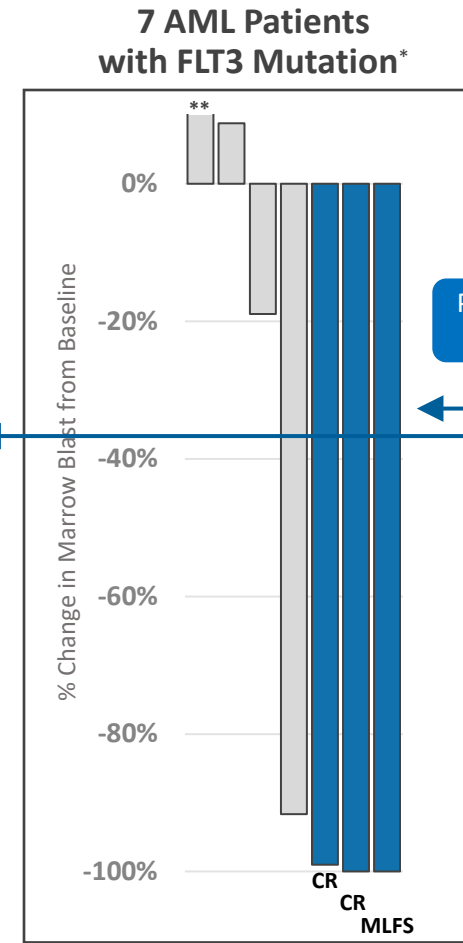
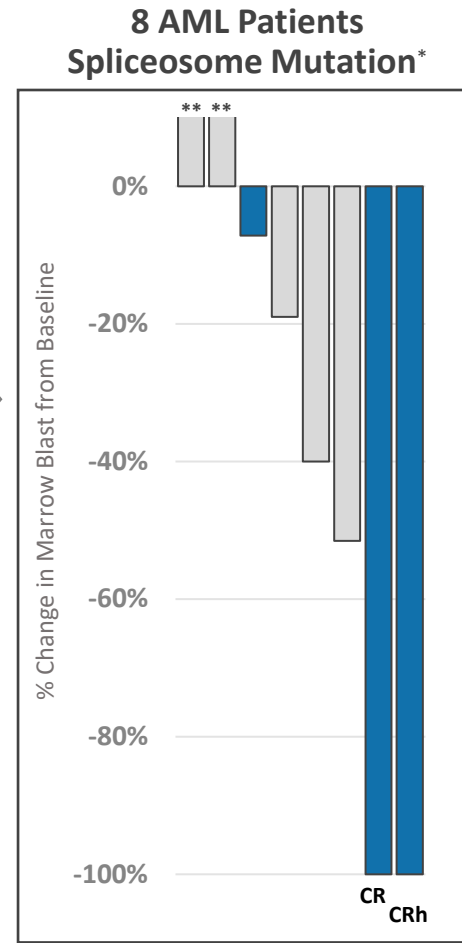
1) Choudhary et al. AACR 2017; 2) Melgar, Sci Transl Med. 2019; 3) Curis AML MDS poster, EHA 2021

Emavusertib Compelling Initial Clinical Data

Showing clear single agent activity where expected in clinical studies



**strongest monotherapy signal
observed where expected
(Spliceosome/FLT3 patients)**



Duration of Responses: 5.6 – 7.0 months

7	AML FLT3*
8	AML Spliceosome*
24	AML Other
17	AML Not Evaluable for Marrow Assessment
12	MDS Spliceosome
13	MDS Other
6	MDS Not Evaluable for Marrow Assessment

84 Total Patients enrolled in monotherapy

Note: 84 total patients enrolled as of Feb 9, 2023 with data cut-off as of Mar 17, 2023;

* Three AML patients had both FLT3 and Spliceosome mutation and are counted in both populations; evaluable patients include all patients whose disease was determined to be evaluable for objective response with baseline and post-treatment marrow assessments

** Denotes blast percent increase > 10%

Potential Cornerstone Treatment for Hematologic Malignancies

Emavusertib inhibits both IRAK4 and FLT3 – key disease drivers in leukemia and lymphoma

Leukemia

Monotherapy targets the two largest **genetically-defined** patient populations in AML/MDS^{a,6-8}

Emavusertib synergizes with existing treatments⁵ as **IRAK4-L is expressed in nearly all AML/MDS patients**

AML/MDS opportunity: 333K patients³

Emavusertib has demonstrated clinical activity across both targeted and non-targeted populations^{1,4,5}

Lymphoma

Initial clinical data show potential to **overcome BTKi resistance** in patients with NHL/CLL¹

Combination with BTKi **blocks both BCR and TLR signaling**, maximizing downregulation of NF- κ B²

NHL/CLL opportunity: 1.9M patients³

^a Patients with *FLT3* mutation or *IRAK4-L* overexpression. 1) Joffe, et al. *Hemasphere*. 2022. June 6(Suppl 3):1011-1012; 2) Guidetti, et al. *AACR Mol Cancer Ther*. 2021;20(Suppl 12):P073; 3) 2022 Prevalence Data DRG Clarivate; 4) Garcia-Manero, et al. *Hemasphere*. 2022. June 6(Suppl 3):30-31; 5) Curis press release. <https://investors.curis.com/2022-12-12-Curis-Announces-Additional-Encouraging-Clinical-Data-from-TakeAim-Leukemia-Study-of-emavusertib-CA-4948-in-Monotherapy-R-R-AML-and-hrMDS>, accessed May 19, 2023; 6) Smith, et al. *Nat Cell Biol*. 2019; 7) Choudhary, et al. *eLife*. 2022;11:378136; 8) Saygin, et al. *J Hematol Oncol*. 2017 Apr 18.

Emavusertib in Leukemia (AML/MDS)

The ideal candidate to address the two largest genetically-defined populations in AML/MDS

Emavusertib addresses the two largest genetically-defined populations in AML/MDS:

- 1) IRAK4-L (>50% of population)¹
- 2) FLT3 (>25% of population)²

- Clear single-agent activity
- Genetically-defined patient population
- Dual targeting of IRAK4 and FLT3 may prevent adaptive resistance observed with current FLT3 inhibitors³



Next Steps **TakeAim Leukemia Study**

- *Monotherapy: R/R AML with FLT3
R/R AML with Spliceosome*
- *Combination: 1st Line (all comers)*

A circular inset image showing a microscopic view of a cell, likely a lymphoma cell, with a textured, blue, and somewhat irregular surface. The cell is centered in the background of the slide.

Emavusertib in Lymphoma
(NHL/CLL)

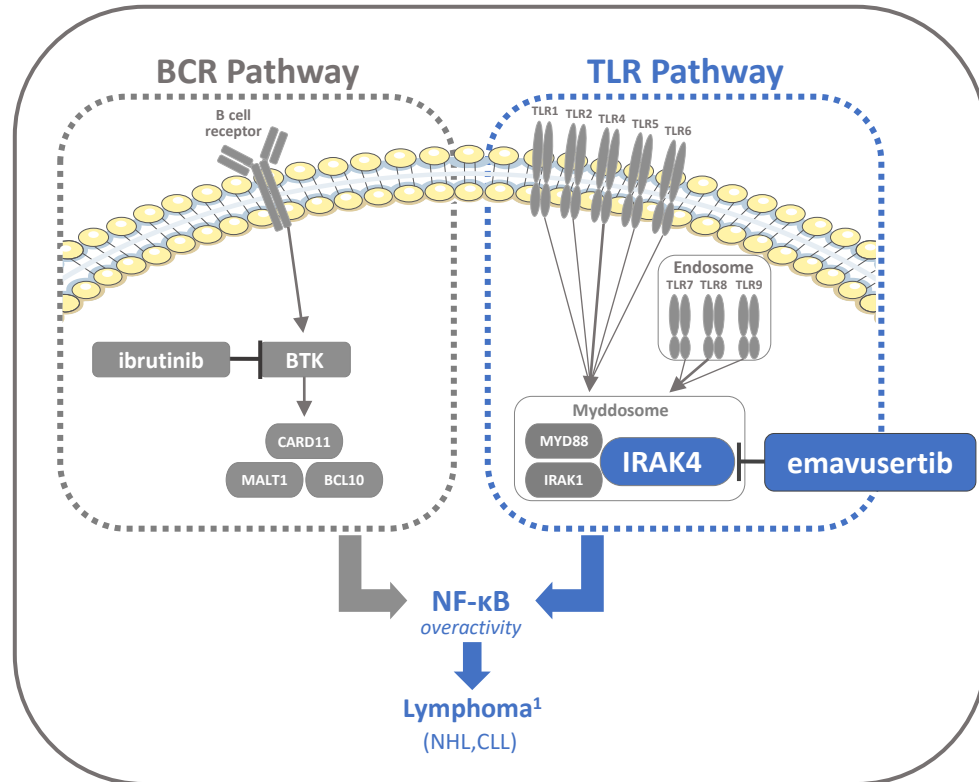
Emavusertib in Lymphoma

Combination therapy provides complimentary inhibition of two pathways that drive NF-κB

NFκB Biology:

Two Pathways Drive NHL/CLL

*BCR and TLR Pathways independently drive NF-κB overactivity
(and NF-κB drives NHL/CLL)*

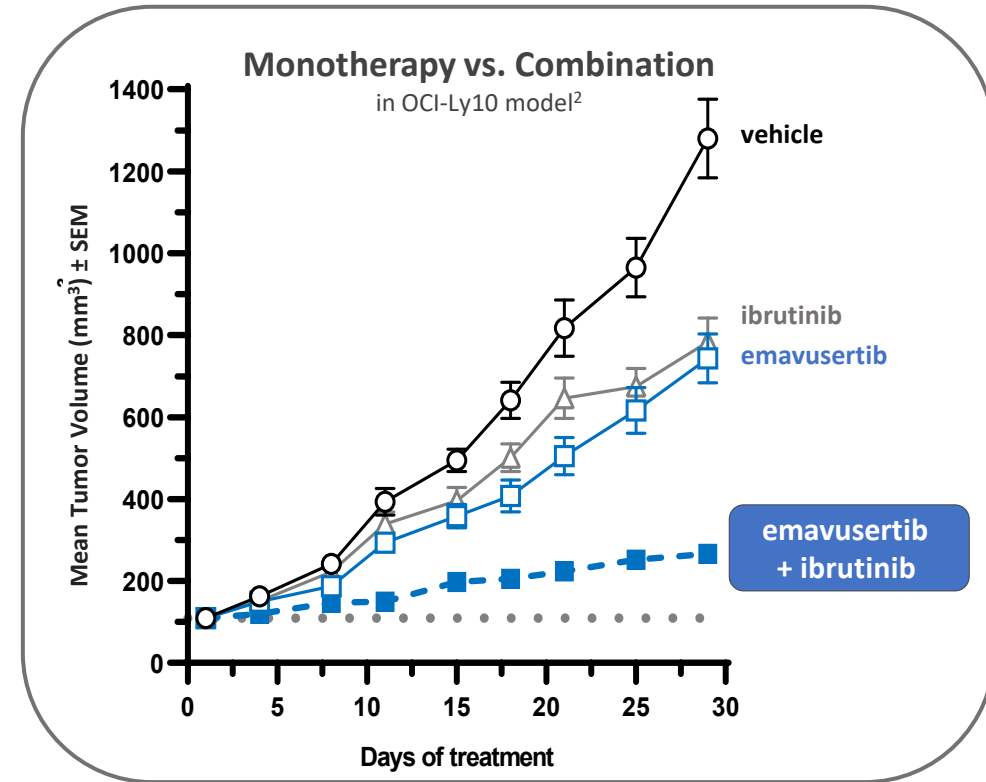


1) IMBRUVICA Package Insert. Rev 08/2018

Clinical Strategy:

Block both pathways with Combination Therapy

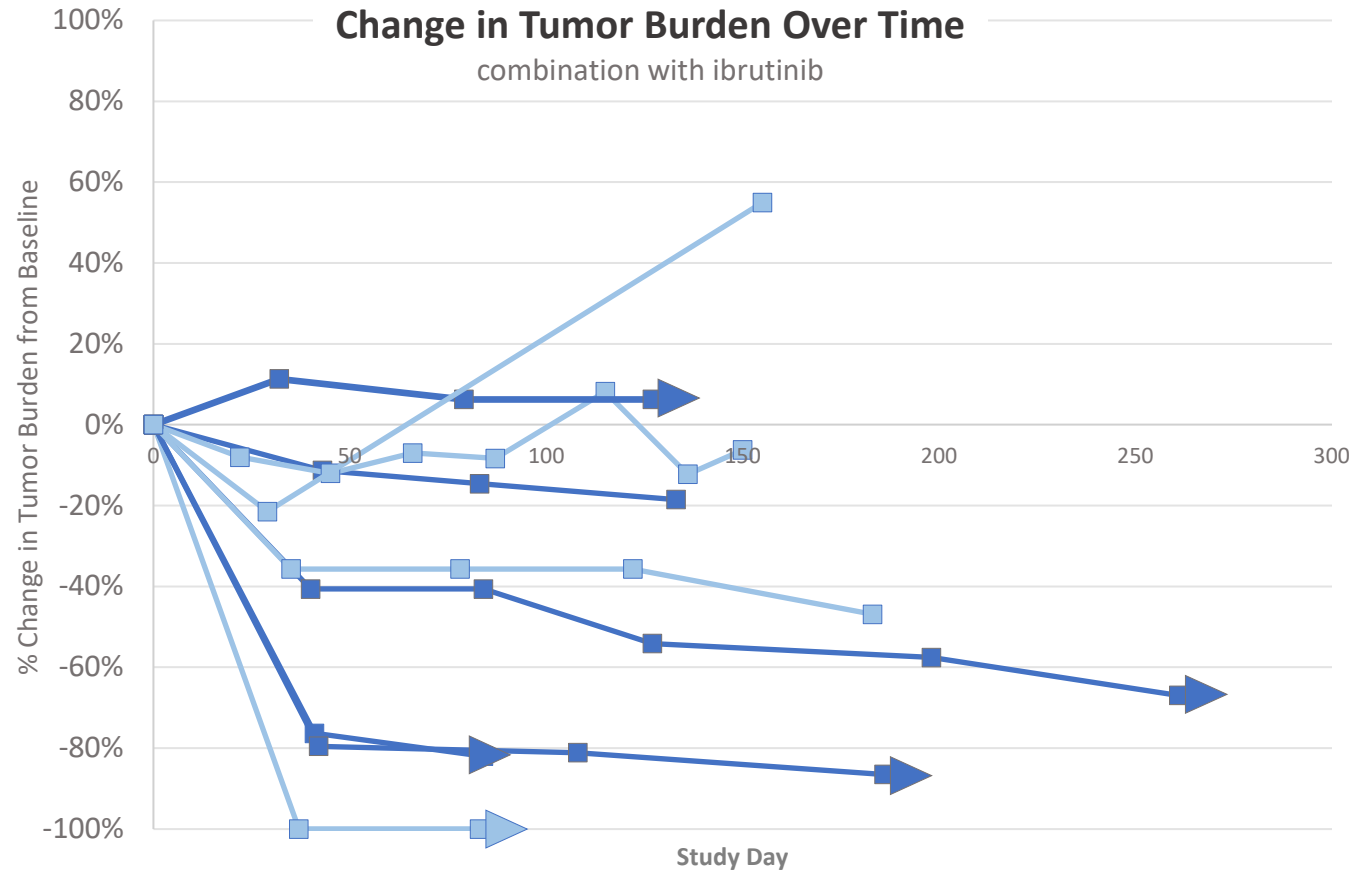
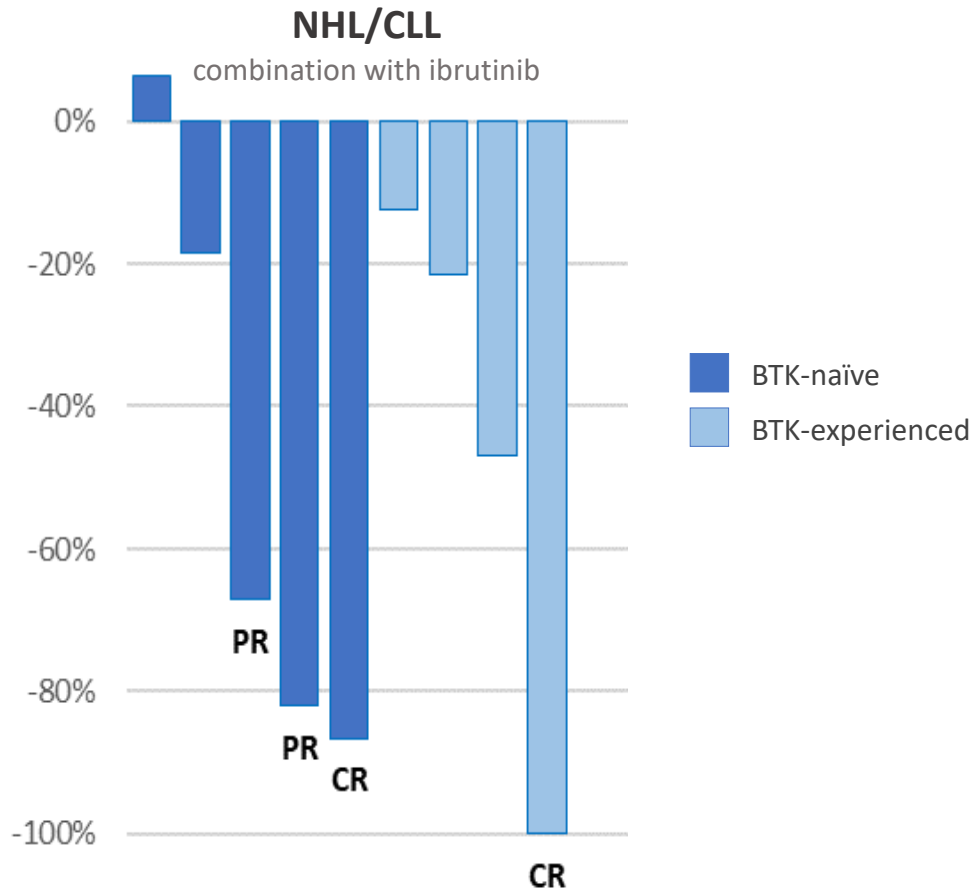
*In preclinical testing, blocking both IRAK4 and BTK
drove tumor reduction better than blocking either one alone*



2) Booher et al. Waldenström Roadmap Symposium 2019

Initial Clinical Data in Lymphoma

Majority of patients achieved decreases in tumor burden, including complete responses



Note: Data from ASCO 2022 poster presentation
Response evaluable patients with baseline and post-treatment disease assessment at data cutoff

Clinical Strategy in Lymphoma

The ideal candidate to combine with BTKi to maximize downregulation of NF-κB

- Patients are currently treated with BTKi because it downregulates NF-κB
- Two pathways drive NF-κB:
 - 1) BCR Pathway: *addressed by blocking BTK*
 - 2) TLR Pathway: *addressed by blocking IRAK4*
- Initial clinical data suggest blocking both pathways may overcome resistance to ibrutinib

The logo for TakeAim, featuring the word "TakeAim" in a blue sans-serif font with a blue arc above the letters "Aim".

Next Steps

TakeAim Lymphoma Study

- *Monotherapy: R/R PCNSL*

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End of Corporate Presentation

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