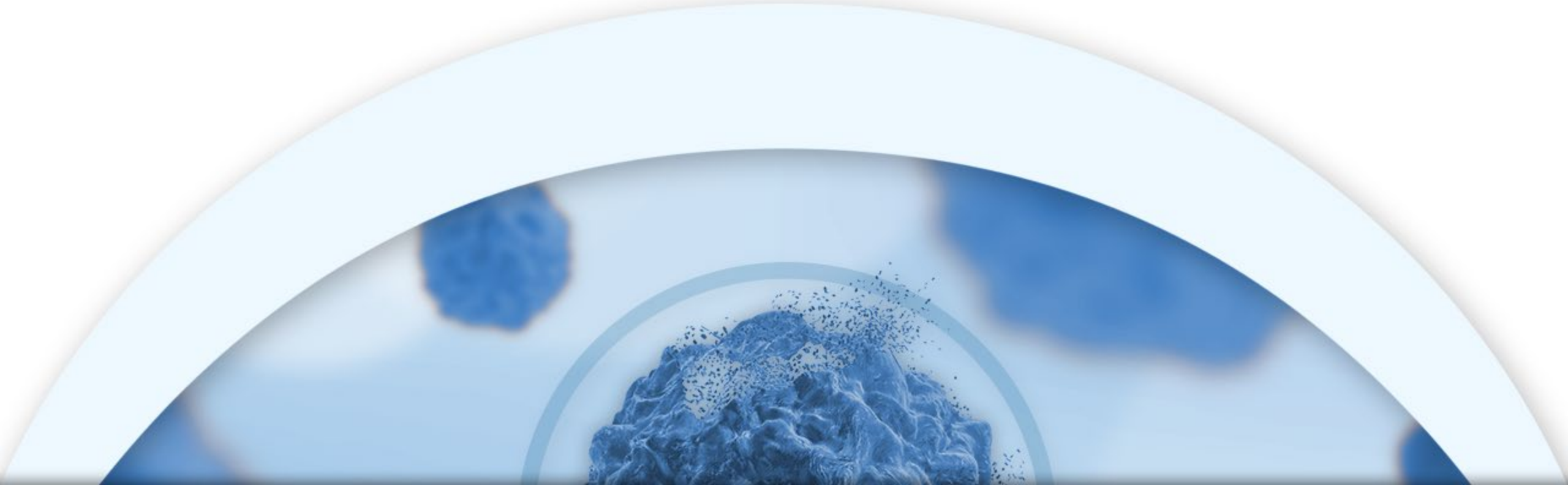
Corporate Presentation

NASDAQ: CRIS



Cautionary Note Regarding Forward Looking Statements

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)”, "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 future clinical and pre-clinical milestones; the timing of future preclinical studies and clinical trials and results of these studies and trials; the clinical and therapeutic potential of our drug candidates; and management’s ability to successfully achieve its 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 may remove the partial clinical hold on the combination therapy phase (Phase 1b) and the expansion phase (Phase 2a) of the Phase 1/2 TakeAim Leukemia trial, or may take further regulatory action with regard to this trial, whether any of our drug candidates will advance further in the clinical development process and whether and when, if at all, they 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 any of our drug candidate discovery and development efforts will be successful; whether any of our drug candidates will be successfully marketed if approved; our ability to achieve the benefits contemplated by our collaboration agreements; management’s ability to successfully achieve its goals; the sufficiency of our cash resources; our ability to raise additional capital to fund our operations on terms acceptable to us or 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 and interim reports filed with the Securities and Exchange Commission 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.

Corporate Overview

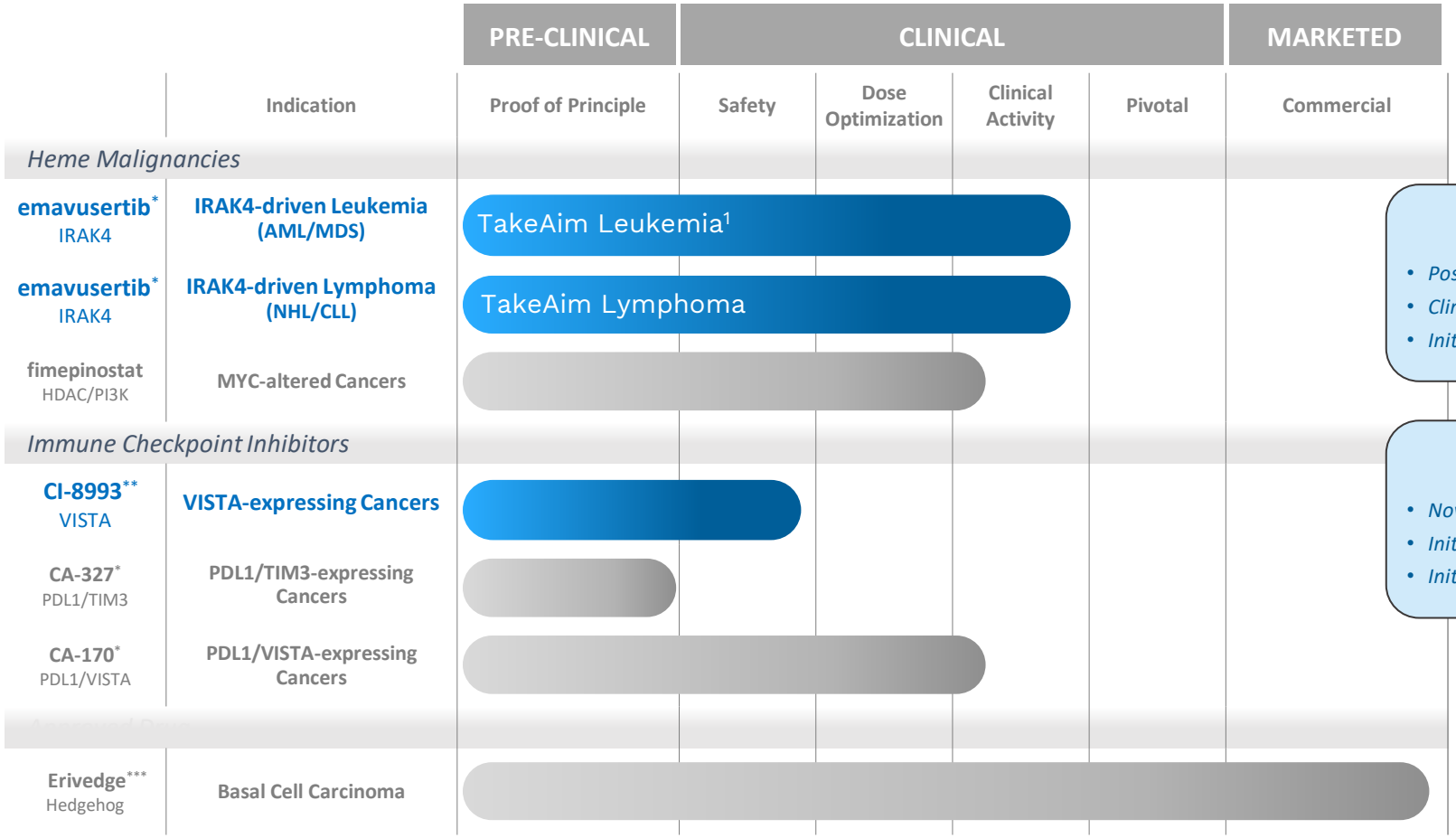
Summary

Investment Thesis	Curis develops novel, first-in-class, cancer therapeutics in areas of significant unmet patient need *Cash runway into 2024 – $107M as of June 30, 2022*
First-in-Class Pipeline	Emavusertib: first-in-class oncology program targeting IRAK4 CI-8993: first-in-class oncology program targeting VISTA
Significant Market Opportunity	AML/MDS: 317K patients[1] (standard of care: HMA) NHL/CLL: 1.8M patients[1] (standard of care: BTKi)
Upcoming Data	2023: emavusertib in AML/MDS (monotherapy) 2023: emavusertib in NHL/CLL (combination with ibrutinib) 2H 2022: CI-8993 in solid tumors (monotherapy)

1) 2022 Prevalence Data DRG Clarivate

Pipeline

Curis develops novel, first-in-class cancer drugs



Two programs are the focus of this presentation

IRAK4 (emavusertib)

- *Positioned to become cornerstone agent in heme malignancies*
- *Clinical PK/PD exposure correlates with 98% target inhibition*
- *Initial clinical data show clear monotherapy activity with complete responses*

VISTA (CI-8993)

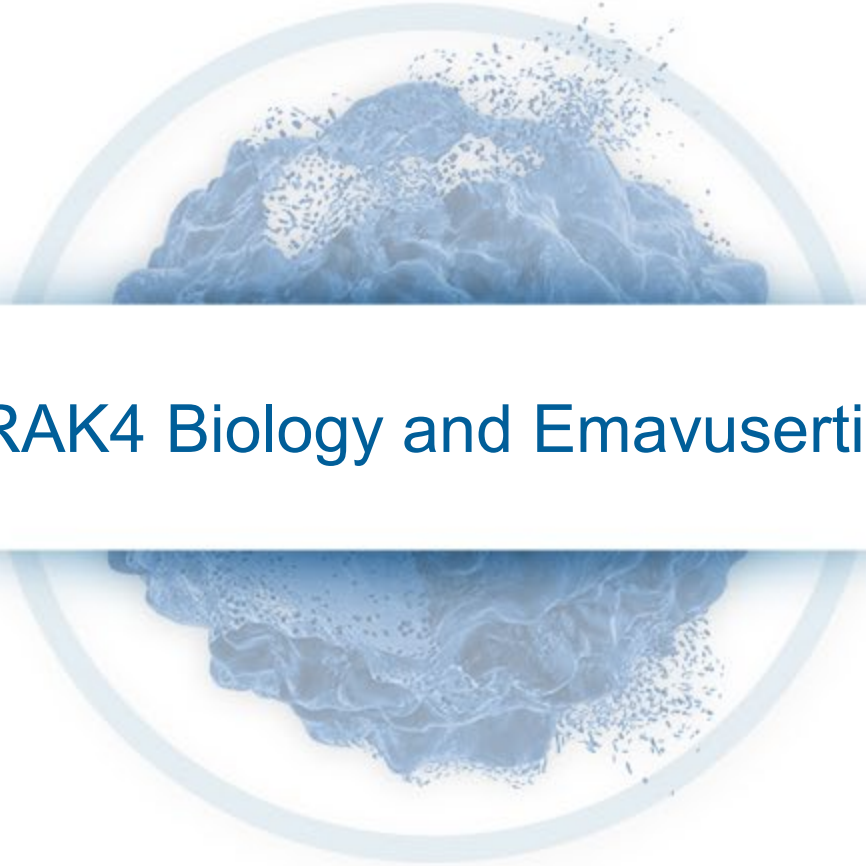
- *Novel immune checkpoint with unique role in T cell activation*
- *Initial safety data show expected immune effects (CRS) are manageable*
- *Initial clinical data show that anti-cancer mechanisms are being activated*

[1] In April 2022, the U.S. Food and Drug Administration ("FDA") placed the TakeAim Leukemia study on partial clinical hold. In August 2022, the FDA notified Curis that it may resume enrollment in the monotherapy dose finding phase of the study. The partial hold remains in place for the combination therapy and expansion phases of the study.

AURIGENE ImmuNext Genentech

* IP licensed from Aurigene
** Exclusive option to license IP from ImmuNext
*** IP licensed to Genentech (Curis receives royalty income)

CURIS



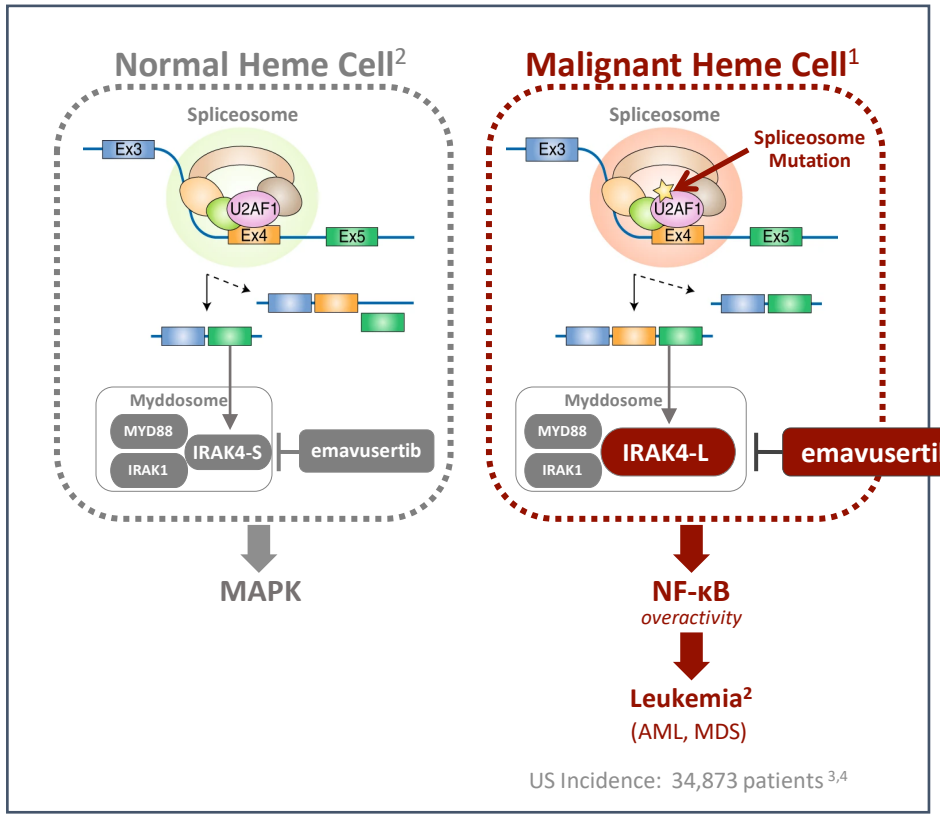
IRAK4 Biology and Emavusertib

IRAK4 Biology and Emavusertib

IRAK4 is a novel and important target across multiple heme malignancies

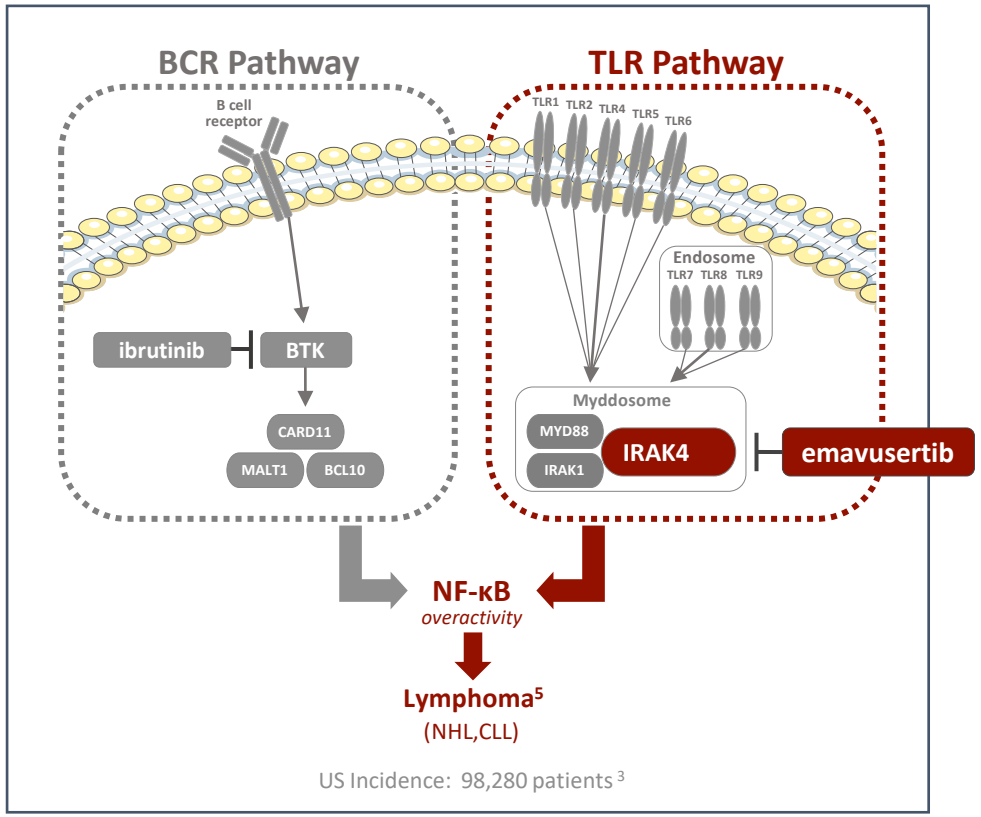
IRAK4 in AML/MDS

Spliceosome mutation drives overexpression of IRAK4-L (which causes constitutive activation of the myddosome)



IRAK4 in NHL/CLL

TLR Pathway is dependent upon IRAK4 for function (2nd pathway driving NF-κB overactivity)



1) Guillamot et al. Nat Cell Biol 2019; 2) Smith et al. Nat Cell Biol 2019; 3) American Cancer Society, Cancer Facts & Figures 2020; 4) Leukemia & Lymphoma Society, Facts and Statistics Overview; 5) IMBRUVICA Package Insert. Rev 08/2018

Emavusertib's Unique Molecular Fingerprint

Targeted design specifically engineered to hit key oncogenic targets

The NCI has selected emavusertib for both clinical and non-clinical studies of IRAK4 inhibition in oncology

NCI Selection for IRAK4

Emavusertib Kinase Interaction Map

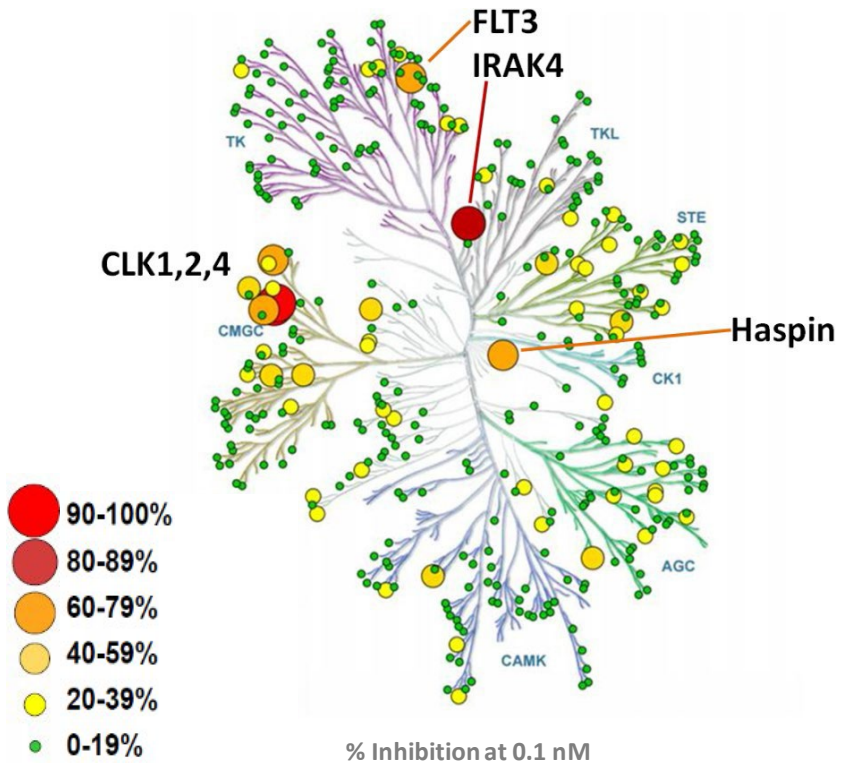


Illustration reproduced courtesy of Cell Signaling Technology

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)

Binds with high affinity to IRAK4

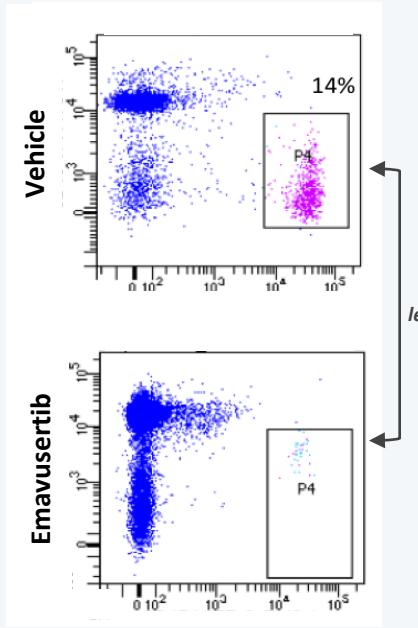
Dual targeting of IRAK4 and FLT3 confers potential efficacy advantage vs. other IRAK4 inhibitors

Emavusertib Preclinical Data

Clear anti-cancer activity suggests broad potential across heme malignancies

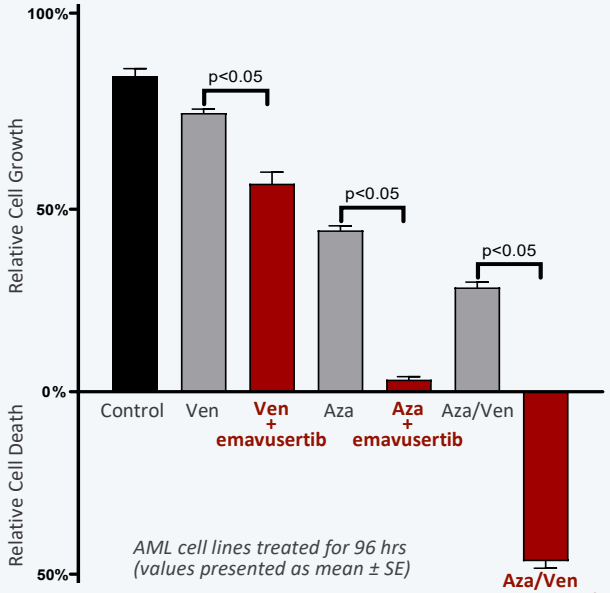
AML/MDS

Monotherapy



emavusertib demonstrates monotherapy activity in patient-derived xenografts[1]

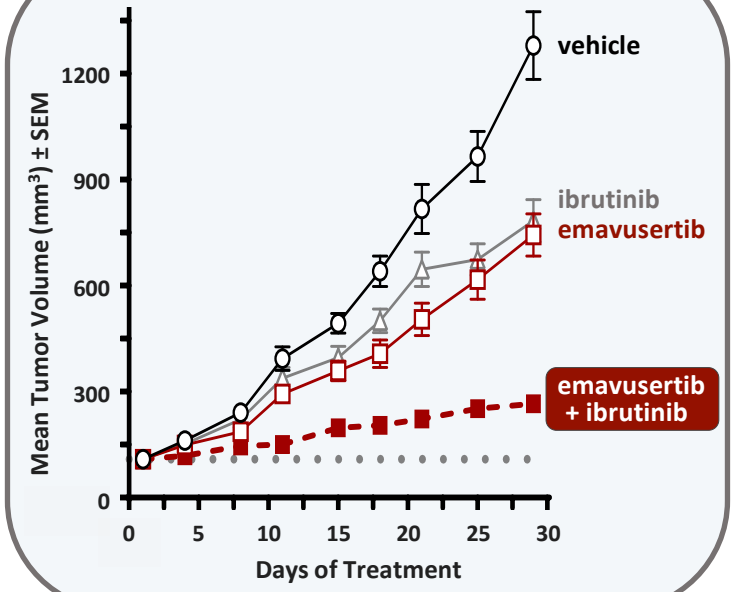
Combination Therapy



emavusertib demonstrates synergy with both azacitidine and venetoclax in THP-1 model[2]

B Cell Cancers

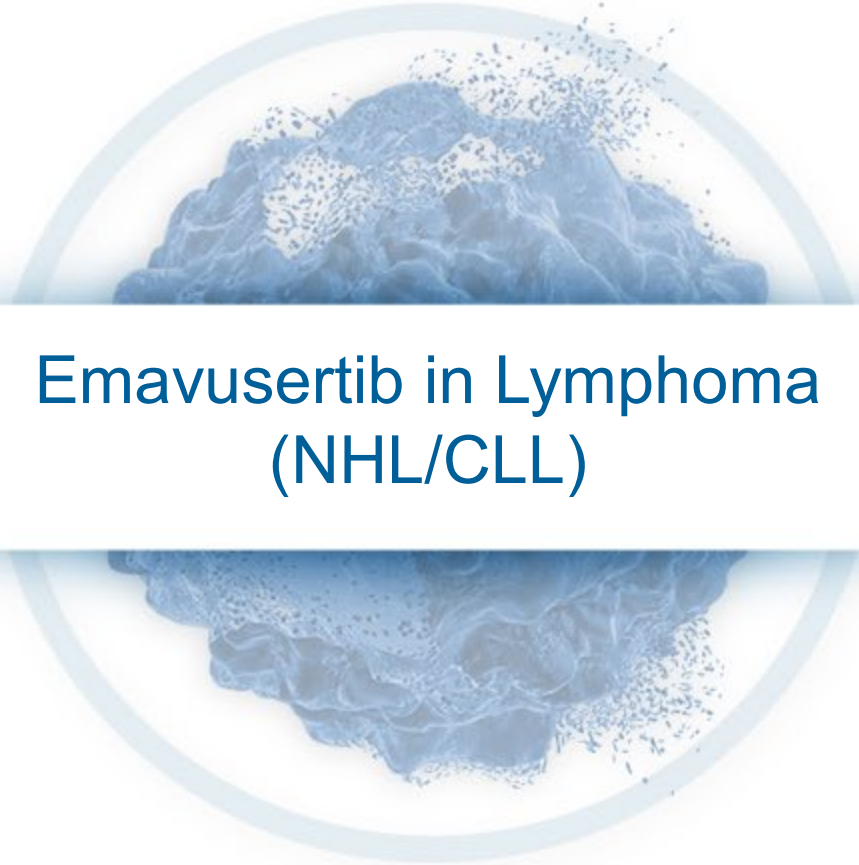
Combination Therapy



emavusertib demonstrates synergy with ibrutinib in OCI-Ly10 model[3]

1) Choudhary et al. AACR 2017; 2) Curis AML MDS poster, EHA 2021; 3) Booher et al. Waldenström Roadmap Symposium 2019

CURIS



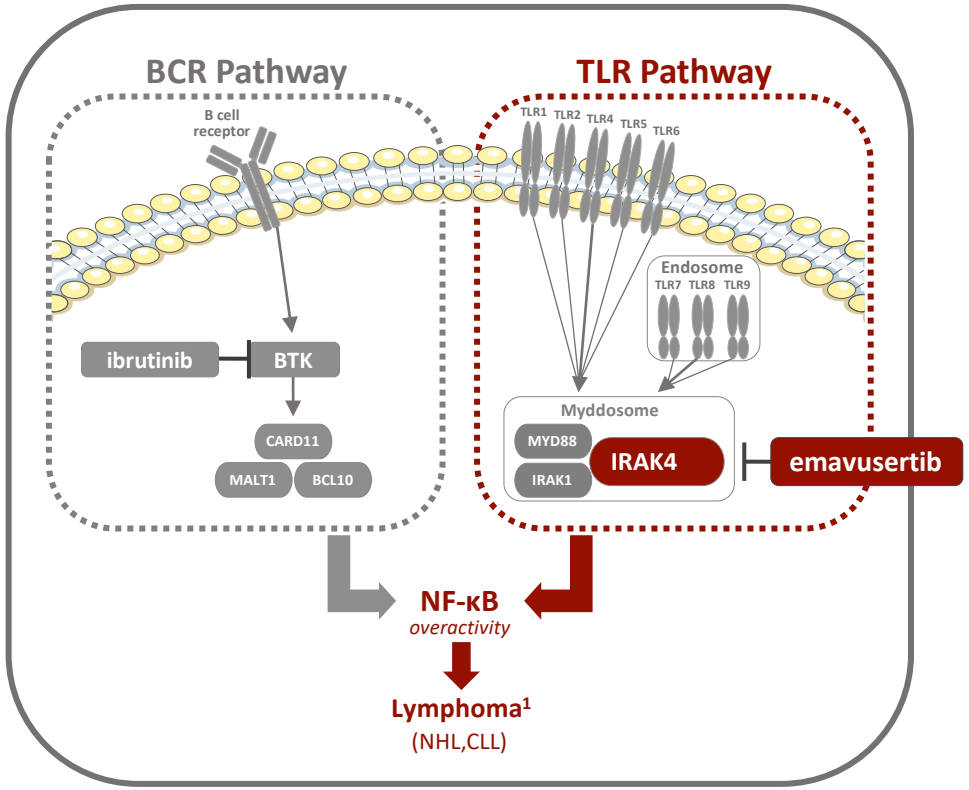
Emavusertib in Lymphoma (NHL/CLL)

Emavusertib in B Cell Cancers

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

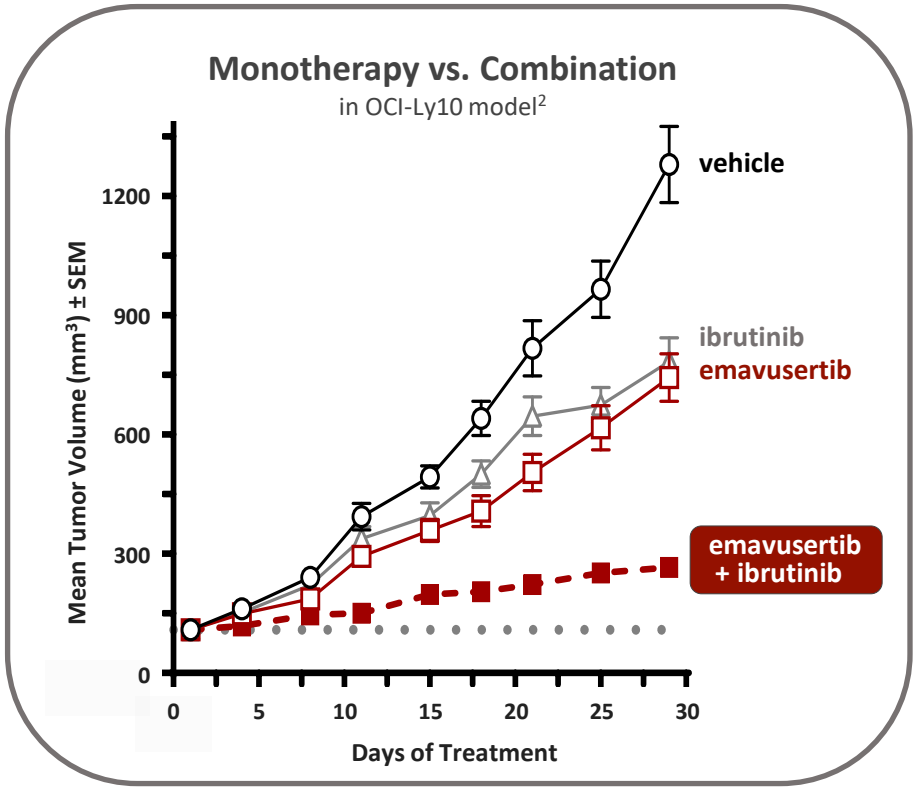
Two Pathways Drive B Cell Cancers

BCR and TLR Pathways independently drive NF-κB overactivity (and NF-κB drives B Cell Cancers)



Clinical Strategy: Use Combination Therapy

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

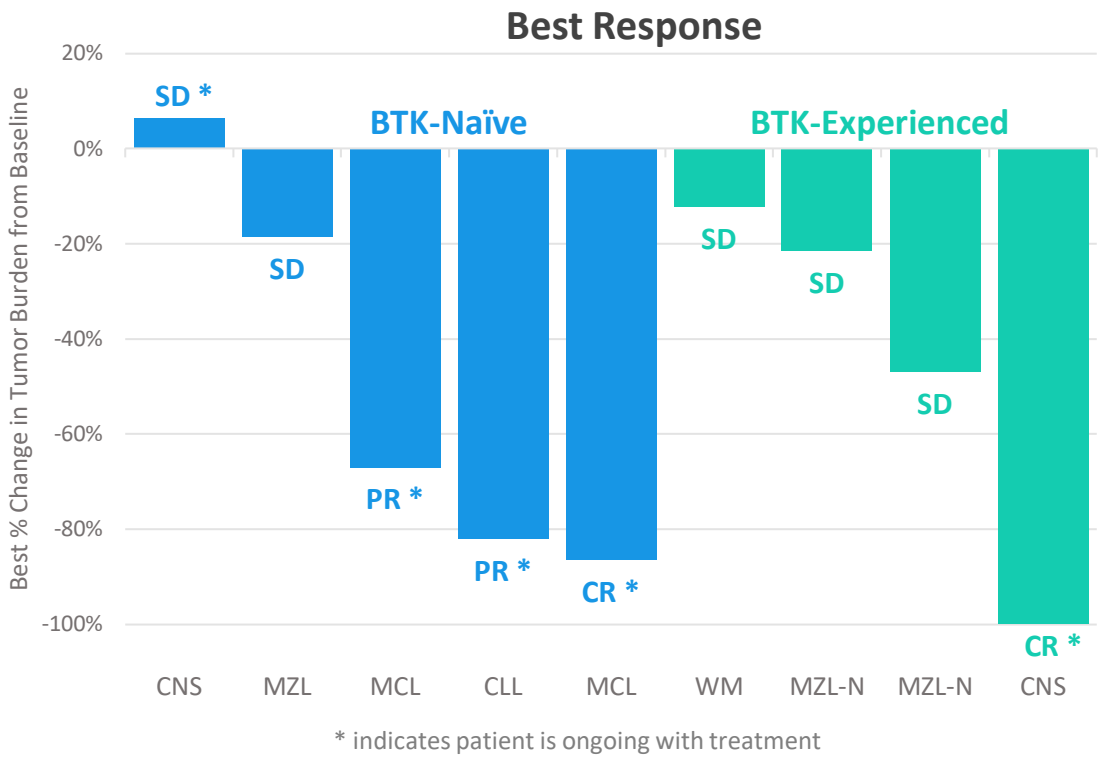


1) IMBRUVICA Package Insert. Rev 08/2018

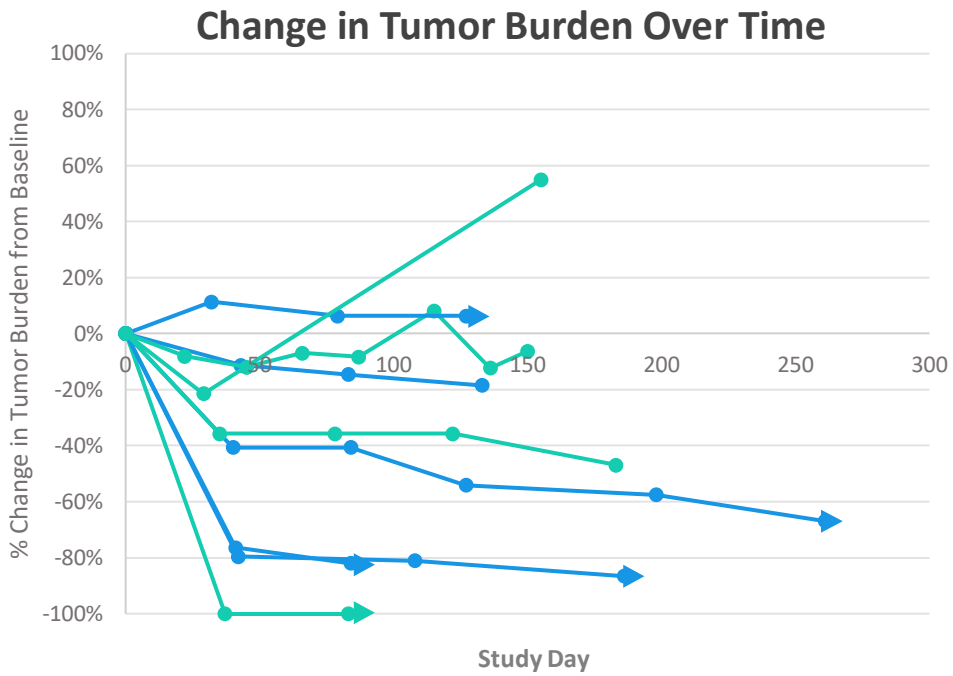
2) Booher et al. Waldenström Roadmap Symposium 2019

Responses Seen in Both BTK-Naïve and BTK-Experienced Patients

Majority of patients achieved decreases in tumor burden



* indicates patient is ongoing with treatment



13 total patients enrolled
9 patients were evaluable for tumor burden
4 patients did not receive pre/post tumor assessments

Data extracted May 6, 2022

Emavusertib in Lymphoma (NHL/CLL)

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

- Patients are 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

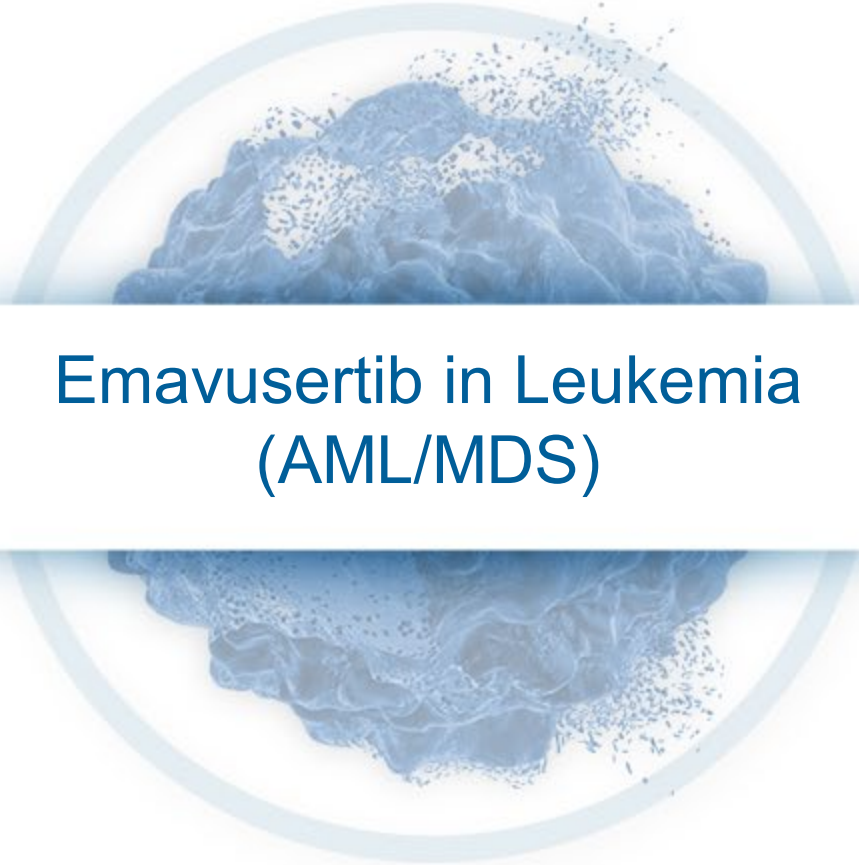
TakeAim

Next Steps

TakeAim Lymphoma Study

- *BTK naïve: MZL, PCNSL, DLBCL*
- *BTK experienced: any NHL subtype*

CURIS

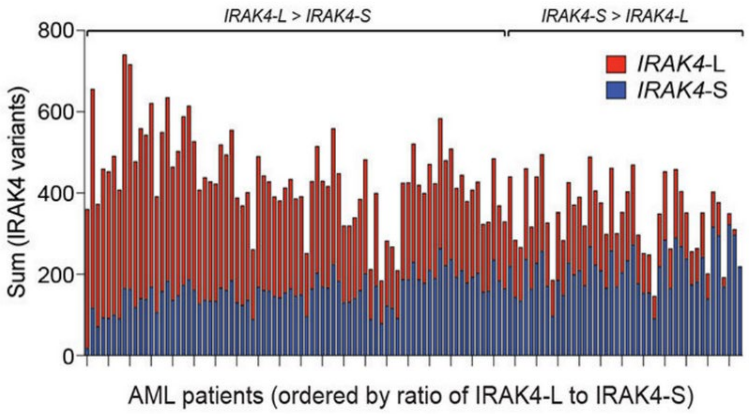


Emavusertib in Leukemia (AML/MDS)

Emavusertib in AML/MDS

Clinical studies designed to leverage the role of IRAK4 and FLT3 in AML/MDS

Disease Driver	% of Patient Population
IRAK4-L	> 50%[1]
FLT3	> 25%[2]
TET2	10-20%[3]
IDH2	9-13%[4]
IDH1	6-10%[4]
CEBPA	~10%[3]



Rationale for Monotherapy

- IRAK4 is the most prevalent genetic target in AML/MDS[1,2]
- IRAK4 signaling is the adaptive response mechanism for FLT3 patients treated with a FLT3 inhibitor[5]
  - *Emavusertib's unique molecular design targets both FLT3 and IRAK4*

Rationale for Combination

- Nearly all patients express some level of IRAK4-L[1]
- Preclinical data demonstrate clear synergy with azacitidine and venetoclax
  - *Even at lower levels, IRAK4 stimulates NF-κB and an array of anti-apoptotic factors beyond BCL2*
  - *Inhibiting IRAK4 with emavusertib enhances the anti-cancer efficacy of aza, ven, and aza/ven combination in preclinical models*

1) Smith et al. Nat Cell Biol 2019; 2) Saygin, et al. J Hematol Oncol. 2017 Apr 18; 3) DiNardo, Cortes. Hematology Am Soc Hematol Educ Program. 2016; 4) DiNardo et al. N Engl J Med 2018; 5) Rabik et al. Ann Transl Med 2020

Encouraging Clinical Activity in R/R AML/MDS

Monotherapy activity in patients with Spliceosome and FLT3 mutations

Best Response	Efficacy
Population #1: AML Spliceosome Patients[1]	
CR/CRh Rate	**2/5 (40%)**
CR	1/5 (20%)
CRh	1/5 (20%)
Population #2: MDS Spliceosome Patients	
Objective Response Rate (ORR)	**4/7 (57%)**
CR	0/7 (0%)
mCR	4/7 (57%)
Population #3: AML FLT3 Patients[1]	
CR/CRh Rate	**1/3 (33%)**
CR	1/3 (33%)
CRh	0/3 (0%)

The CR and CRh patients are both MRD-negative

1 mCR patient went to Stem Cell Transplant (SCT)

FLT3 mutation eradicated in 2 out of 3 patients

Data extraction date: Dec 16, 2021.

1) Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation).

Response criteria per 2017 ELN Criteria for AML and Modified IWG Criteria for MDS:
CR = Complete Remission
CRh = CR with partial hematologic recovery
mCR = marrow CR

Initial Emavusertib Data Compare Favorably to Existing Therapies

Potential to meaningfully improve outcomes in R/R AML patients with spliceosome mutation

Most Commonly Used Therapies in R/R AML Patients without FLT3 Mutation[1]

Emavusertib	Decitabine[2,3]	Azacitidine[2,4]	LoDAC[5]
IRAK4 Inhibitor	*HMA*	*HMA*	*Chemotherapy*
• 40% CR/CRh rate (2 of 5 patients)	• ~16% CR rate	• 17% CR/CRi rate	• ~13% ORR
• No dose-limiting myelosuppression	• Myelosuppressive	• Myelosuppressive	• Myelosuppressive and Black Box Warning
• Oral Administration	• IV Administration	• IV or SC Administration	• IV Administration

patients achieving CR/CRh have remained on emavusertib >6 months

- Spliceosome mutations occur in ~10% of AML patients[6]
- There are no effective therapies for patients who are R/R to Ven/HMA
- mOS 2-4 months[7]

1) Source: CancerMPact Treatment Architecture U.S. AML, Cerner Enviza, www.cancermpact.com, accessed January 3, 2022. Patients with wild type FLT3 and IDH. Excludes Investigational Therapies and anti-CD33; 2) Product Package Insert; 3. Ritchie et al, Leuk Lymphoma 2013; 4) Itzykson et al, Leuk Res 2014; 5) Frikha et al, Bulletin du Cancer 1996; 6) DiNardo et al, Hematology Am Soc 2016; 7) Maiti et al. Haemtologica 2021

Initial emavusertib data compare favorably vs. historical responses with mainstay treatments for R/R AML patients with wild type FLT3/IDH

AML Spliceosome Mutation

Clear Unmet Need in Relapsed/Refractory MDS

Current standard of care offers little therapeutic benefit to patients

Most Commonly Used Therapies in R/R MDS[1]

Emavusertib	Chemotherapy[2]	Decitabine[3]	Azacitidine[3]
IRAK4 Inhibitor	*Chemotherapy*	*HMA*	*HMA*
• 57% mCR rate (4 of 7 patients) • No dose-limiting myelosuppression • Oral Administration	• ~8% ORR • Myelosuppressive and Black Box Warning • IV Administration	• 2nd line response data unavailable • Myelosuppressive • IV Administration	• 2nd line response data unavailable • Myelosuppressive • IV or SC Administration

- Spliceosome mutations (U2AF1/SF3B1) are the most prominent mutations in MDS (~30% of MDS patients)[5]
- No effective therapies for patients R/R to HMA (chemo is standard of care)
- mOS 4-6 months[6]

1) CancerMPact Treatment Architecture U.S. AML, Cerner Enviza, www.cancermpact.com, accessed January 3, 2022. Excludes Investigational Therapies; 2) Prébet et al, JCO 2011.; 3) Product Package Insert.; 4) Jabbour et al Cancer 2010; Prébet et al., JCO 2011; Duong et al, Clin Lymphoma Myeloma Leuk, 2013; 5) Ochi Cancers 2021.; 6) Jabbour et al Cancer 2010.

Initial emavusertib data compared favorably vs. historical responses with the mainstay treatment for R/R MDS patients

MDS Spliceosome Mutation

Emavusertib May Address Unmet Need in R/R AML Patients with FLT3 Mut

No approved therapies for patients R/R to FLT3 inhibitors

Most Commonly Used Therapies in R/R AML Patients with FLT3 Mutation[1]

Emavusertib	Gilteritinib[2,3]	Azacitidine[2]	Decitabine[2]
IRAK4 Inhibitor	*FLT3 Inhibitor*	*HMA*	*HMA*
• 33% CR (1 of 3 patients) • No dose-limiting myelosuppression • Oral Administration	• ~12% CR • No dose-limiting myelosuppression • Oral Administration	• 2nd line response data unavailable • Myelosuppressive • IV or SC Administration	• 2nd line response data unavailable • Myelosuppressive • IV Administration

1) CancerMPact Treatment Architecture U.S. AML, Cerner Enviza, www.cancermpact.com, accessed January 3, 2022. Excludes Investigational Therapies and anti-CD33; 2) Product Package Insert; 3) Perl et al NEJM 2019; 4) Saygin, et al. J Hematol Oncol. 2017; 5) Melgar, Sci Transl Med. 2019

- ~30% of AML patients have FLT3 mutation[4]
- Dual inhibition of IRAK4 and FLT3 may lead to increased efficacy, as signaling through IRAK4 drives resistance to FLT3 inhibitors[5]

IRAK4/FLT3 inhibition may improve efficacy in R/R AML patients with FLT3 mutation[5]

AML
FLT3
Mutation

Emavusertib in Leukemia (AML/MDS)

The ideal candidate to address the two largest genetic populations in AML/MDS

Emavusertib addresses the two largest genetic populations in AML/MDS:

1) IRAK4 (>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 inhibitors[3]

TakeAim

Next Steps

TakeAim Leukemia Study

- *Monotherapy: Spliceosome, FLT3 mutation*
- *Combination: all other AML/MDS patients*

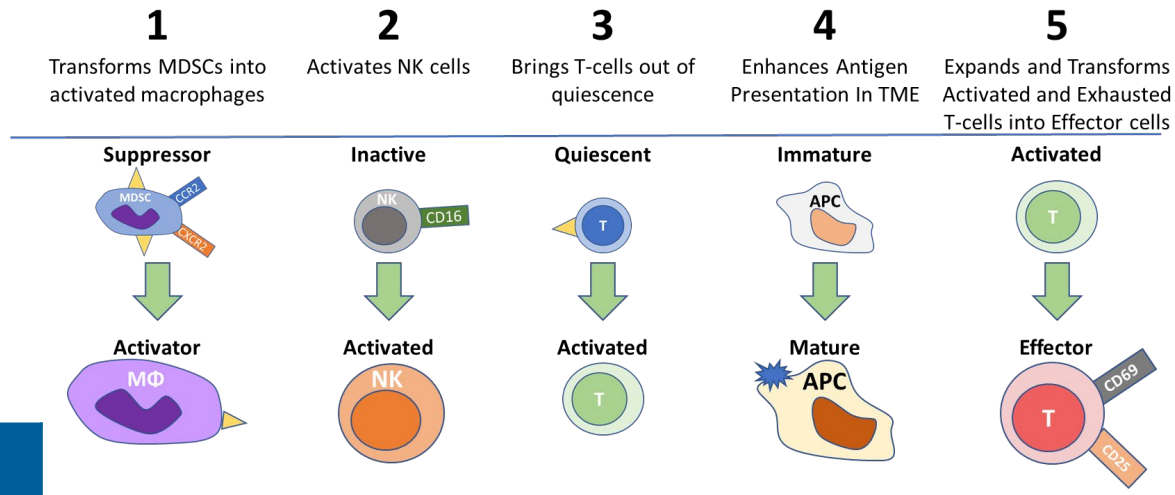
1) Smith et al. Nat Cell Biol 2019; 2) Saygin, et al. J Hematol Oncol. 2017 Apr 18; 3) Melgar, Sci Transl Med. 2019

CURIS

VISTA Biology and CI-8993

CI-8993: Novel Checkpoint Inhibitor

Published research suggests VISTA has a broad role among checkpoint inhibitors



Target					
VISTA (CI-8993)	☑	☑	☑	☑	☑
PD-1 (Pembro, Nivo, etc.)	☑	☒	☒	☒	☑
PD-L1 (Atezo, Durva, etc.)	☒	☒	☒	☒	☑
CTLA-4 (Ipi)	☒	☒	☒	☒	☑
TIM3	☑	☒	☒	☒	☑
LAG3	☒	☒	☒	☒	☑
OX40	☒	☒	☒	☒	☑
TIGIT	☒	☒	☒	☒	☑

We believe VISTA inhibition has potential for broad application in many tumor types in monotherapy and in combination with existing checkpoint inhibitors

Checkpoint Inhibitors Approved in Multiple Malignancies:

- Melanoma
- Lung Carcinoma
- Renal Cell Carcinoma
- Head & Neck Squamous Cell Carcinoma
- Lymphoma
- Hepatocellular Carcinoma
- Merkel Cell Carcinoma
- Gastric/Gastroesophageal Adenocarcinoma
- Cervical Carcinoma
- Cutaneous Squamous Cell Carcinoma
- Breast Carcinoma
- Esophageal Carcinoma
- Uterine Carcinoma
- Urothelial Carcinoma
- Genomic Alterations (e.g., MSI-high)

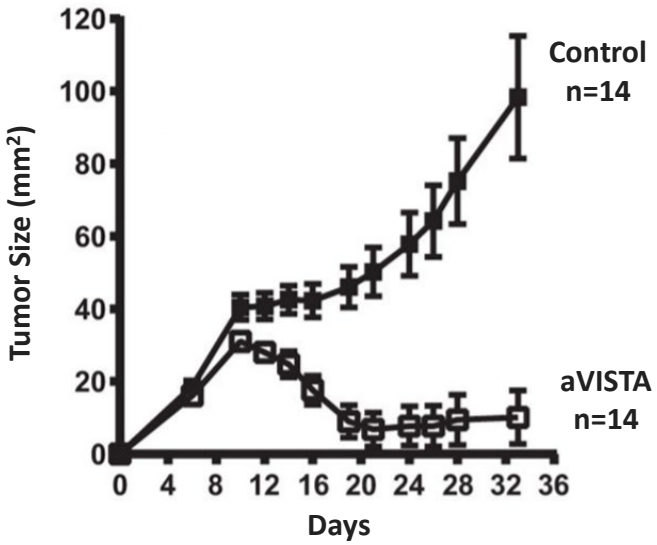
Sources: Curis & ImmuNext internal data, Curis 2021 VISTA Symposium.

CI-8993 Preclinical Data

Clear single-agent activity; potential to transform immune-oncology treatment in combination

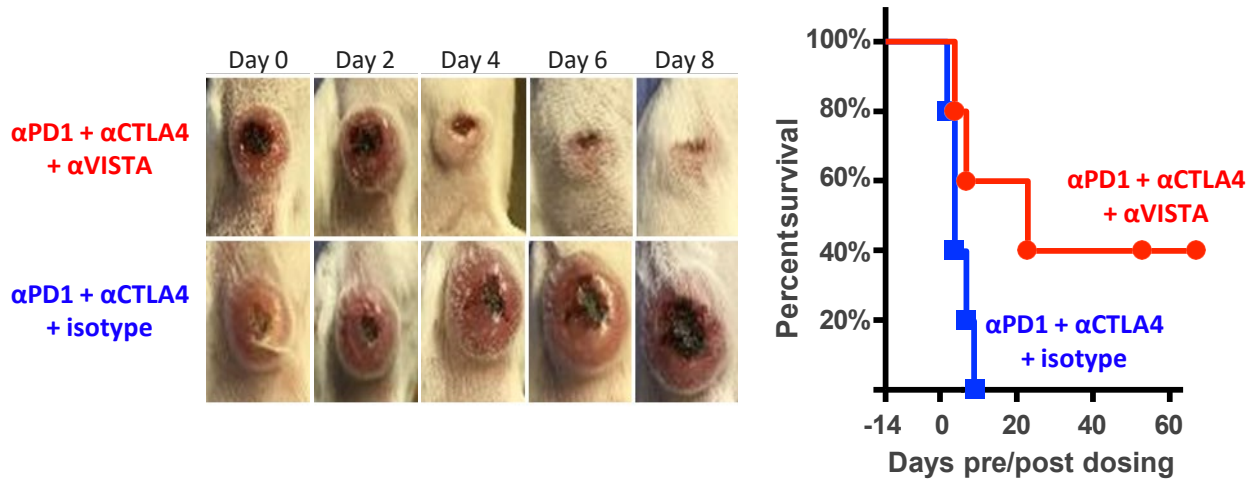
Monotherapy

Anti-VISTA inhibited tumor growth in B16ova melanoma model[1]



Combination Therapy

Anti-VISTA inhibited xenograft growth in checkpoint resistant CT26 model[2]



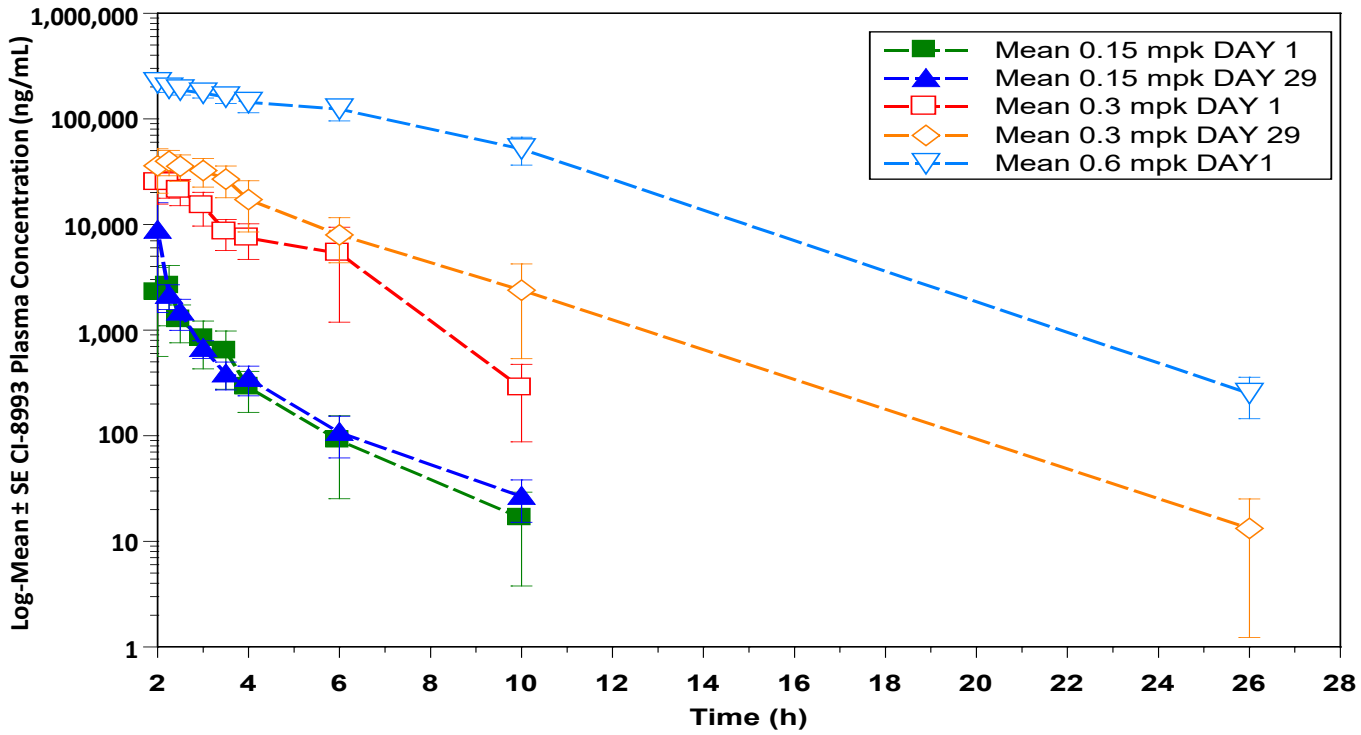
1) Le Mercier et al. Cancer Res. 2014 Apr 1

2) J. Lines, IEBMC Conference 2019

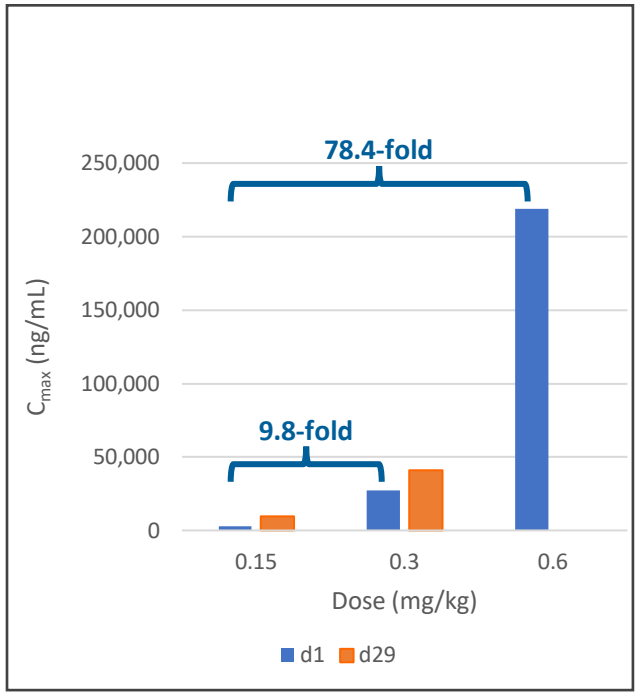
CI-8993 Initial Clinical Data

CI-8993 is demonstrating a favorable PK profile

Plasma Concentration



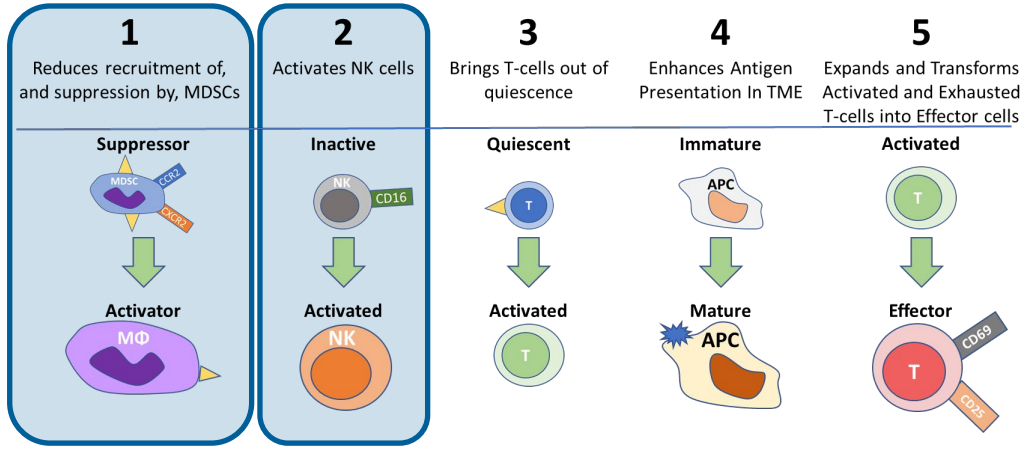
C_{max} Levels



Saturation kinetics in C_{max} data ("sink effect")
suggest potential for broad bioavailability at higher dose levels

CI-8993 Initial Clinical Data

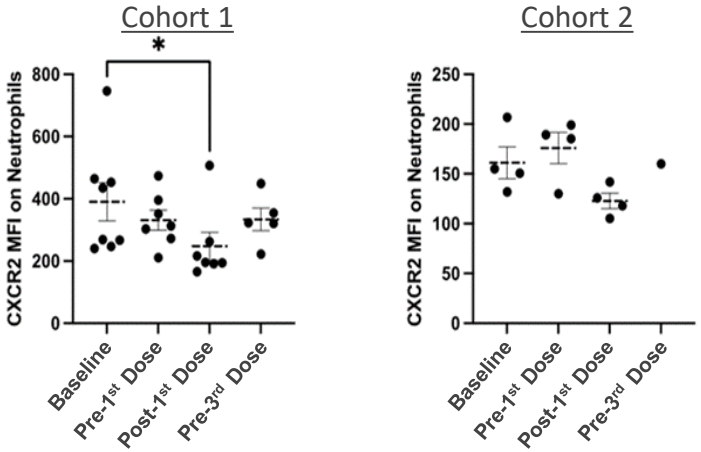
Initial data show reduction of MDSCs entering tumor & increased NK cell activation



1 Decreased recruitment of MDSCs

Decreased CXCR2 on granulocytes

CI-8993 reduces MDSCs (↓CXCR2 and ↓CCR2); MDSCs suppress anti-tumor immunity and impair efficacy of other checkpoint inhibitors

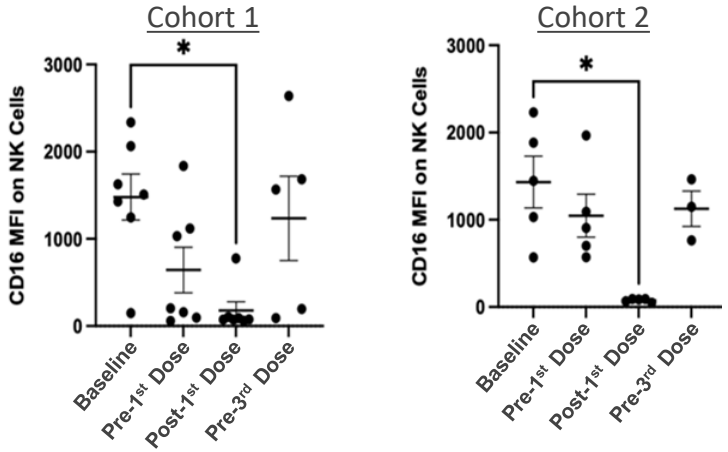


Similar finding for CCR2 on monocytes

2 NK Cell Activation

Decreased CD16 on NK cells

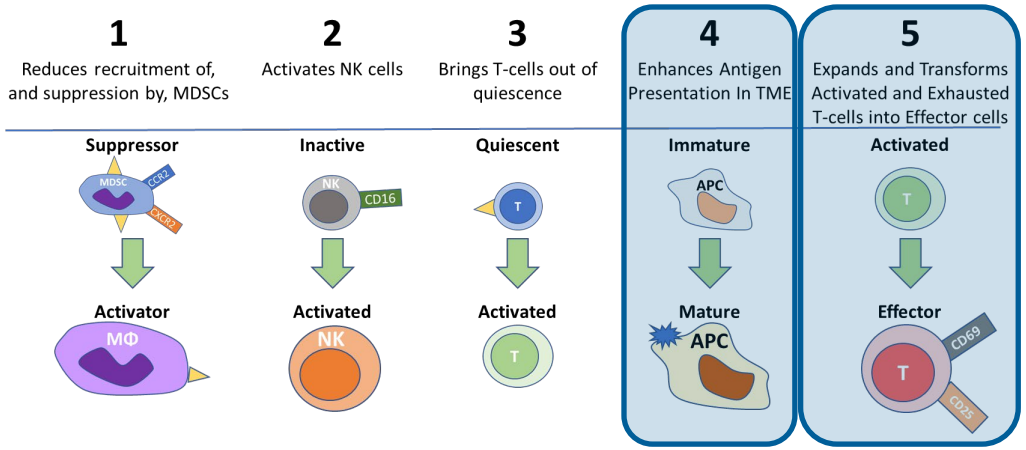
CI-8993 activates NK cells (↓CD16 signifies NK activation); activated NK cells exert an important anti-tumor function via the innate immune system



* p<0.05

CI-8993 Initial Clinical Data

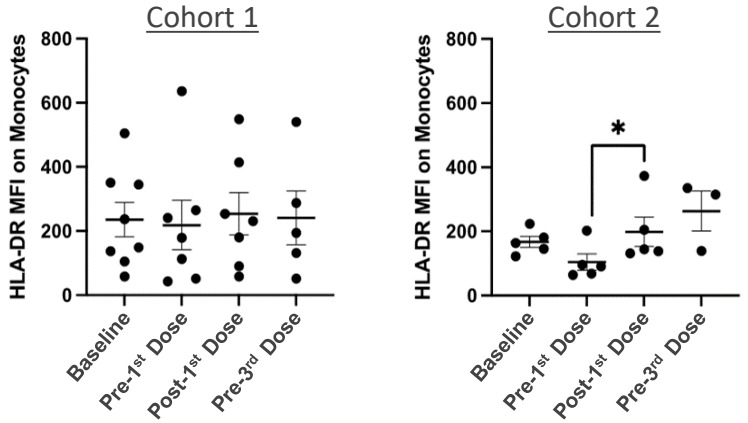
Initial data show enhanced antigen presentation & increased T cell activation factors



4 Enhanced Antigen Presentation

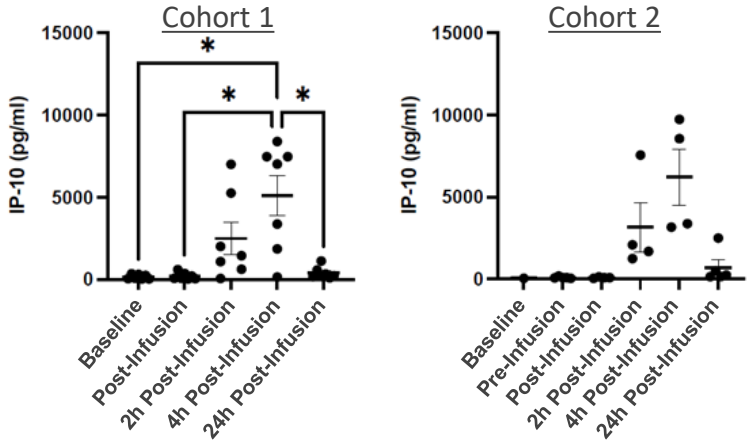
Increased HLA-DR on Monocytes

CI-8993 enhances antigen presentation (↑HLA-DR); antigen presentation allows the immune system to recognize the tumor and attack it



5 Release of T-Cell Activating Factors

Increased Secretion of IP10



CI-8993 increases T-cell factors (↑IP10 and ↑MIP1α); these stimulate T-cell expansion and transformation into effector T-cells

Similar finding for MIP1α

* p<0.05

CI-8993 Encouraging Progress at Early Dose Levels

First-in-class CI-8993 has potential for broad applicability in immune checkpoint therapy

- Favorable PK profile
- Saturation kinetics ("sink effect") appear to be addressed with increase in dose level
- Initial clinical data suggest multiple anti-cancer mechanisms are being activated in patients

Next Steps in Dose Escalation

- *Looks for additional signs of anti-cancer activity and determine RP2D*

Corporate Overview

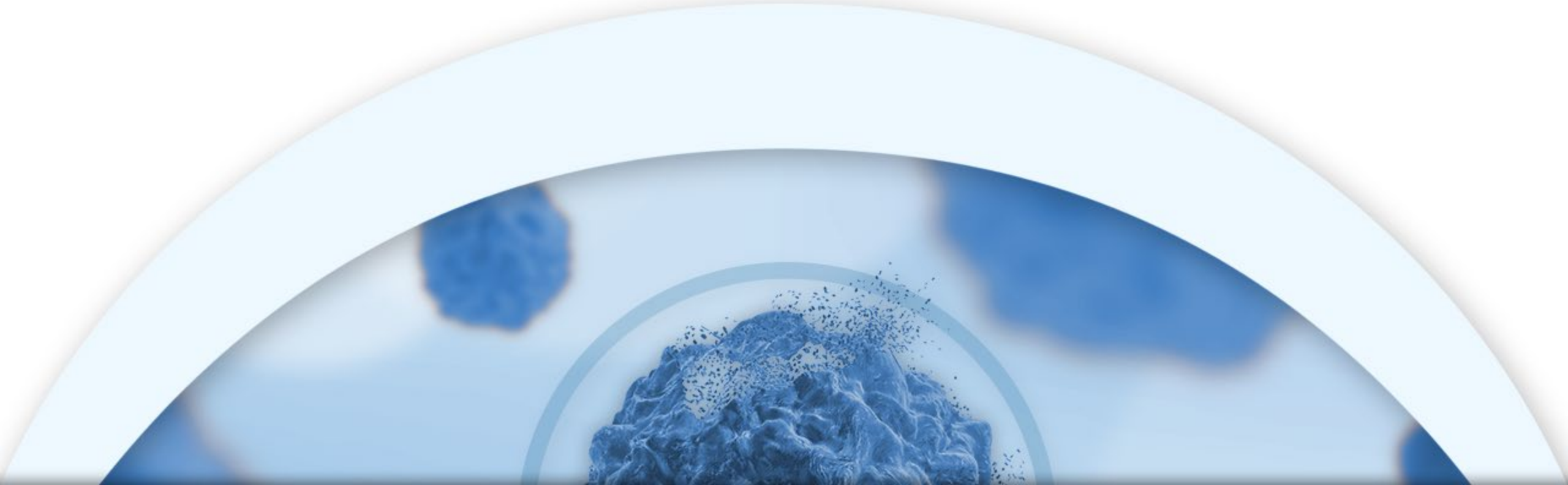
Summary

Investment Thesis	Curis develops novel, first-in-class, cancer therapeutics in areas of significant unmet patient need *Cash runway into 2024 – $107M as of June 30, 2022*
First-in-Class Pipeline	Emavusertib: first-in-class oncology program targeting IRAK4 CI-8993: first-in-class oncology program targeting VISTA
Significant Market Opportunity	AML/MDS: 317K patients[1] (standard of care: HMA) NHL/CLL: 1.8M patients[1] (standard of care: BTKi)
Upcoming Data	2023: emavusertib in AML/MDS (monotherapy) 2023: emavusertib in NHL/CLL (combination with ibrutinib) 2H 2022: CI-8993 in solid tumors (monotherapy)

1) 2022 Prevalence Data DRG Clarivate

End of Corporate Presentation

NASDAQ: CRIS



CURIS

APPENDIX

Emavusertib PK/PD

Attractive PK profile supports BID dosing and high target suppression

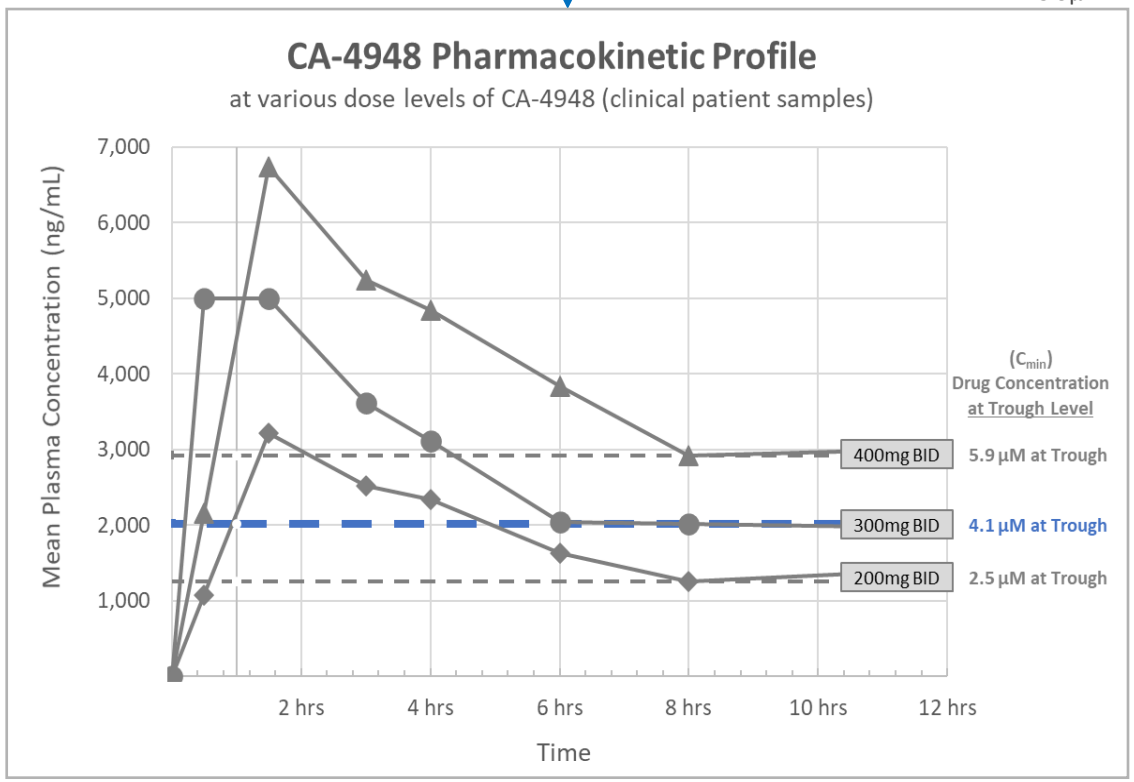
Attractive PK Profile

- Half-life of ~6 hours
- Supports BID dosing regimen

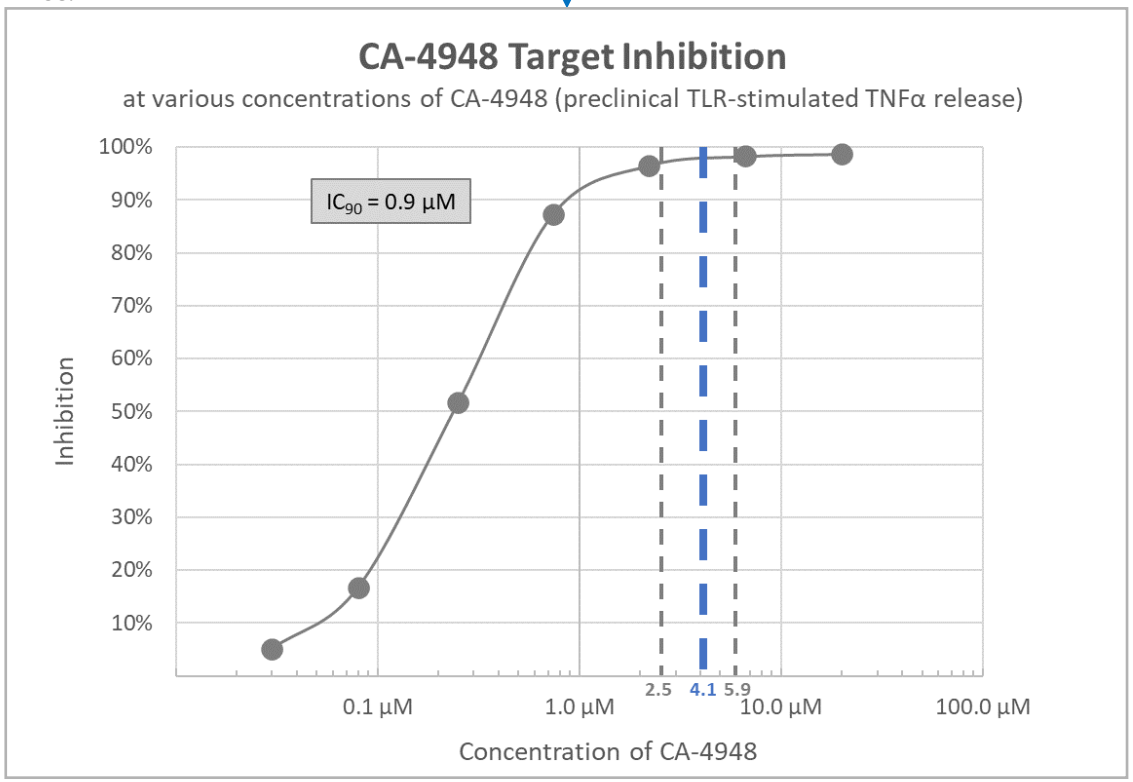
Trough Exposure	Dose	Inhibition
2.5µM	200mg	97%
4.1µM	**300mg**	**98%**
5.9µM	400mg	98%

High Target Suppression

- Exposure at RP2D correlates with 98% inhibition



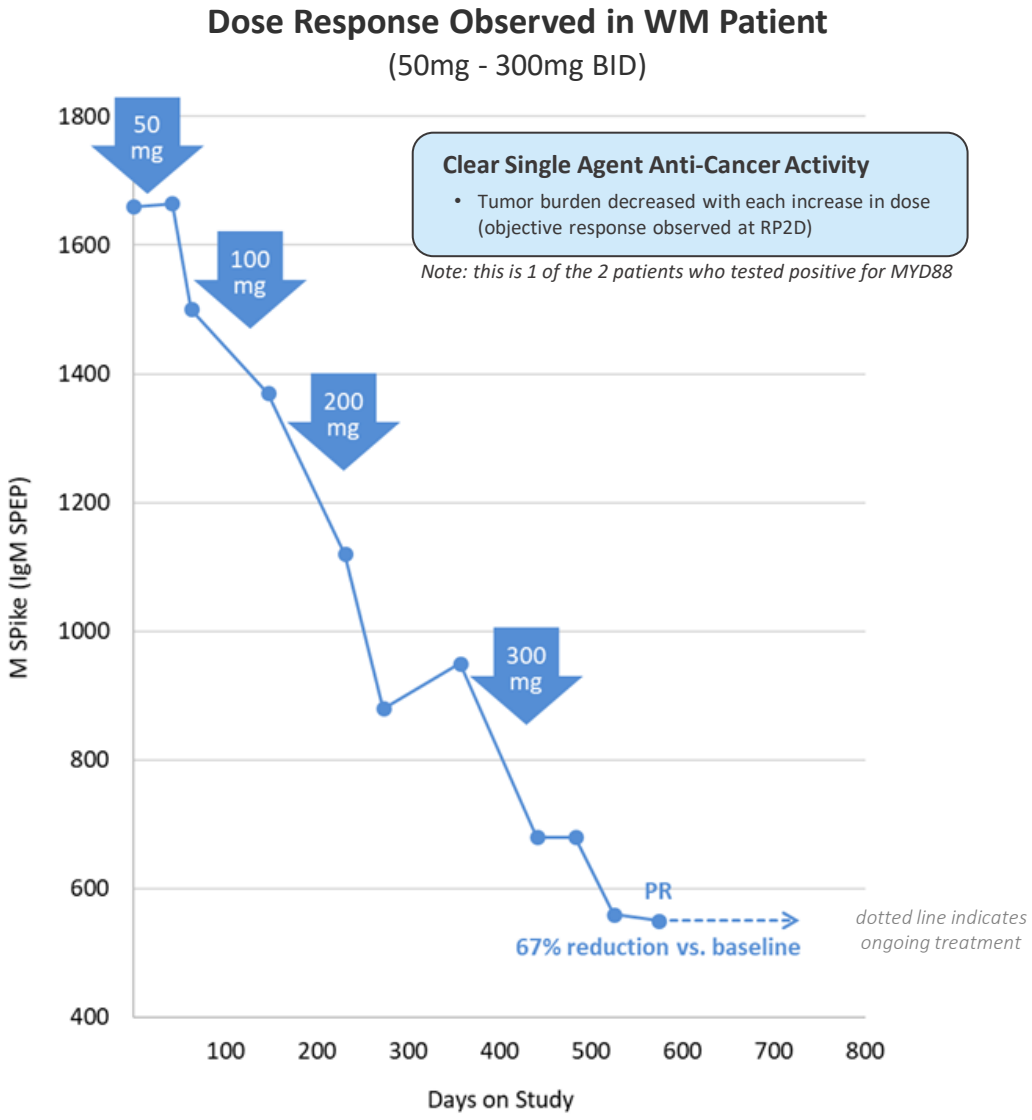
Data from TakeAim lymphoma clinical study



Data from preclinical study of target inhibition

Dose Response in Single Patient at Multiple Dose Levels

Patient in dose escalation phase of TakeAim Lymphoma study



Clear dose response observed

Tumor burden reduced with each increased dose

Emavusertib Clinical Plan

Ongoing clinical studies in AML/MDS and B cell cancers

AML/MDS Monotherapy

(relapsed/refractory)

Patients with Targeted Mutation

- Patients with spliceosome mutation
- Patients with FLT3 mutation

Supports rapid regulatory path

- *Spliceosome mutation is a leading cause of IRAK4-L overexpression[1]*
- *Signaling through IRAK4 is an adaptive response mechanism for FLT3 patients treated with a FLT3 inhibitor[2]*

AML/MDS Combination Therapy

(relapsed/refractory)

Patients without Targeted Mutation

- HMA-naïve, emavusertib + HMA
- Venetoclax naïve, emavusertib + venetoclax

Supports use in broad population

- *Clinical data show emavusertib reduces tumor burden in the significant majority of evaluable patients*
- *Preclinical data demonstrate synergy with azacitidine and venetoclax*

B Cell Cancers Combination Therapy

(relapsed/refractory)

Patients with IRAK4 Pathway activation

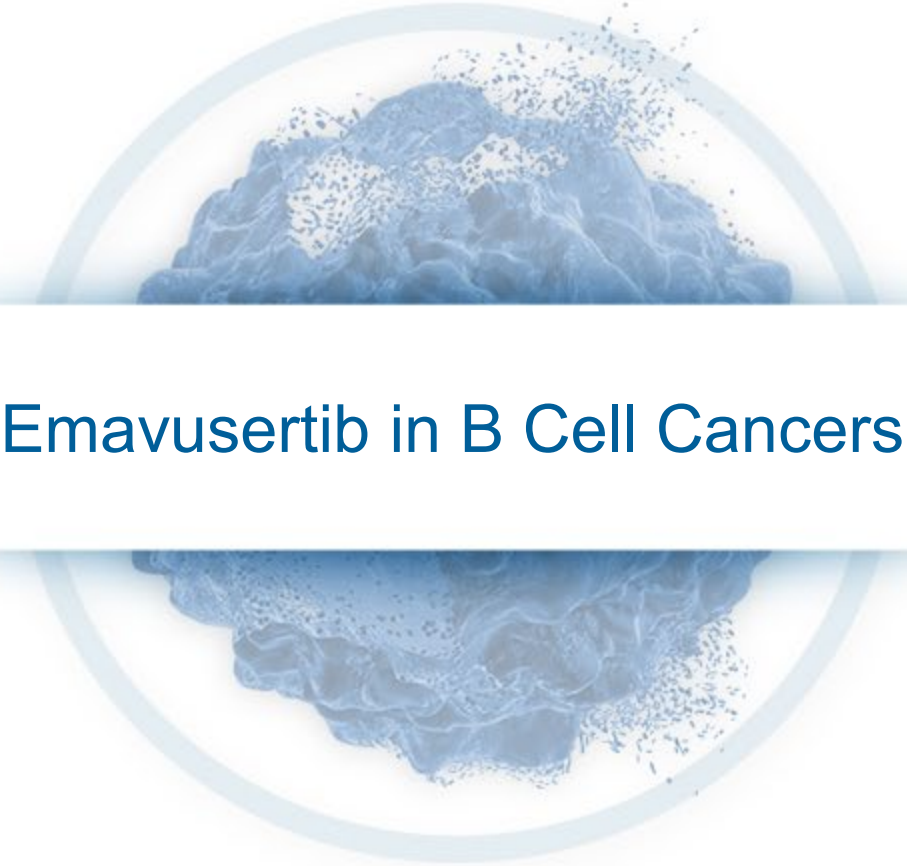
- BTKi-naïve, Marginal Zone Lymphoma
- BTKi-naïve, Primary CNS Lymphoma
- BTKi-naïve, ABC-DLBCL
- Patients (any tumor type) who have relapsed after adaptive resistance to ibrutinib

Maximizes speed and probability of success

- *Marginal Zone Lymphoma, Primary CNS Lymphoma, and ABC-DLBCL are aggressive indications associated with TLR/IRAK4 Pathway activity*
- *If patients who relapsed on ibrutinib can get clinical response with combination, it is likely impact of adding emavusertib*

1) Smith et al. Nat Cell Biol 2019; 2) Rabik et al. Ann Transl Med 2020

CURIS



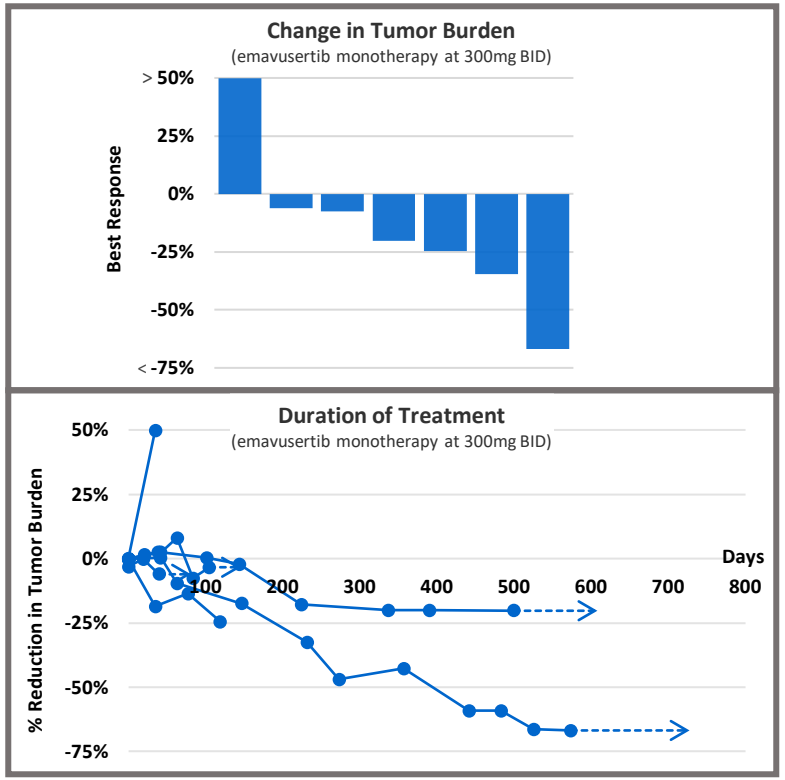
Emavusertib in B Cell Cancers

Emavusertib in B Cell Cancers

Proof-of-Concept demonstrated with monotherapy; Combination therapy study in progress

Monotherapy

Ph1 proof-of-concept study
demonstrated durable tumor reduction in monotherapy



2020 American Society of Hematology (ASH) Conference Presentation

Combination Therapy

Blocking both IRAK4 and BTK
may be better than blocking either one alone

4 Targeted Patient Populations

- BTKi naïve, Marginal Zone Lymphoma
- BTKi naïve, Primary CNS Lymphoma
- BTKi naïve, ABC-DLBCL
- Patients (any tumor type) who have relapsed after adaptive resistance to ibrutinib

TakeAim Lymphoma Study in Progress

---

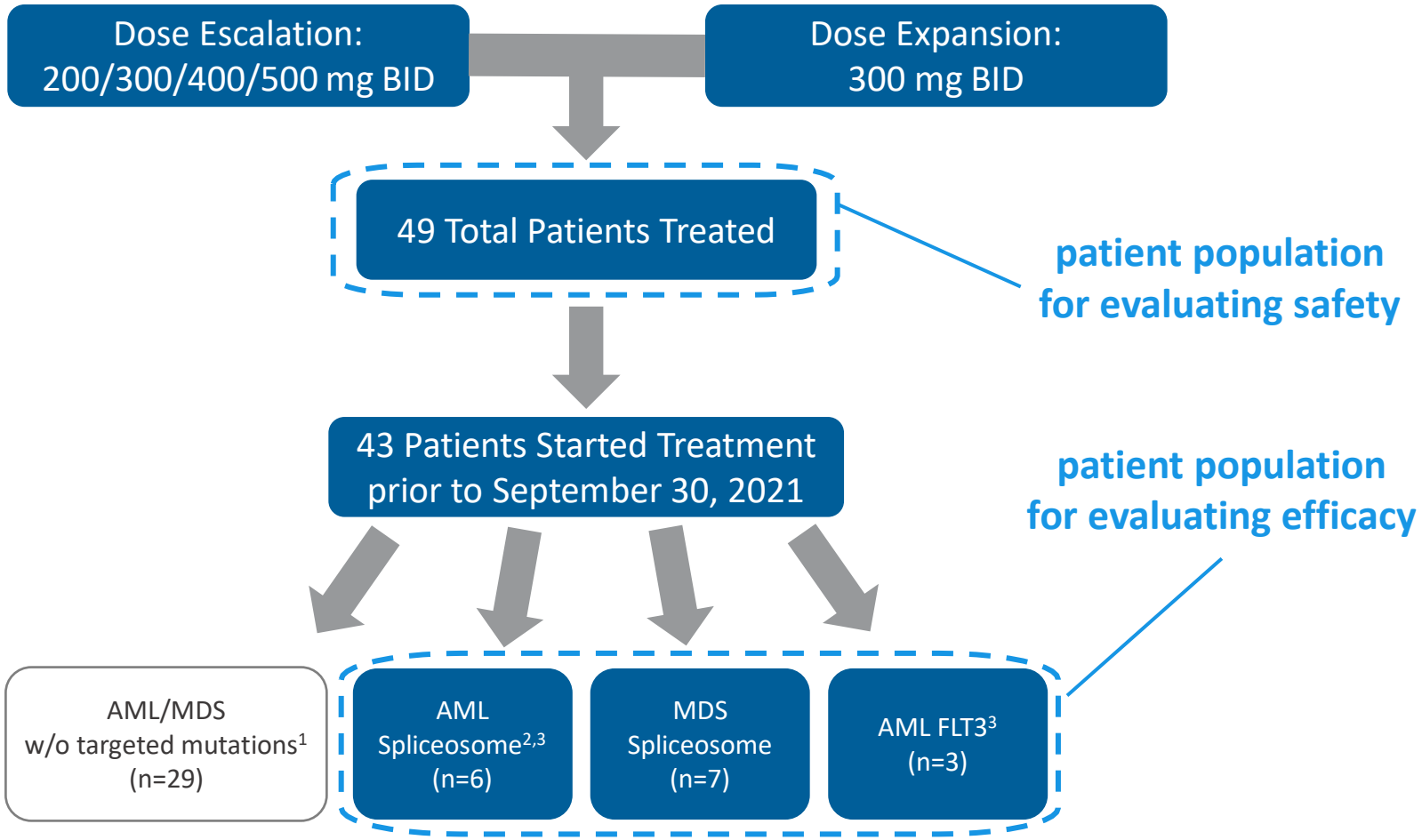
initial data coming in 1H 2022

CURIS

Emavusertib in AML/MDS

Emavusertib in AML and MDS

TakeAim Leukemia Trial - Open-label, single arm, Phase 1/2 dose escalation and expansion study



Study Objectives

1°: Determine maximum tolerated dose
Determine recommended Phase 2 dose

2°: Pharmacokinetic (PK) profile
Preliminary anti-cancer activity

Study Population

- Relapsed/Refractory AML or high-risk MDS
- ECOG performance Status of ≤ 2
- Age ≥ 18 years

Dosing

- Oral, Twice Daily (BID) Dosing
- 28-day cycles

Data extraction date: Dec 16, 2021
1) These are non-targeted patients, due to lack of Spliceosome or FLT3 mutation, this population will be addressed in the combination therapy study; 2) One patient was not response evaluable because of discontinuation due to patient decision;
3) Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation)

Safety Profile for emavusertib

49 total patients with AML/MDS treated with emavusertib

Recommended Phase 2 Dose

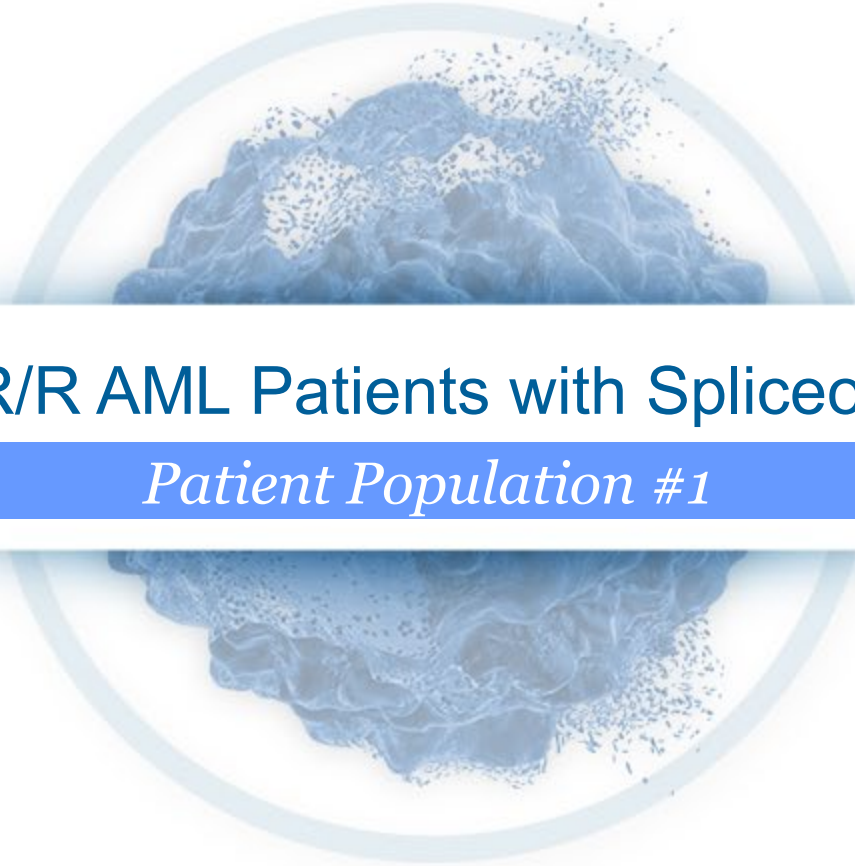
Grade 3+ Treatment-Related Adverse Event	200 mg BID (N = 3)		300 mg BID (N = 26)		400 mg BID (N = 17)		500 mg BID (N = 3)	
	n (%)		n (%)		n (%)		n (%)	
Number of patients having grade 3+ treatment-related AEs	1	(33.3)	6	(23.1)	6	(35.3)	2	(66.7)
Alanine aminotransferase increased	1	(33.3)	0		0		0	
Blood creatine phosphokinase increased	0		1	(3.8)	0		0	
Dizziness	1	(33.3)	0		0		0	
Dyspnoea	0		0		1	(5.9)	0	
Enterobacter infection	0		0		1	(5.9)	0	
Fatigue	0		0		1	(5.9)	0	
Gastrointestinal haemorrhage	0		1	(3.8)	0		0	
Hypophosphataemia	0		1	(3.8)	0		0	
Hypotension	0		1	(3.8)	0		0	
Lipase increased	0		2	(7.7)	0		0	
Platelet count decreased	0		1	(3.8)	0		0	
Presyncope	0		0		1	(5.9)	0	
Rhabdomyolysis	0		1	(3.8)	2	(11.8)	1	(33.3)
Syncope	0		0		0		1	(33.3)

Data extraction date: Dec 16, 2021.

1. Data for the two patients that have escalated from 300 mg BID to 400 mg BID were included in the 400 mg BID dose group.

Well-tolerated and manageable AE profile at Recommended Phase 2 Dose

No dose-limiting myelosuppression reported, which is a life-threatening problem characteristic of many cancer treatments, making emavusertib favorable for combinations



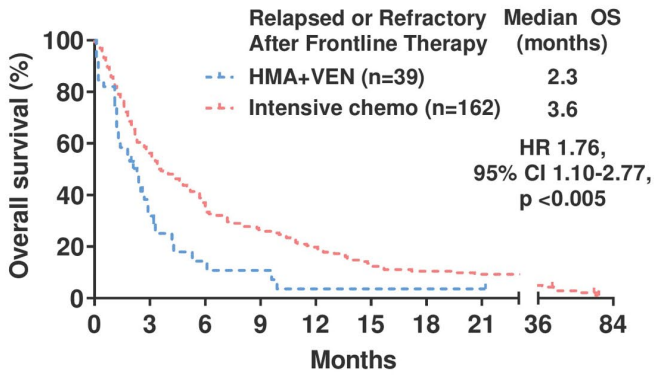
Clinical Data: R/R AML Patients with Spliceosome Mutation

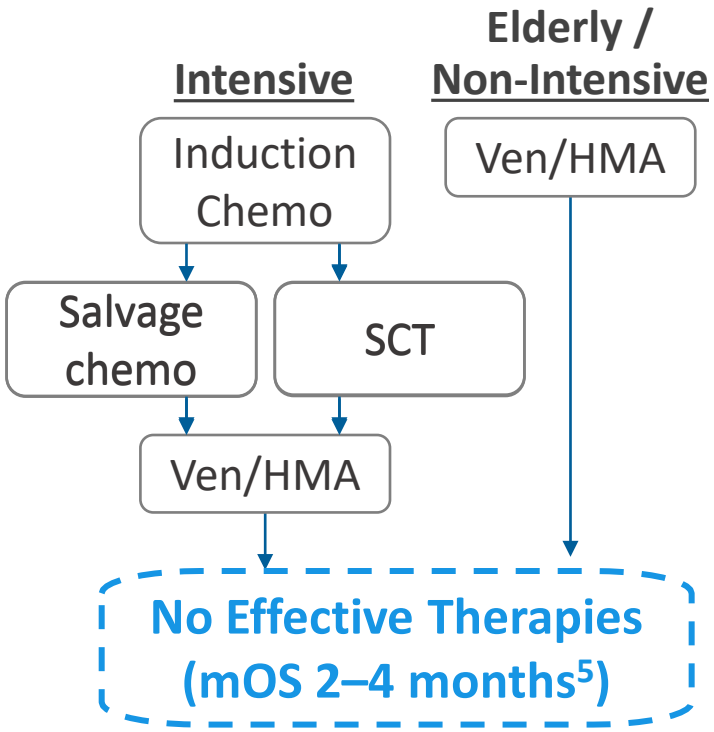
Patient Population #1

Unmet Need for R/R AML Patients with Spliceosome Mutation

No approved targeted therapies and no unified standard of care for these patients

- Spliceosome mutations occur in ~10% of AML patients[1]
  - These mutations create a chronic inflammatory marrow microenvironment[2], which impairs hematologic recovery[3]
  - Ability to achieve CR is impaired in patients with U2AF1/SF3B1 mutation[4]
- There are no effective therapies for patients R/R to Ven/HMA
  - no unified standard of care





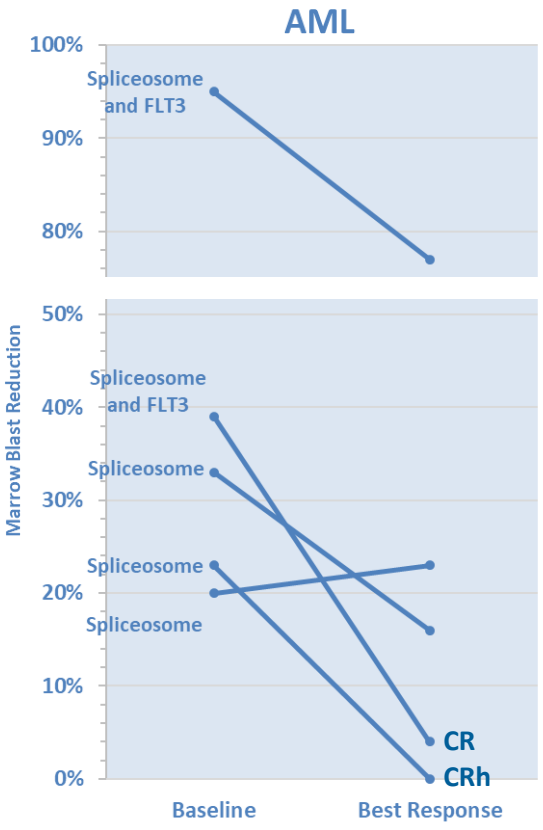
Opportunity to meaningfully improve outcomes in R/R AML patients with spliceosome mutations

AML Spliceosome Mutation

1) DiNardo et al, Hematology Am Soc 2016; 2) Smith et al. Nat Cell Biol 2019; 3) Trowbridge JEM 2021. Ochi Cancers 2021. Hou, Oncotarget 2016; 4) Hou, Oncotarget 2016; 5) Maiti et al. Haemtologica 2021

Encouraging Clinical Activity in R/R AML Patients with Spliceosome Mutation

Achieved 40% CR/CRh rate, with treatment duration >6 months to date in responding patients



Dx	Dose (BID)	Risk Category (ELN)	Baseline Molecular Mutations	Prior Therapies		Duration on emavusertib (mos)	Blasts Baseline	Blasts Best Response[1]	% Change
				# Lines	Therapy				
sAML	300 mg	Intermediate	RUNX1, WT1, SF3B1	1	decitabine	7	23	0	-100% (CRh)
sAML	300 mg	Intermediate	U2AF1, FLT3, BCOR, WT1	1	decitabine/venetoclax	6+	39	4	-90% (CR)
AML	300 mg	Intermediate	U2AF1, NRAS	4	cytarabine/idarubicin, decitabine/venetoclax, fludarabine/cyclophosphamide /methotrexate, azacitidine	2.5	33	16	-52%
AML	300 mg	Adverse	FLT3, SF3B1, NRAS, PTPN11, RAD21, RUNX1, TET2, GATA, STAT3	4	cytarabine/daunorubicin, decitabine, decitabine/venetoclax, gilteritinib	2.6	95	77	-19%
sAML	400 mg	Adverse	SF3B1, DNMT3A, P53	1	azacitidine/venetoclax	2	20	23	15%

Data extraction date: Dec 16, 2021; "+" in Duration of Treatment indicates the patient remains on treatment as of the date of data extraction.
1) Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation).

Emavusertib achieved CR/CRh responses,
despite transformed AML being historically highly resistant to treatment

AML Spliceosome Mutation

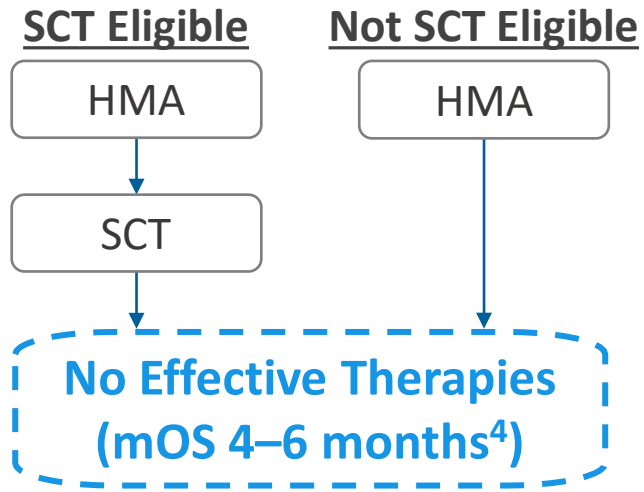
Clinical Data: R/R MDS Patients with Spliceosome Mutation

Patient Population #2

Spliceosome Mutations Common in MDS

Large unmet need for R/R MDS patients with spliceosome mutation

- Spliceosome mutations (U2AF1/SF3B1) are the most prominent mutations in MDS, accounting for ~30% of all MDS patients[1]
  - These mutations create a chronic inflammatory marrow microenvironment[2], which impairs hematologic recovery[3]
- There are no effective therapies for patients R/R to HMA: chemotherapy is standard of care



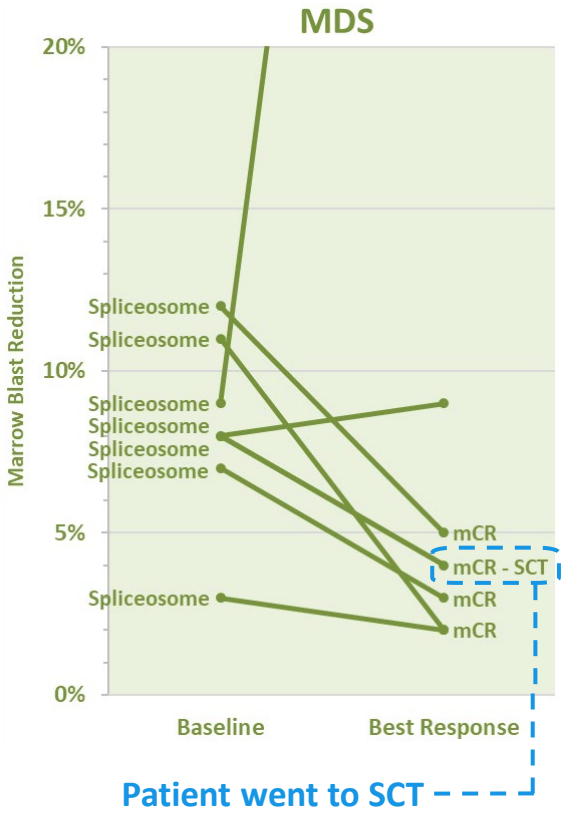
Current standard of care offers limited therapeutic benefit to patients

MDS Spliceosome Mutation

1) Ochi Cancers 2021.; 2) Smith et al. Nat Cell Biol 2019.; 3) Trowbridge JEM 2021. Ochi Cancers 2021.; 4) Jabbour et al Cancer 2010; Prebet et al., JCO 2011; Duong et al, Clin Lymphoma Myeloma Leuk, 2013.

Encouraging Clinical Activity in R/R MDS Patients with Spliceosome Mutation

Marrow blast reduction achieved in 5 of 7 patients, including 4 marrow CRs



Dx	Dose (BID)	IPSS-R	Baseline Molecular Mutations	Prior Therapies		Duration on emavusertib (mos)	Blasts Baseline	Blasts Best Response	% Change
				# Lines	Therapy				
MDS	200 mg	Very High Risk	U2AF1 ,ASXL1, NF1, PHF6, GFI1, KDM6A, TET2	1	azacitidine	5.7	11	2	-82% (mCR)
MDS	300 mg	Very High Risk	U2AF1, DNMT3A, BCOR, STAG2, BCORL1, ETV6, SETBP1	1	magrolimab/azacitidine	3.3+	12	5	-58% (mCR)
MDS	400 mg	Very High Risk	SF3B1, RUNX1, NFE2	2	lenalidomide, guadecitabine	4.3	7	3	-57% (mCR)
MDS	300 mg	High Risk	SF3B1, DNMT3A, ASXL1, TET2, EZH2	2	azacitidine, canakinumab	0.9 *(went to SCT)*	8	4	-50% (mCR)
MDS	300 mg	High Risk	U2AF1, ASXL1	4	lenalidomide, azacitidine, cyclosporine, decitabine	5.3+	3	2	-33%
MDS	300 mg	Very High Risk	SF3B1, ASXL1, NF1, SH2B3, RUNX1, PHF6, CBL, GFI1, EZH2	3	ipilimumab/azacitidine, quizartinib/azacitidine, azacitidine/venetoclax/ pevonedistat	1.6	8	9	13%
MDS	400 mg	Very High Risk	U2AF1, ASXL1, BCOR, DNMTA, GATA2, SETBP1	1	azacitidine	1.2	9	62	>100%

Data extraction date: Dec 16, 2021; "+" in Duration of Treatment indicates the patient remains on treatment as of the date of data extraction.

Consistent tumor burden reduction in targeted population with limited options

MDS Spliceosome Mutation

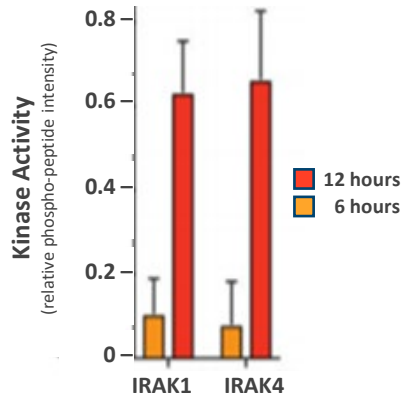
Clinical Data: R/R AML Patients with FLT3 Mutation

Patient Population #3

Emavusertib in AML/MDS with FLT3 Mutation

IRAK4 inhibition is synergistic with, and prevents adaptive resistance to, FLT3 inhibition

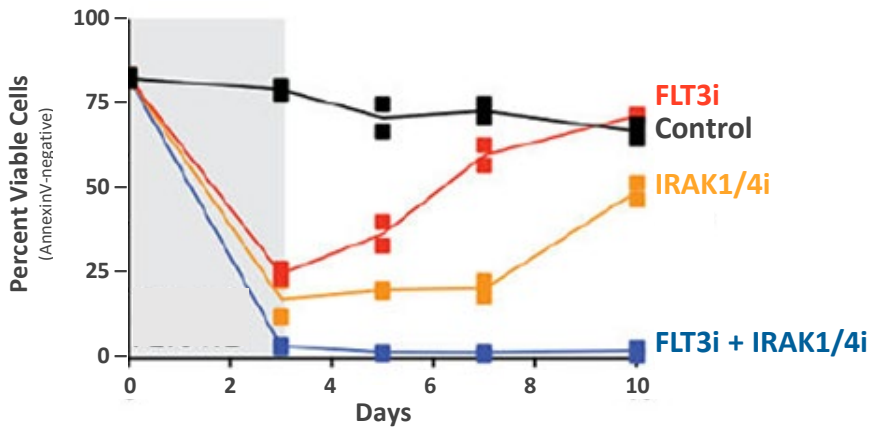
IRAK Activity
increases after treatment with FLT3i



IRAK4 activity increases after treatment of MLL-AF9 FLT3-ITD cells with FLT3i (quizartinib)

IRAK4 activity also shown to increase in patients during gilteritinib treatment

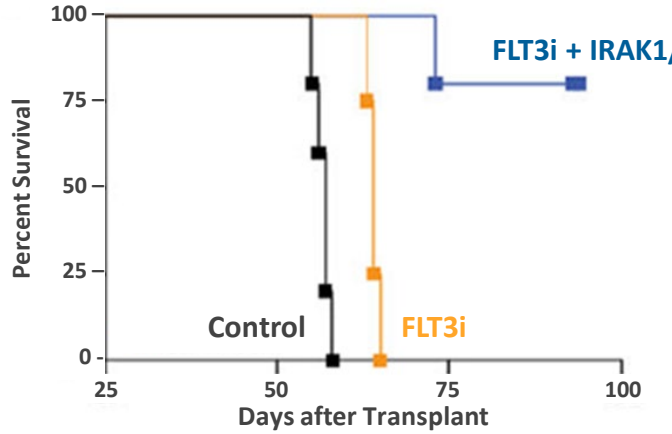
IRAK1/4i Synergy with FLT3i



Combination of IRAK1/4 and FLT3 inhibition (quizartinib) is synergistically cytotoxic

Viability of MLL-AF9; FLT3-ITD cells treated for 3 days with DMSO (vehicle control), quizartinib (0.5 µM), IRAKi (10 µM), or quizartinib and IRAKi

Leukemia-free Survival
IRAK1/4i + FLT3i Combination vs FLT3i alone



Mice die if treated FLT3i (quizartinib) alone, but survive if treated with combination of IRAK1/4i and FLT3i

Leukemia-free survival of NRGS mice xenografted with AML-019

Preclinical data demonstrates synergistic effect of dual inhibition

AML
FLT3
Mutation

Source: Melgar, Sci Transl Med. 2019.

Encouraging Clinical Activity in R/R AML Patients with FLT3 Mutation

Achieving disease modification in heavily pretreated patients with emavusertib monotherapy

Dx	Dose (BID)	Risk Category (ELN)	Baseline Molecular Mutations	Prior Therapies		Duration on emavusertib (mos)	Blasts Baseline	Blasts Best Response[1]	% Change
				# Lines	Therapy				
AML	400 mg	Adverse	FLT3 ***(eradicated at C3D1)***, ASXL1, BCOR, CEBPA *(eradicated at C3D1)*, CSF3R, EZH2, NRAS, RUNX1 (X3), STAG2, TET2(X2,1) *(eradicated at C3D1)*	2	decitabine/venetoclax, gilteritinib ***(refractory to gilteritinib)***	5.1	60	5	-92%
sAML	300 mg	Intermediate	FLT3 ***(eradicated at C4D1)***, BCOR *(eradicated at C4D1)*, U2AF1 *(decreased to 1.3 VAF at C4D1)*, WT1 *(eradicated at C4D1)*	1	decitabine/venetoclax	6.2+	39	4	-90% (CR)
AML	300 mg	Adverse	FLT3, SF3B1, NRAS, PTPN11, RAD21, RUNX1, TET2, GATA, STAT3	4	cytarabine/daunorubicin, decitabine/PCM-075, decitabine/venetoclax, gilteritinib	2.6	95	77	-19%

Data extraction date: Dec 16, 2021; "+" in Duration of Treatment indicates the patient remains on treatment as of the date of data extraction.
1) Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation).

Significant marrow blast reduction and
FLT3 mutation eradicated in 2 out of 3 patients

AML
FLT3
Mutation

CURIS

VISTA Biology and CI-8993

Incorporated Learnings from CI-8993 Prior Clinical Study

Pharmacodynamic activity (cytokine release) observed in initial clinical study

CI-8993 is the first anti-VISTA monoclonal antibody (IgG1κ) to be studied in clinical trials

- Janssen initiated a Ph1 study in 2016 and enrolled 12 patients[1]
- Transient Cytokine Release Syndrome (CRS) was observed in several patients at 0.15mg/kg
- Transient grade 3 CRS-associated encephalopathy observed at 0.3mg/kg, after which Janssen halted the study

CI-8993 Protocol Designed to Manage Expected CRS

- CRS is likely an on-target effect; indicates the drug is hitting the target and inducing immune response
- NCCN guidelines were issued in 2018; oncology community now familiar with managing CRS
- Desensitizing step-dose of CI-8993, and pre/post-infusion medication, administered to mitigate CRS

1) ClinicalTrials.gov, Trial #NCT02671955

CI-8993 Clinical Plan: Phase 1 Dose Escalation Study

On-going clinical study to determine safety

Phase 1 Dose Escalation Study Design

Patient Population

- Patients with advanced refractory solid tumors (includes mesothelioma, melanoma, NSCLC, TNBC)

Treatment

- Bi-weekly dosing
- Plan to mitigate potential toxicities by co-medication and step dosing (desensitization)

Objectives

- Safety, PK/PD, tolerability during dose escalation
- Anti-cancer activity during expansion

Protocol Designed to Manage Expected CRS

- CRS is likely an on-target effect; indicates drug is hitting the target and inducing immune response
- NCCN guidelines were issued in 2018; oncology community now familiar with managing CRS
- Desensitizing step-dose of CI-8993, and pre/post-infusion medication, administered to mitigate CRS

NSCLC: Non-Small Cell Lung Cancer; TNBC: Triple Negative Breast Cancer

CI-8993 Has Demonstrated Favorable Safety Profile

Successfully managed expected CRS at all levels dosed to date

All Grades Treatment-Related Adverse Events Occurring in 2+ Patients	0.15 mg/kg (N = 7)		0.3 mg/kg (N = 5)	
	n (%)		n (%)	
Number of patients having any grade treatment-related AEs	4	(57.1)	4	(80.0)
Headache	3	(42.9)	1	(20.0)
Chills	2	(28.6)	1	(20.0)
Alanine aminotransferase increased	1	(14.3)	1	(20.0)
Fatigue	2	(28.6)	0	
Hypotension	0		2	(40.0)

Grade 3+ Treatment-Related Adverse Events	0.15 mg/kg (N = 7)		0.3 mg/kg (N = 5)	
	n (%)		n (%)	
Number of patients having grade 3+ treatment-related AEs	0		1	(20.0)
Leukopenia	0		1	(20.0)

Data extraction date: Dec 11, 2021.
One additional patient experienced grade 2 treatment-related AE after receiving step dose and chose not to proceed to full dose.

Expected stimulation of immune response-related AEs

Successfully managed at all levels dosed to date

CI-8993 has successfully cleared dose level where Janssen observed DLT