

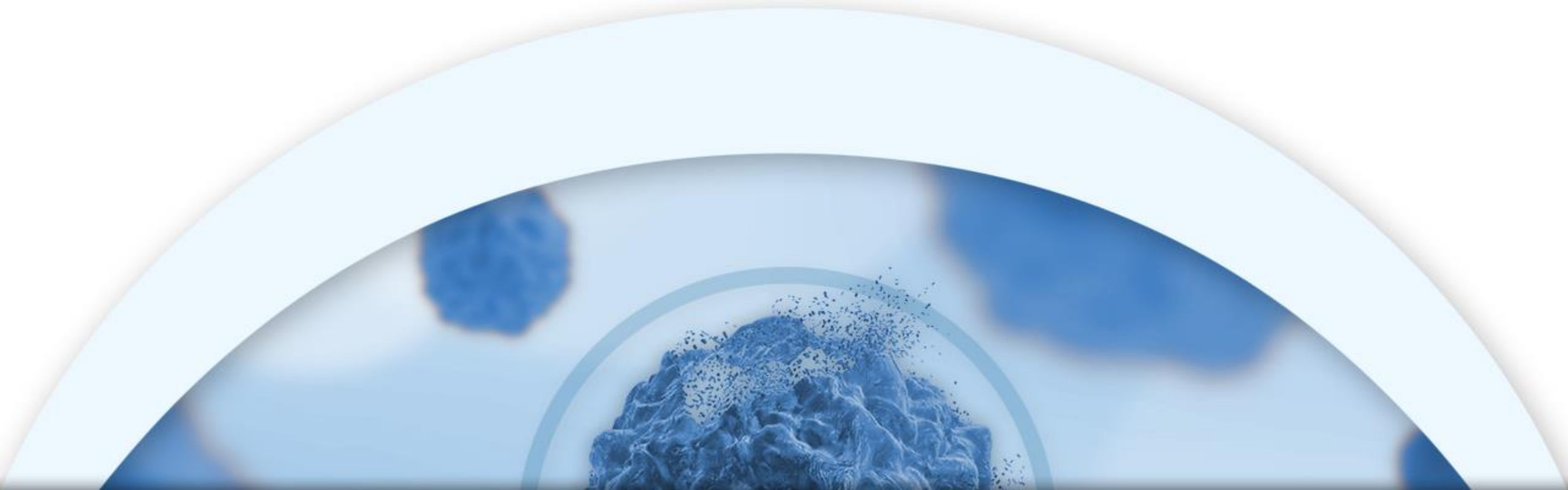


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## Corporate Presentation

*NASDAQ: CRIS*

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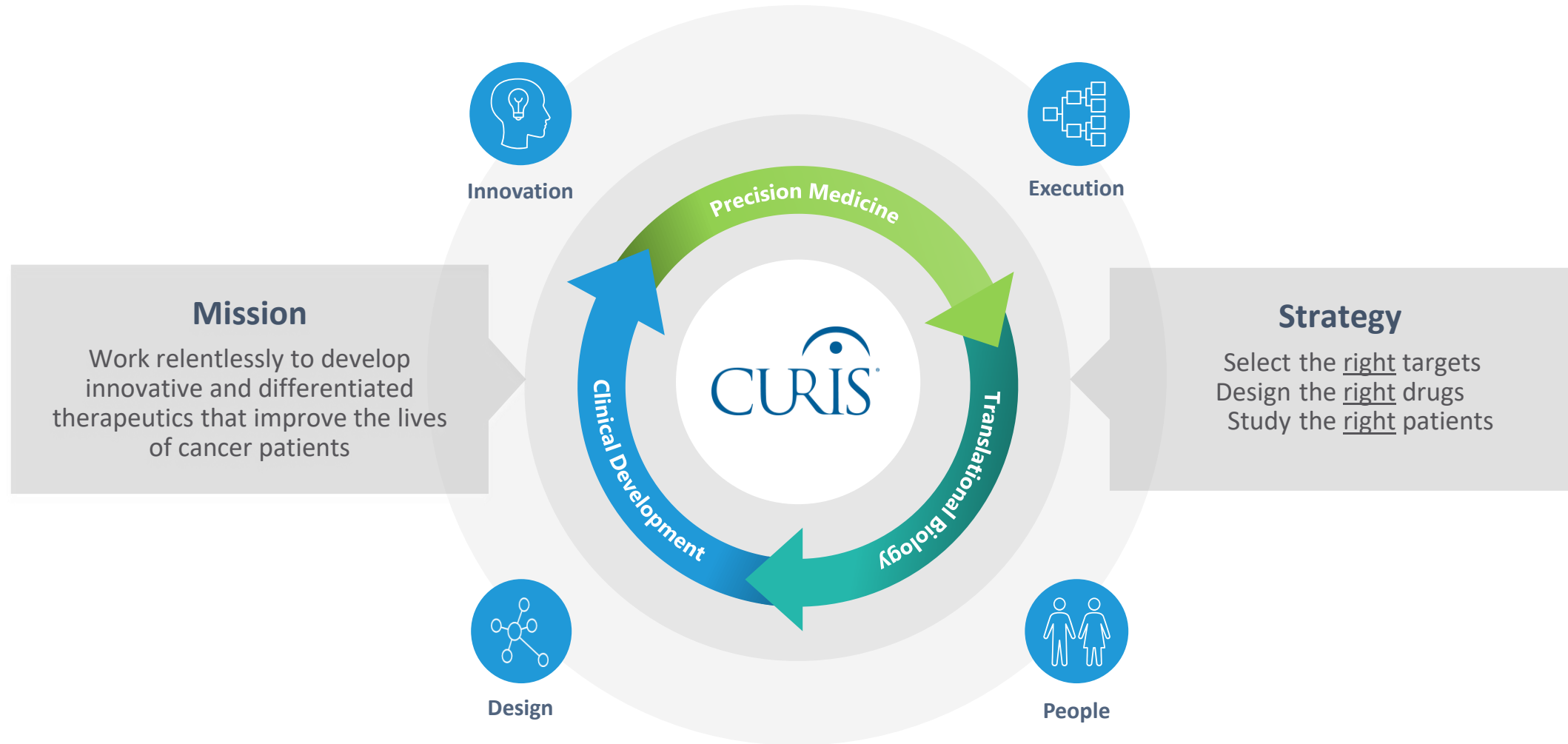
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This presentation contains certain forward-looking statements about Curis, Inc. (“we,” “us,” or the “Company”) within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as “expect(s),” “believe(s),” “will,” “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 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 U.S. Food and Drug Administration 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](http://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.

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# Curis Mission & Strategy

*Developing the New Generation of Targeted Cancer Drugs*



<b>Investment Thesis</b>	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need
<b>Robust Pipeline</b>	<p>CA-4948: first-in-class inhibitor of IRAK4 in oncology <i>There are no drugs currently approved that block the entire TLR pathway</i></p> <p>CI-8993: first-in-class antagonist of VISTA <i>There are no drugs currently approved for VISTA inhibition</i></p> <p>Fimepinostat: first-in-class suppressor of MYC <i>There are no drugs currently approved for MYC inhibition</i></p>
<b>Corporate</b>	<ul style="list-style-type: none"><li>• Experienced management team with proven capabilities</li><li>• Curis R&amp;D pioneered the first-in-class inhibitor of the Hedgehog pathway (Erivedge®) partnered with and commercialized by Genentech/Roche for advanced basal cell carcinoma</li><li>• Cash, cash equivalents and investments of approximately \$20.5M as of Dec 31, 2019</li></ul>

## *Progressing through Clinical Studies on the Path to Potential Registration*



# Pipeline

## Of Oncology Drug Candidates



		PRE-CLINICAL	CLINICAL				MARKETED
Indication		Proof of Principle	Safety	Dose Optimization	Clinical Activity	Pivotal	Commercial
<i>Heme Malignancies</i>							
<b>CA-4948*</b> IRAK4	MYD88/TLR-altered NHL	[Progress bar]					
<b>CA-4948*</b> IRAK4	AML/MDS patients w/ spliceosome mutations	[Progress bar]					
<b>Fimepinostat</b> HDAC/PI3K	MYC-altered Cancers	[Progress bar]					
<i>Immune Checkpoint Inhibitors</i>							
<b>CI-8993**</b> VISTA	VISTA-expressing/infiltrated Cancers	[Progress bar]					
<b>CA-327*</b> PDL1/TIM3	PDL1/TIM3-expressing Cancers	[Progress bar]					
<b>CA-170*</b> PDL1/VISTA	PDL1/VISTA-expressing Cancers	[Progress bar]					
<i>Basal Cell Carcinoma</i>							
<b>Erivedge***</b> Hedgehog	Basal Cell Carcinoma	[Progress bar]					

\* IP licensed from Aurigene  
 \*\* Option to license IP from ImmuNext  
 \*\*\* IP licensed to Genentech (Curis receives royalty income)

A circular inset image showing a microscopic view of a cell cluster, likely a tumor, with a blue and white color scheme. The cluster is composed of numerous small, interconnected cells, some appearing more densely packed than others. The background of the inset is light blue.

## Targeted Programs in Heme Malignancies

*CA-4948: In development for treatment of TLR-altered cancers*

# CA-4948 Overview

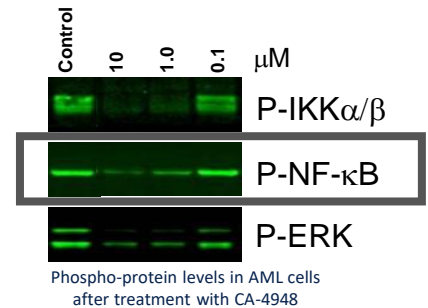
## First-in-Class Inhibitor of IRAK4 in Oncology

Profile	
Value Proposition	<ul style="list-style-type: none"> <li>• First-in-class IRAK4 inhibitor in cancer</li> <li>• Specific malignancies in Lymphoma are characterized by overactivity of the myddosome in the TLR pathway (which is dependent upon IRAK4)</li> <li>• Specific malignancies in Leukemia are characterized by spliceosome mutations that lead to overexpression of IRAK4-L (the oncogenic isoform of IRAK4)</li> <li>• Composition-of-matter IP extends into 2035</li> </ul>
Population	<p>Lymphoma: Patients w/ over-activated myddosome/TLR pathway; Patients treated w/ ibrutinib (IRAK4i has strong synergy with BTKi)</p> <p>Leukemia: Patients whose tumors have splicing mutations that overexpress IRAK4-L</p>
Product Candidate Description	<ul style="list-style-type: none"> <li>• Potent and orally bioavailable inhibitor of IRAK4 for treatment of MYD88-altered lymphomas and spliceosome-mutated leukemia</li> </ul>

Designed to be best-in-class  
IRAK4 inhibitor<sup>1</sup>

Kinase	Affinity
	K <sub>d</sub> (nM)
IRAK4	23
IRAK1	12,000
IRAK2	>20,000
IRAK3	8,500

Potent suppressor  
of signal transduction<sup>2</sup>



1) Data from Curis preclinical study

2) Booher et al. AACR 2017 (poster #1168)



# CA-4948 Mechanism of Action

## *In Development for Patients with MYD88/TLR-Altered Disease*

*Inhibiting either of these two pathways should provide benefit to patients with B cell lymphoma, CA-4948 targets oncogenic activity in the TLR pathway by blocking IRAK4*

### Oncogenic

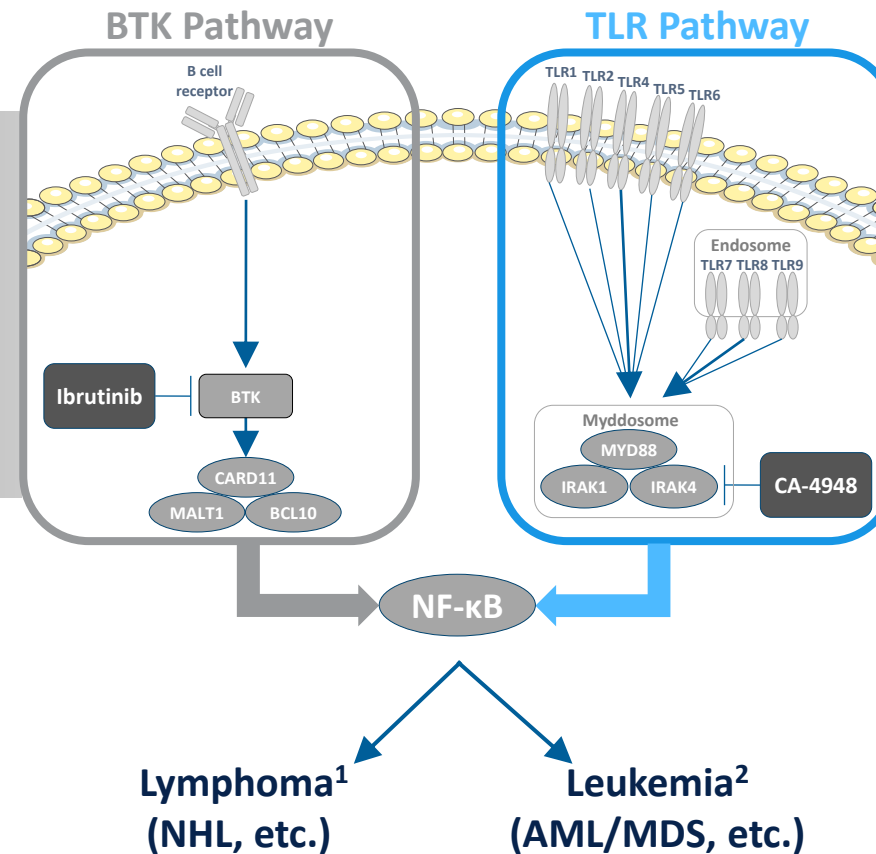
- Dysregulation drives excessive B Cell proliferation

### Pathway validated

- MCL, MZL, CLL, Waldenström's macroglobulinemia<sup>1</sup>

### BTK inhibition effective

- Ibrutinib is FDA approved



### Oncogenic

- Dysregulation drives excessive B cell proliferation<sup>2,3</sup>

### Dependent upon IRAK4

- Signaling requires myddosome, which requires IRAK4

### Strong Synergy

- Inhibition highly synergistic with BTK inhibition

1) IMBRUVICA Package Insert. Rev 08/2018

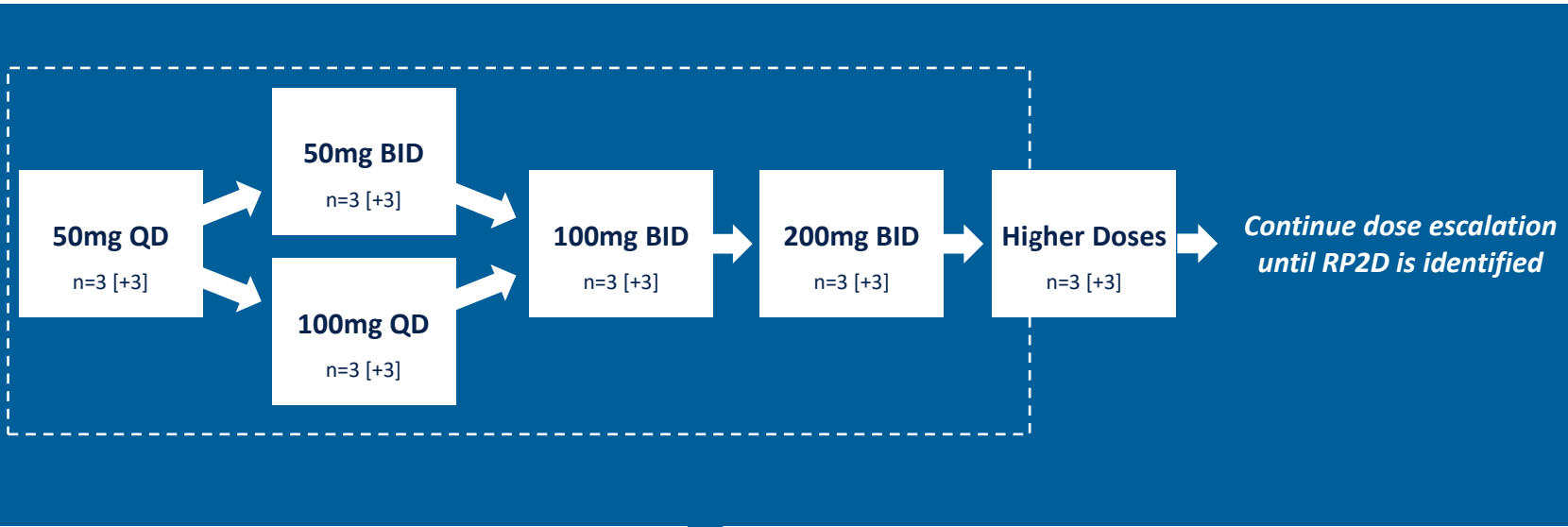
2) Ngo et al. Nature. 2011 Feb 3;470(7332):115-9

3) Küppers et al. J Exp Med. 2015. 212(13): 2184

4) Smith et al. Nat Cell Biol 2019

# CA-4948 in Lymphoma

## *Preliminary Phase 1 Data Demonstrate Tolerability, PK, PD, and Anti-Cancer Activity*



**Preliminary Phase 1 Data Readout**

- Generally well tolerated
- Favorable PK profile, PD, and anti-cancer activity
- 5 of 6 patients dosed at 200mg or higher have seen reduction
- Report updated safety and efficacy data in 2020

### **Patient Population**

- Patients with R/R Lymphoma (incl DLBCL, WM, and patients with MYD88-altered disease)

### **Treatment**

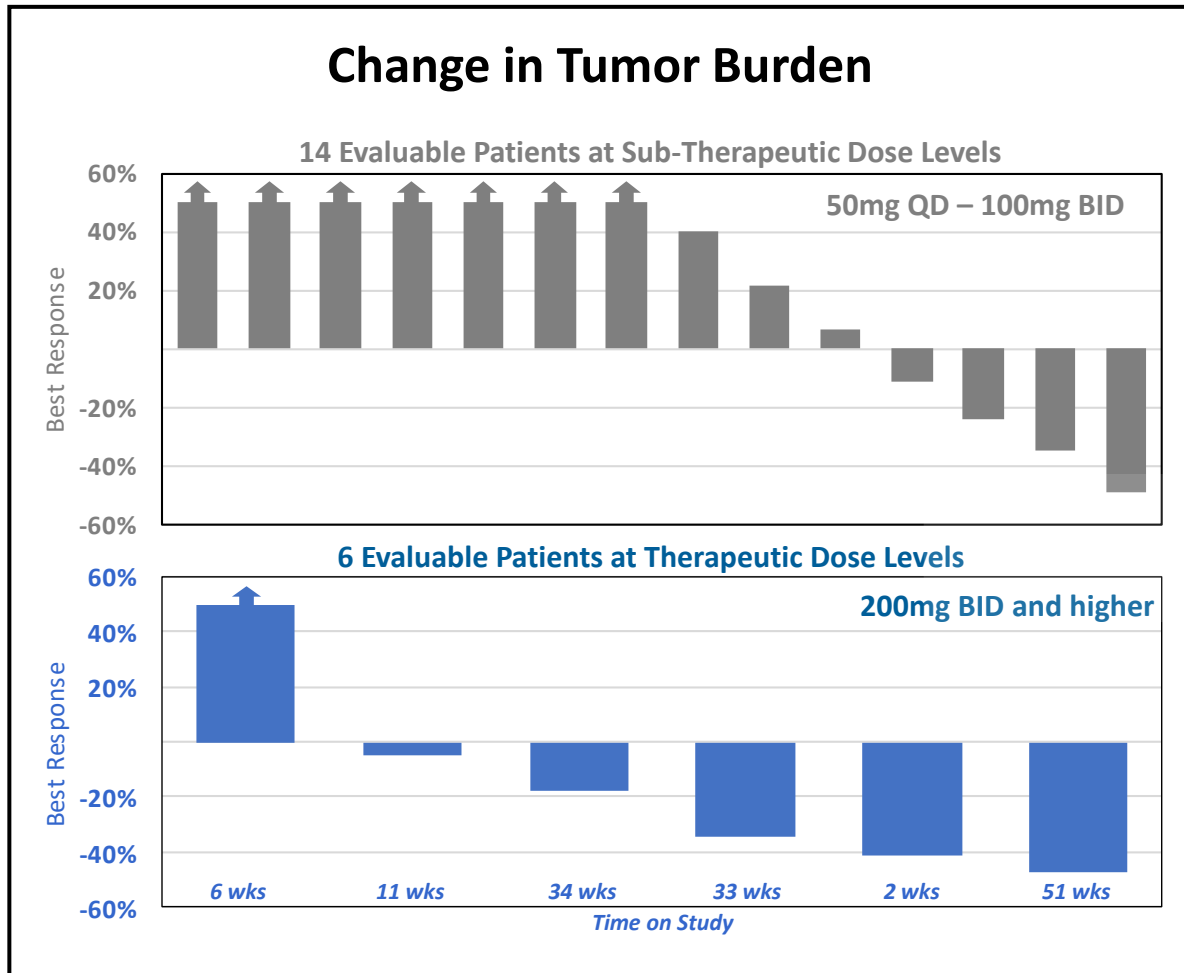
- Oral, once-daily (QD) or twice-daily (BID), dosing in continuous 21-day cycles

### **Objective**

- Safety/tolerability during dose escalation
- Efficacy during expansion

# CA-4948 in Lymphoma

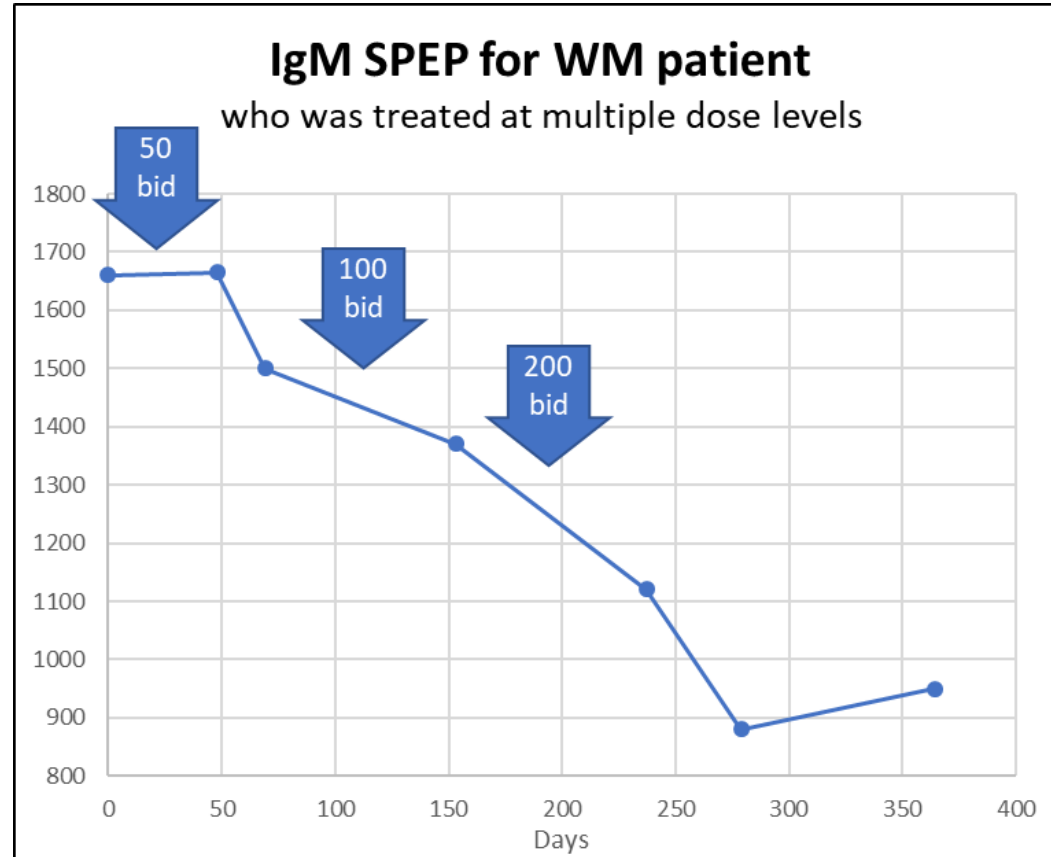
*Single Agent Dose Response Observed as Phase 1 Study Advances to Therapeutic Dose Levels*



**Dose Response Observed**  
*5 of 6 patients experienced tumor reduction (avg reduction of 29%) as dose increased to therapeutic levels (200mg and higher)*

# CA-4948 in R/R Lymphoma

*Single Agent Dose Response Observed as Phase 1 Study Advances to Therapeutic Dose Levels*



**Dose Response Observed**  
*Increased tumor reduction observed  
as patient increased dose*

# CA-4948 in R/R Lymphoma

*Combination with BTKi leads to Potent Anti-Cancer Activity in MYD88-altered DLBCL Models*

## Preclinical Anti-Cancer Activity

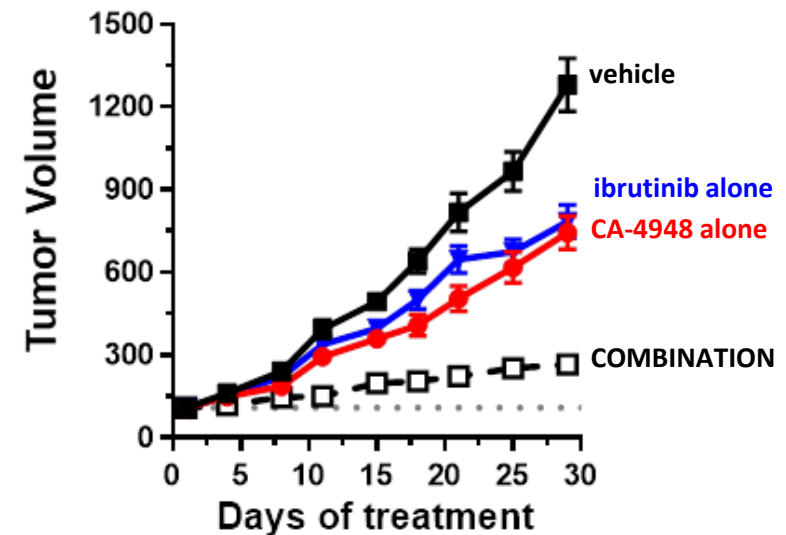
### Potent as Single Agent

- Anti-cancer activity demonstrated in MYD88-altered DLBCL
- Interim readout in dose escalation study shows clear dose response
- We intend to continue dose escalation to further enhance efficacy until MTD / R2PD

### Strong Synergy in Combination

- Anti-cancer activity demonstrated to be highly synergistic with BTK inhibition
- Evaluating potential clinical development strategies for CA-4948 with BTKi to assess anti-cancer activity

Preclinical Anti-Cancer Activity  
in MYD88-altered DLBCL<sup>1</sup>  
(OCI-Ly10)



1) Data from Curis preclinical study; Booher, et al. 4<sup>th</sup> Waldenstrom Roadmap Symposium

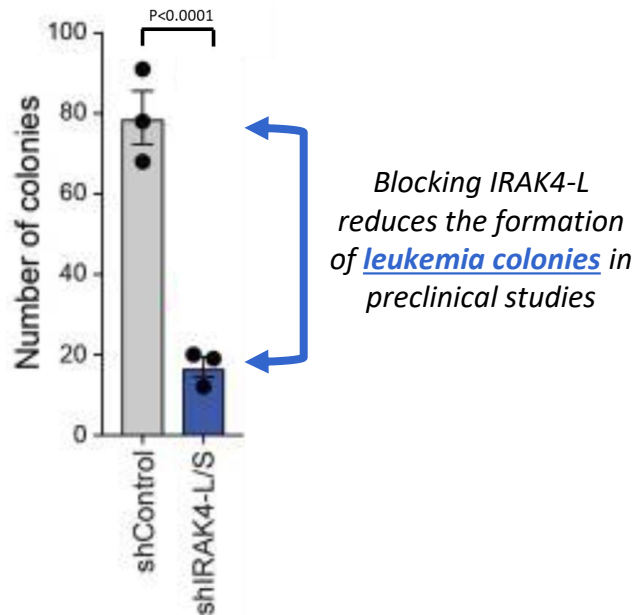
## Additional Regulatory Path Identified in AML/MDS

### Specific Genetic Mutations Lead to Expression of the Long Isoform of IRAK4 (IRAK4-L)

*Oncogenic IRAK4-L, which is driven by spliceosome mutations (incl. SF3B1 and U2AF1), is preferentially expressed >50% of AML/MDS patients*

#### IRAK4-L is Oncogenic

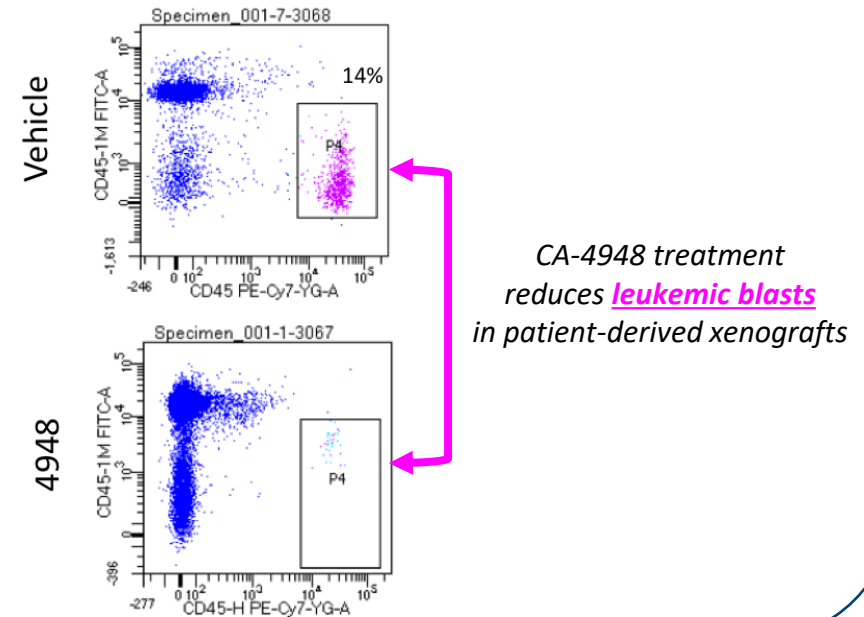
IRAK4-L provides a genetic link to oncogenic immune signaling in AML/MDS



Smith et al. Nat Cell Biol. 2019

#### CA-4948 Directly Targets IRAK4

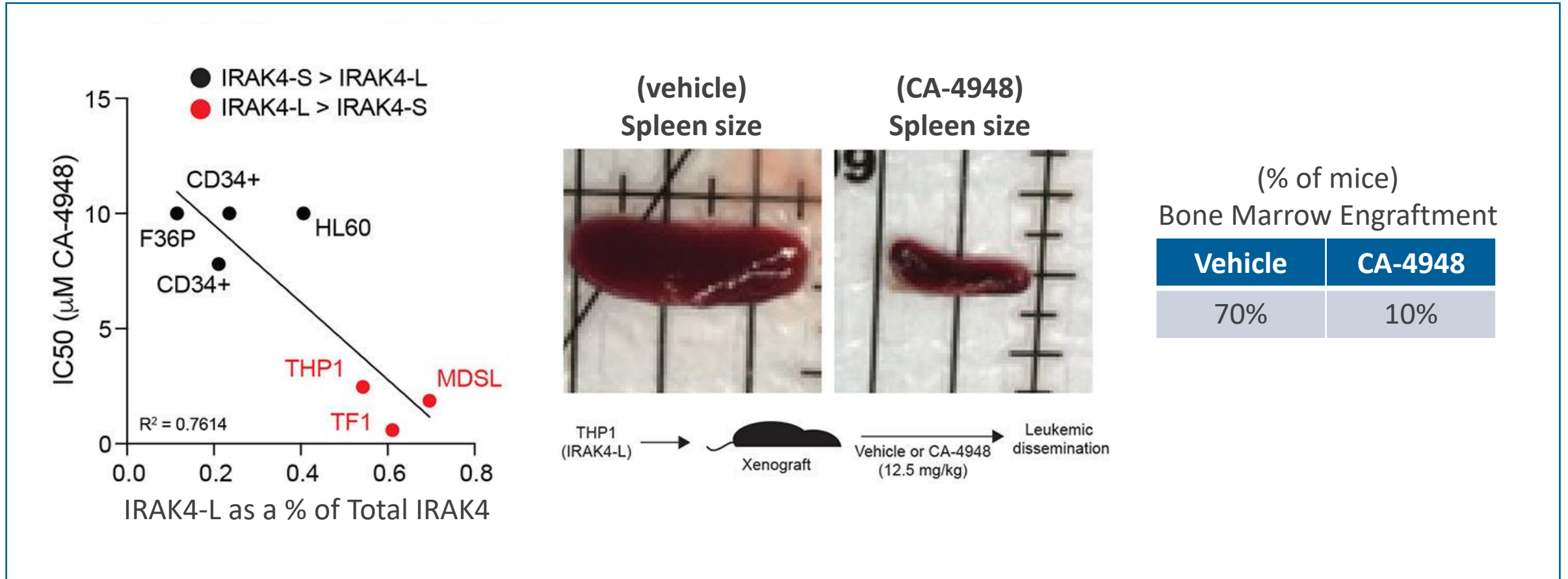
Direct inhibition of the protein associated with disease (IRAK4) may offer a potential path to accelerated approval



Choudhary et al. AACR 2017

# CA-4948 in AML/MDS

*Overexpression of IRAK4-L is a Strong Predictor of Sensitivity to CA-4948*



Smith et al. 2019



*Monoclonal Antibody Immune Checkpoint Inhibitor*

*CI-8993: In development for treatment of VISTA-expressing cancers*



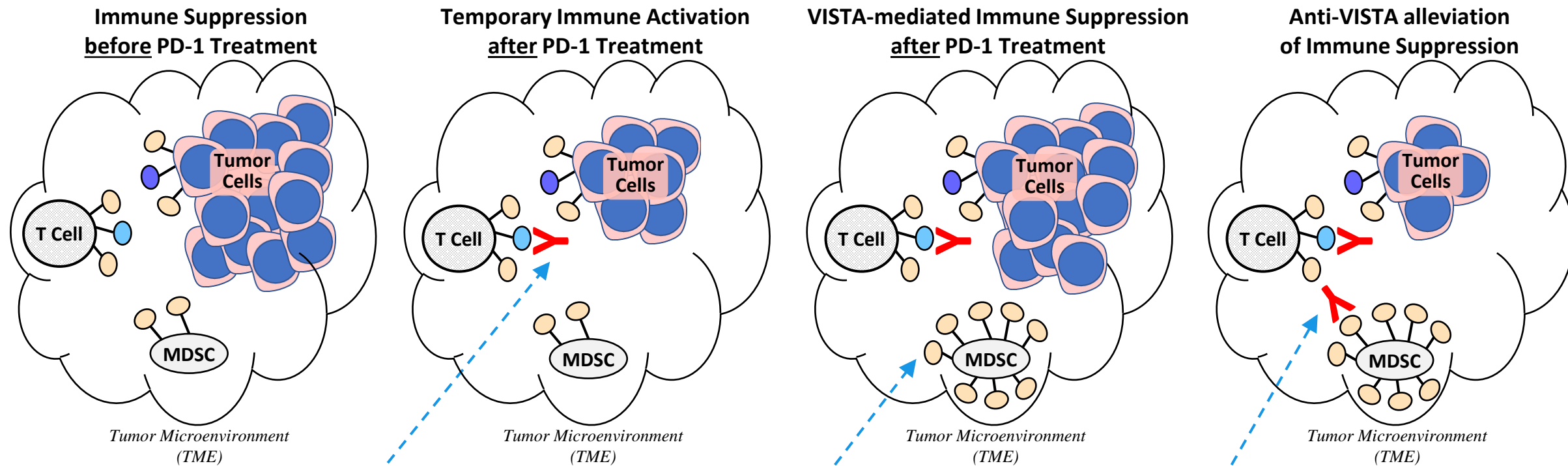
# CI-8993 Overview

## *In Development for Patients with VISTA Expressing Cancers*

<i>Profile</i>	
Value Proposition	<ul style="list-style-type: none"><li>• First-in-class monoclonal antibody antagonist of VISTA</li><li>• No anti-VISTA drugs currently in the clinic</li><li>• Composition-of-matter IP extends into 2034</li></ul>
Population	<ul style="list-style-type: none"><li>• Patients with VISTA-expressing cancers, including Mesothelioma, NSCLC, and TNBC</li><li>• All patients who will receive PD1/PDL1 or CTLA4 antibody therapy</li><li>• Patients who have developed resistance to PD1/PDL1 or CTLA4 antibody therapy</li></ul>
Product Description	<ul style="list-style-type: none"><li>• Monoclonal antibody developed by ImmuNext/Janssen in partnership with Randy Noelle's lab at Dartmouth (the co-discoverer of VISTA)</li></ul>

## Illustrative Example of VISTA's Role in Immune Suppression

**In Pre-Clinical Testing<sup>1</sup>, Blocking VISTA Results in:**  
 Reduced suppressive mediators and enhanced antigen presentation of MDSCs  
 Altered chemotaxis (reduced traffic of MDSCs into the TME)



**Blocking PD-1**  
 activates T cells in some patients

**Blocking PD-1**  
 also causes up to 5x increase in VISTA expression  
 and re-suppression of T cell activity<sup>2</sup>

**Blocking VISTA**  
 re-activates anti-tumor immune function<sup>1</sup>



<sup>1</sup> Data from ImmuNext preclinical studies  
<sup>2</sup> Gao et al. Nature. 2017. 23: 551-555

A circular inset image showing a microscopic view of a cell cluster, likely a tumor, with a blue and white color scheme. The cluster is composed of numerous small, interconnected cells, some appearing more densely packed than others. The background of the inset is light blue.

## Targeted Programs in Heme Malignancies

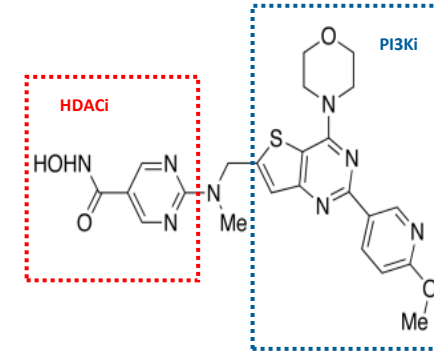
*Fimepinostat: In development for treatment of MYC-altered cancers*

# Fimepinostat Overview

*In Development for Patients with MYC-Altered Cancers*

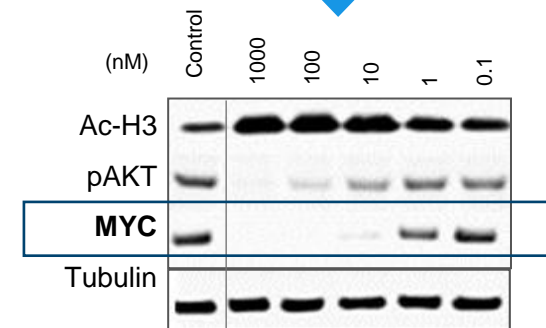
Profile	
Value Proposition	<ul style="list-style-type: none"> <li>• First-in-class drug candidate with demonstrated anti-cancer activity as a single agent in MYC-altered patients in Ph1 and Ph2 trials</li> <li>• Composition-of-matter IP extends into 2032</li> </ul>
Population	<ul style="list-style-type: none"> <li>• Patients with MYC-altered cancer</li> <li>• (&gt;50% of all cancers are effected by MYC)<sup>3</sup></li> <li>• Collaborating with DarwinHealth on characterization of biomarkers and tumor type alignments to identify potential therapeutic opportunities</li> </ul>
Product Candidate Description	<ul style="list-style-type: none"> <li>• Potent and orally bioavailable dual inhibitor of HDAC and PI3K enzymes<sup>1</sup></li> <li>• Favorable safety profile in over 200 patients</li> </ul>

**Mechanism #1**  
The HDAC component  
Suppresses  
MYC transcription<sup>2</sup>



**Mechanism #2**  
The PI3K component  
Enhances  
MYC destruction<sup>2</sup>

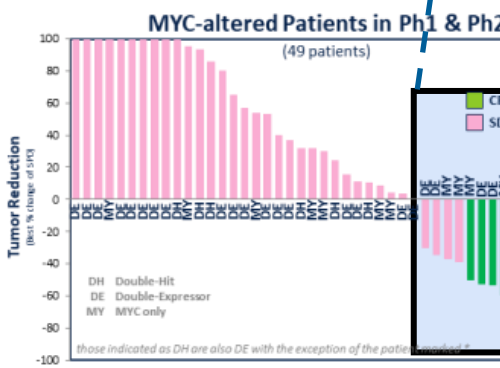
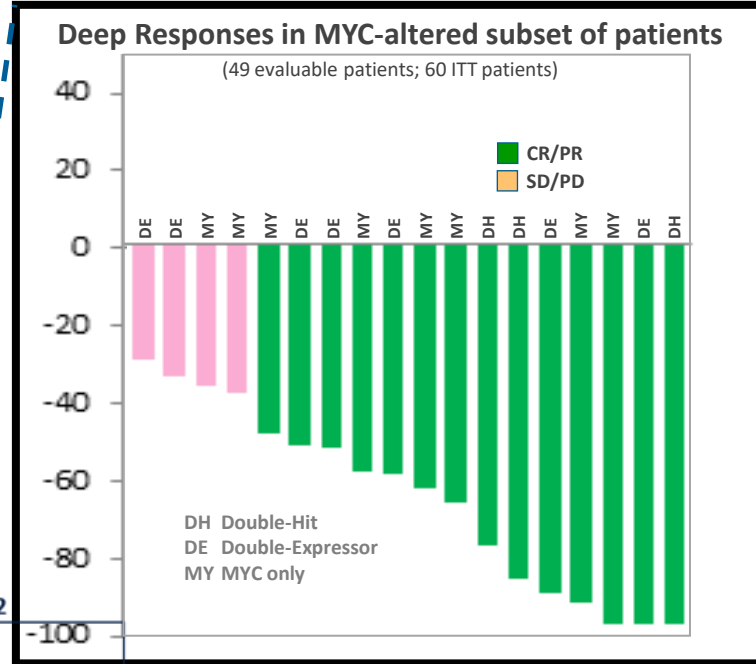
Dual Mechanism leads to  
potent and dose-dependent downregulation of MYC protein



Protein levels in DLBCL cells after treatment with Fimepinostat (Curis Preclinical Study)

1) Qian et.al. Clin Cancer Res. 2012. 18: 4104  
 2) Sun et.al. Mol Cancer Ther. 2017. 6: 285  
 3) Chen et al. Nature. 2018 Feb 23. 3:5

# Fimepinostat Clinical Data Provides Strong Rationale For Development in MYC-Altered Lymphoma



## Monotherapy Anti-Cancer Activity

### Deep responses

- 8 complete responses (CR); 6 partial responses (PR)
- 2 patients able to proceed to transplant

### Durable responses

- Median duration = 13.6 months

### Fast Track designation received

- Following FDA review of clinical data

Evaluating potential therapeutic opportunities for fimepinostat in research collaboration with DarwinHealth

## Summary

<b>Investment Thesis</b>	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need
<b>Robust Pipeline</b>	<p>CA-4948: first-in-class inhibitor of IRAK4 in oncology <i>There are no drugs currently approved that block the entire TLR pathway</i></p> <p>CI-8993: first-in-class antagonist of VISTA <i>There are no drugs currently approved for VISTA inhibition</i></p> <p>Fimepinostat: first-in-class suppressor of MYC <i>There are no drugs currently approved for MYC inhibition</i></p>
<b>Potential Upcoming Catalysts</b>	<ul style="list-style-type: none"><li>• Updated efficacy data for CA-4948 Phase 1 study in NHL</li><li>• Initiation of CA-4948 Phase 1 study in AML/MDS patients with spliceosome mutations</li><li>• Initiation of CI-8993 dose escalation Phase 1 study</li></ul>

## Leadership Team

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End of Corporate Presentation

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