

Corporate Presentation

NASDAQ: CRIS



Cautionary Note Regarding Forward Looking Statements



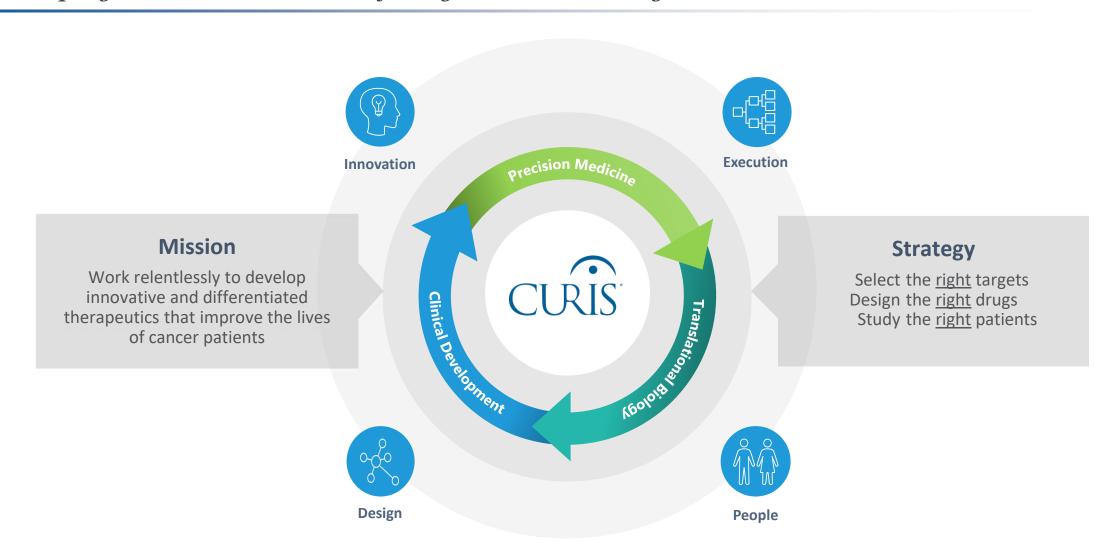
This presentation contains certain forward-looking statements about Curis, Inc. ("we," "us," or the "Company") within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "expect(s)," "believe(s)," "may," "anticipate(s)," "focus(es)," "plans," "mission," "strategy," "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. You are cautioned not to place undue reliance on these forwardlooking 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



Company



Overview

Investment Thesis	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need	
Robust Pipeline	CA-4948: first-in-class inhibitor of IRAK4 in oncology There are no drugs currently approved for IRAK4 inhibition in oncology CI-8993: first-in-class antagonist of VISTA There are no drugs currently approved for VISTA inhibition Fimepinostat: first-in-class suppressor of MYC There are no drugs currently approved for MYC inhibition	
Corporate	 Experienced management team with proven capabilities Curis R&D pioneered the first-in-class inhibitor of the Hedgehog pathway (Erivedge®) partnered with and commercialized by Genentech/Roche for advanced basal cell carcinoma Cash and investments of \$23.6M as of Sep 30, 2020 (in addition to \$30M stock purchase commitment from Aspire Capital) 	

Evolution of Curis



Progressing through Clinical Studies on the Path to Potential Registration

2018 2019 2020 **Define Registration Path Initial Clinical Data** Target Discovery Report preliminary efficacy data for Work with investigators and FDA to Determine R2PD of CA-4948 in NHL and CA-4948 Ph1 study in NHL define path to potential registration determine optimal clinical path Evaluate new published research in Capitalize on newly identified opportunity Identify patient populations and IRAK4-L expression and the potential in AML/MDS and initiate a Ph1 study of initiate clinical studies opportunity for CA-4948 in AML/MDS CA-4948 in patients expressing IRAK4-L Report efficacy data for CA-170 study • Capitalize on unique clinical experience (small molecule targeting VISTA) in with VISTA by in-licensing the leading mesothelioma monoclonal antibody program (CI-8993) and initiating a Ph1 study in solid tumors

Pipeline



All Curis programs are novel, first-in-class



ImmuNext ** Option to license IP from ImmuNext

Genetich *** IP licensed to Genentech (Curis receives royalty income)





Targeted Programs in Heme Malignancies

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

CA-4948 Overview



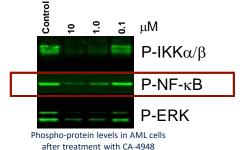
First-in-Class Inhibitor of IRAK4 in Oncology

Profile		
Value Proposition	 First-in-class IRAK4 inhibitor in cancer Specific malignancies in Lymphoma are characterized by overactivity of the myddosome in the TLR pathway (which is dependent upon IRAK4) Specific malignancies in Leukemia are characterized by spliceosome mutations that lead to overexpression of IRAK4-L (the oncogenic isoform of IRAK4) Composition-of-matter IP extends into 2035 	
Population	Lymphoma: All patients treated with ibrutinib (IRAK4i has strong synergy with BTKi) Leukemia: >50% of AML/MDS patients (the population which overexpresses IRAK4-L)	
Product Candidate Description	 Potent and orally bioavailable inhibitor of IRAK4 for treatment of MYD88-altered lymphomas and spliceosome-mutated leukemia 	

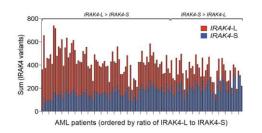
Designed to be best-in-class IRAK4 inhibitor¹

	Aillilly	
Kinase	K _d (nM)	
IRAK4	23	
IRAK1	12,000	
IRAK2	>20,000	
IRAK3	8,500	

In Lymphoma:
Potent suppressor
of NF-κB signal transduction²



In Leukemia: >50% of AML/MDS patients overexpress IRAK4-L³



¹⁾ Data from Curis preclinical study

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

³⁾ Smith et al. Nat Cell Biol 2019



Mechanism of Action

The TLR Pathway is a primary and independent activator of NF-κΒ and is oncogenic in both Lymphoma and Leukemia

Oncogenic

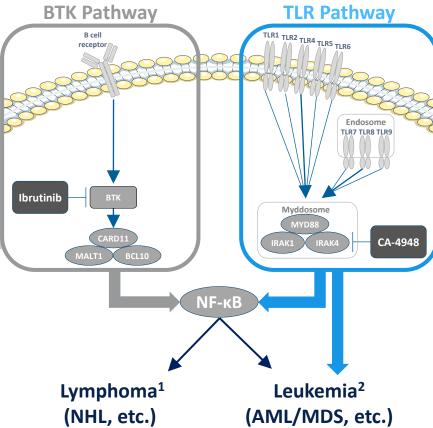
Dysregulation drives excessive B Cell proliferation

Pathway validated

MCL, MZL, CLL, Waldenström's macroglobulinemia¹

BTK inhibition effective

Ibrutinib is FDA approved



Oncogenic

Dysregulation drives excessive B cell proliferation^{2,3}

Dependent upon IRAK4

Signaling requires myddosome, which requires IRAK4

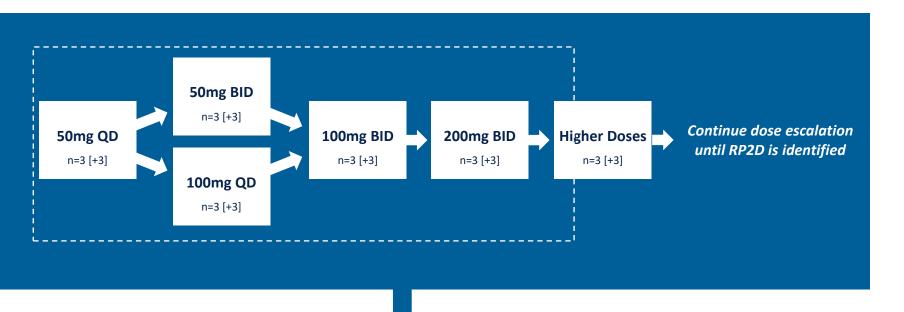
Strong Synergy

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



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



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

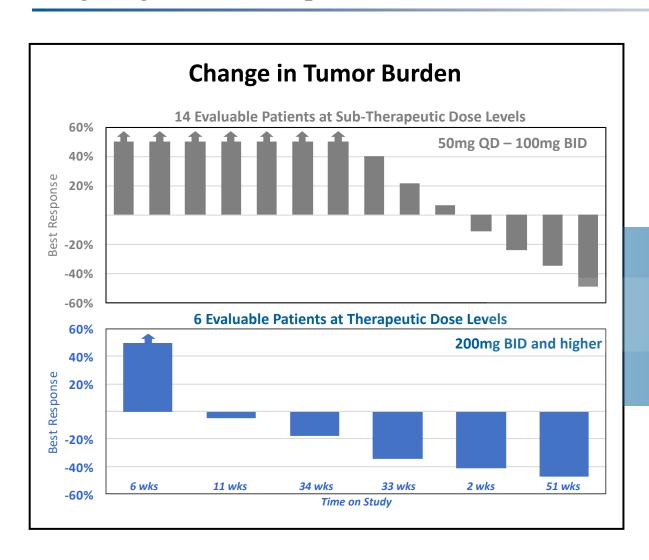
- Safety/tolerability during dose escalation
- Efficacy during expansion

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



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

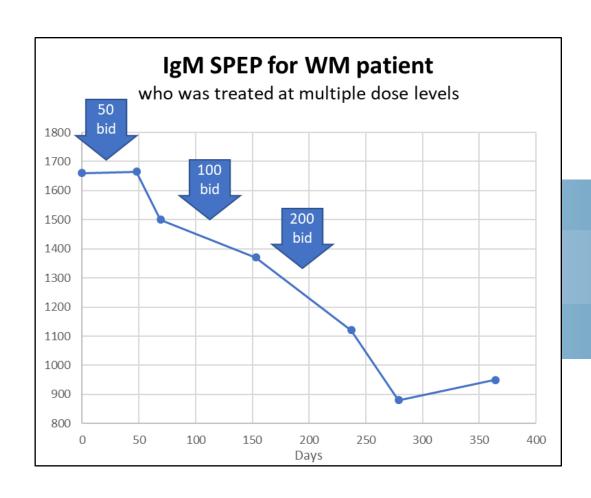


Dose Response Observed

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



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



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

Preclinical Anti-Cancer Activity

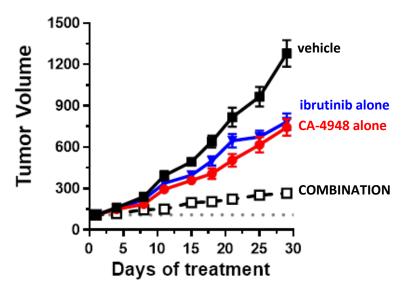
Potent as Single Agent

- 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 DLBCL¹ (OCI-Ly10)



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

CA-4948 in AML/MDS



Additional Regulatory Path Identified in AML/MDS

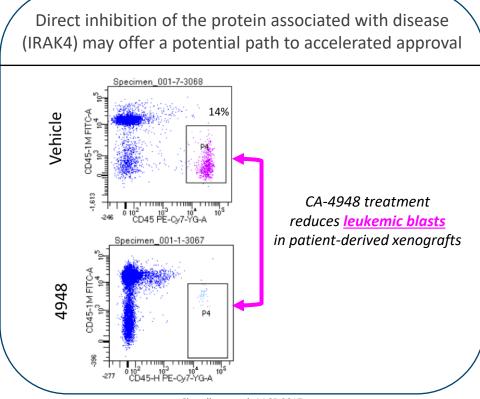
Specific Genetic Mutations Lead to Expression of the Long Isoform of IRAK4 (IRAK4-L)

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 Number of colonies Blocking IRAK4-L reduces the formation of leukemia colonies in preclinical studies shControl

Smith et al. Nat Cell Biol. 2019

CA-4948 Directly Targets IRAK4

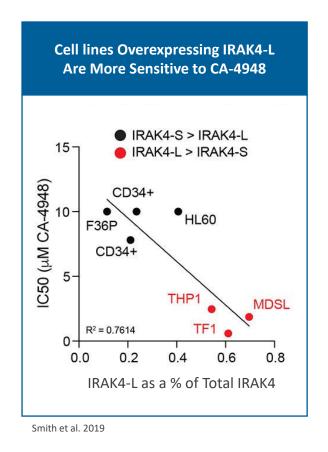


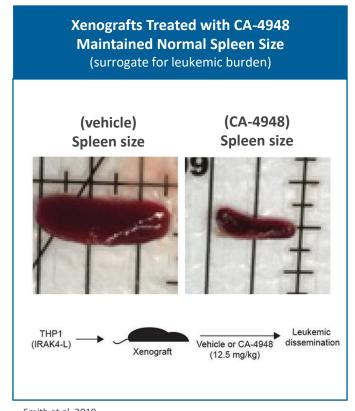
Choudhary et al. AACR 2017

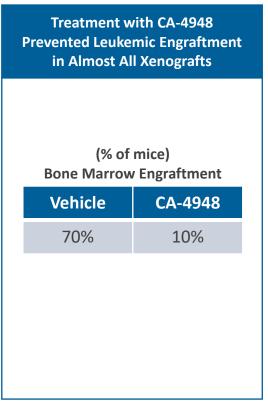
CA-4948 in AML/MDS



Preclinical data supporting opportunity in AML/MDS







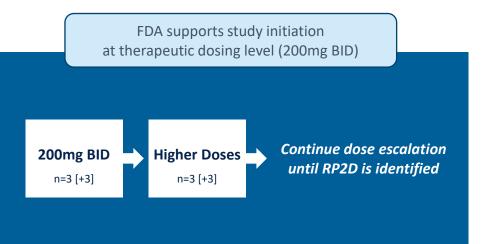
Smith et al. 2019 Smith et al. 2019

otein	IRAK4-L 1	DD	Kinase Domain	460
Prot	IRAK4-S	1	Kinase Domain	336

CA-4948 in AML/MDS



Phase 1 Study Design



Patient Population

• Patients with R/R AML and High Risk MDS

Treatment

• Oral, twice-daily (BID), dosing in continuous 28-day cycles

Objective

- Safety/tolerability during dose escalation
- Efficacy during expansion

Upcoming Milestones

- ✓ Initiated Ph1 study in Q2 2020
- Report initial data by end of 2020





Monoclonal Antibody Immune Checkpoint Inhibitor

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

CI-8993 Overview



In Development for VISTA Expressing and Infiltrated Cancers

Profile	
Value Proposition	 First-in-class monoclonal antibody antagonist of VISTA No anti-VISTA drugs currently in the clinic Composition-of-matter IP extends into 2034
Population	 Patients with VISTA-expressing cancers (incl. Mesothelioma, NSCLC, and TNBC) Patients receiving PD1/PDL1 or CTLA4 antibody therapy (or those who have already received it and have developed resistance to it)
Product Description	 Monoclonal antibody developed by ImmuNext/Janssen in partnership with Randy Noelle's lab at Dartmouth (the co-discoverer of VISTA) IND cleared to proceed by FDA in June 2020

CI-8993 Target Background



VISTA is a Major Checkpoint Regulator

RESEARCH ARTICLE SUMMARY

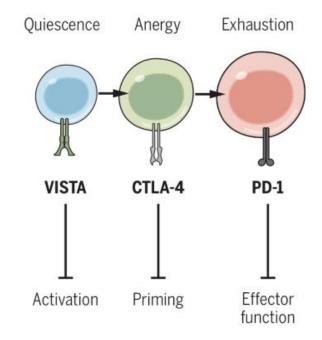
T CELLS

VISTA is a checkpoint regulator for naïve T cell quiescence and peripheral tolerance

Mohamed A. ElTanbouly*, Yanding Zhao*, Elizabeth Nowak, Jiannan Li, Evelien Schaafsma, Isabelle Le Mercier, Sabrina Ceeraz, J. Louise Lines, Changwei Peng, Catherine Carriere, Xin Huang, Maria Day, Brent Koehn, Sam W. Lee, Milagros Silva Morales, Kristin A. Hogquist, Stephen C. Jameson, Daniel Mueller, Jay Rothstein, Bruce R. Blazar, Chao Cheng†, Randolph J. Noelle†

- CTLA-4, PD-1, and VISTA are the three main players in controlling checkpoint blockade
- VISTA controls early T cell activation events
- Blockade of VISTA will allow for an expanded T cell response against tumors

Integration of VISTA with other wellestablished negative checkpoint regulators of T cell activation

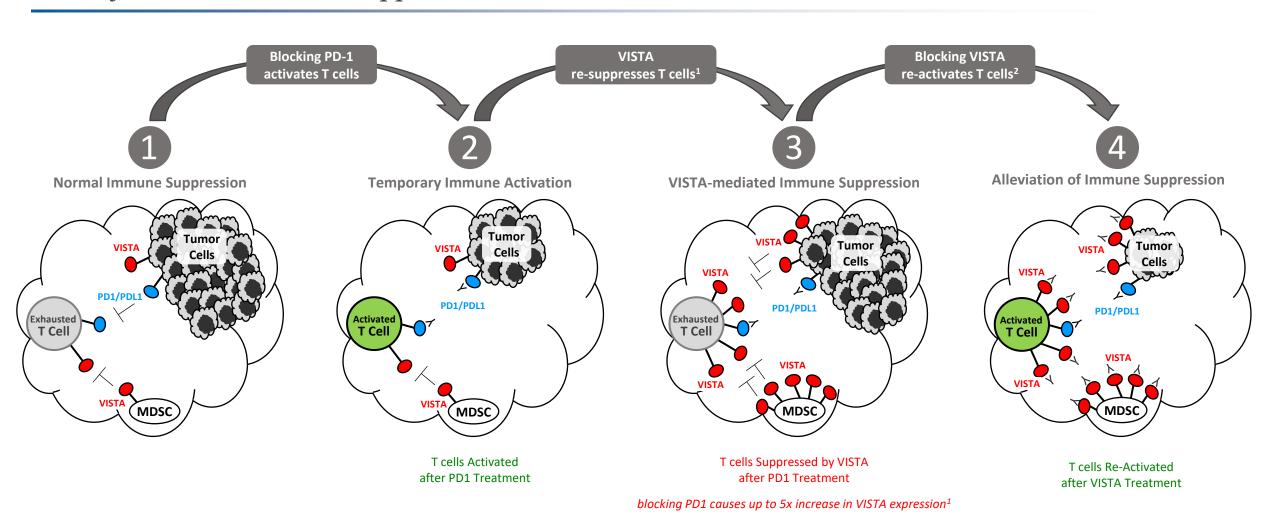


Eltanbouly et al. Science. 2020

CI-8993 Target Background



Role of VISTA in Immune Suppression in the Tumor Microenvironment (TME)



¹ Gao et al. Nature. 2017. 23: 551–555

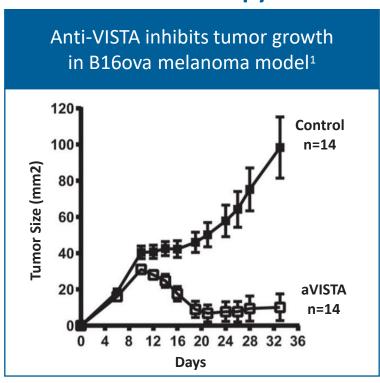
² Data from ImmuNext preclinical studies

CI-8993 Preclinical Data



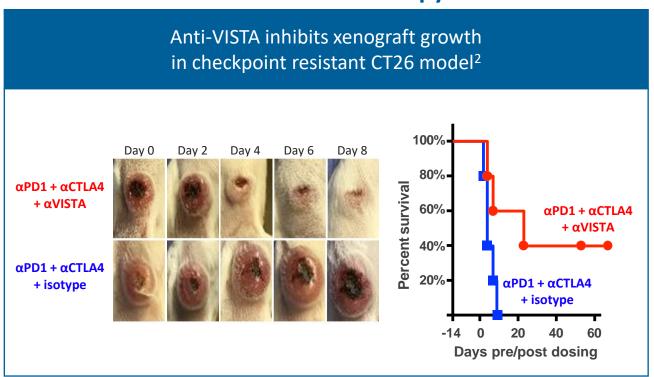
Preclinical efficacy demonstrated in both monotherapy & combination therapy

Monotherapy



¹ LeMercier 2014

Combination Therapy



² 2019 IEBMC Conference

CI-8993 Clinical Plan



Phase 1 dose escalation study to begin in 2H 2020

Curis Design for Ph1 Dose Escalation Study



Patient Population

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

Treatment

- · Bi-weekly dosing
- Mitigate potential toxicities by desensitization, premedication, dosing interval and duration

Objective

- Safety, PK/PD, tolerability during dose escalation
- Efficacy during expansion

Prior clinical development of CI-8993:

CI-8993 was originally developed by Janssen (JNJ-61610588)

- JNJ licensed VISTA IP from ImmuNext in 2012 and initiated a Ph1 study in 2016
- 12 patients were enrolled; initial dose level was 0.005mg/kg
- Low-grade transient Cytokine Release Syndrome (CRS) seen at 0.15mg/kg and above

JNJ halted study after 1 DLT at sub-therapeutic dose level

- The only patient treated at 0.3mg/kg experienced grade 3 CRS-associated encephalopathy after 36hrs on treatment
- Patient was initially treated w/antibiotics; symptoms resolved after treatment with tocilizumab
- JNJ opted to halt the study and return IP to ImmuNext

Target range for expected efficacy (0.5 - 2.0 mg/kg) was never reached

Curis Ph1 Study Incorporates Key Learnings from Janssen Ph1 Study

- CRS is likely an on-target toxicity; indicates drug is hitting the target and inducing inflammatory response
- Oncology community now familiar with managing CRS;
 NCCN guidelines were issued in 2018
- Shared plan for managing CRS and enabling escalation to therapeutic dose levels with FDA
- FDA approved IND in June 2020





Targeted Programs in Heme Malignancies

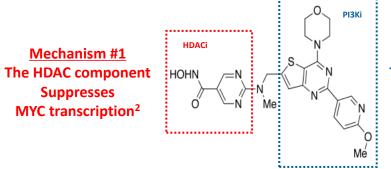
Fimepinostat: In development for treatment of MYC-altered cancers

Fimepinostat Overview



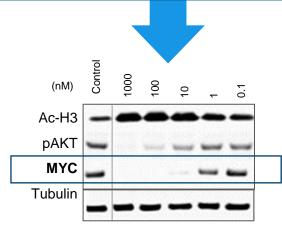
In Development for Patients with MYC-Altered Cancers

Profile		
Value Proposition	 First-in-class drug candidate with demonstrated anti-cancer activity as a single agent in MYC-altered patients in Ph1 and Ph2 trials Composition-of-matter IP extends into 2032 	
Population	 Patients with MYC-altered cancer (>50% of all cancers are effected by MYC)³ Collaborating with DarwinHealth on characterization of biomarkers and tumor type alignments to identify potential therapeutic opportunities 	
Product Candidate Description	 Potent and orally bioavailable dual inhibitor of HDAC and PI3K enzymes¹ Favorable safety profile in over 200 patients 	



Mechanism #2
The PI3K component
Enhances
MYC destruction²

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



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

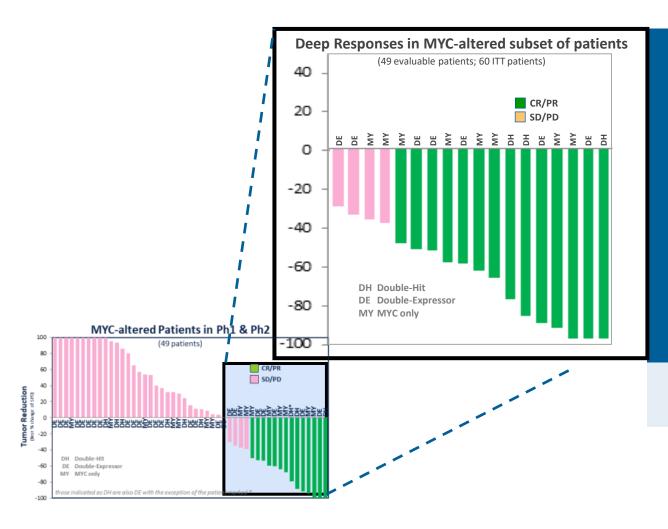
¹⁾ Qian et.al. Clin Cancer Res. 2012. 18: 4104

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

Company



Summary

Investment Thesis	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need	
Robust Pipeline	CA-4948: first-in-class inhibitor of IRAK4 in oncology There are no drugs currently approved for IRAK4 inhibition in oncology CI-8993: first-in-class antagonist of VISTA There are no drugs currently approved for VISTA inhibition Fimepinostat: first-in-class suppressor of MYC There are no drugs currently approved for MYC inhibition	
Potential Catalysts	2H 2020: Updated efficacy data for CA-4948 Ph1 study in NHL 2H 2020: Initial efficacy data of CA-4948 Ph1 study in AML/MDS patients 2H 2020: Initiation of CI-8993 dose escalation Ph1 study	

Curis

CURIS

Leadership Team





















End of Corporate Presentation

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