CURIS

Corporate Presentation

NASDAQ: CRIS

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 forwardlooking 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 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.

Curis Mission & Strategy Developing the New Generation of Targeted Cancer Drugs





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			
	Fimepinostat: first-in-class suppressor of MYC There are no drugs currently approved for MYC inhibition			
Robust Pipeline	CA-4948: first-in-class suppressor of the TLR Pathway There are no drugs currently approved that block the entire TLR pathway			
	CA-170*: first-in-class suppressor of VISTA There are no drugs currently approved for VISTA inhibition			
	Experienced management team with proven capabilities			
Corporate	 Curis R&D profeered the FDA-approved, inst-in-class suppressor of the Hedgenog pathway (Envedges) partnered with and commercialized by Genentech and Roche for advanced basal cell carcinoma in adults Cash, cash equivalents and investments of approximately \$28M as of Sept 30, 2019 			

*Based on initial data no further patients will be enrolled in the study. We are currently evaluating future studies for CA-170.

Evolution of Curis





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Pipeline of Oncology Drug Candidates



PRECLINICAL		CLINICAL				MARKETED	
	Indication	Proof of Principle	Safety	Dose Optimization	Clinical Activity	Pivotal	Commercial
Heme Malign	Heme Malignancies						
Fimepinostat HDAC/PI3K	MYC-altered Cancers	FDA Fa	ist Track Des	signation			
CA-4948 * IRAK4	MYD88/TLR-altered DLBCL, WM						
CA-4948 * IRAK4	IL-1R/TLR-altered AML, MDS						
Immune Checkpoint Inhibitors							
CA-170 * VISTA/PDL1	VISTA-expressing Cancers						
CA-327 * TIM3/PDL1	TIM3-expressing Cancers						
Approved Drug							
Erivedge** Hedgehog	Basal Cell Carcinoma						

AURIGENE * IP licensed from Aurigene

Generation ** IP licensed to Generatech (Curis receives royalty income)



Targeted Programs in Heme Malignancies

Fimepinostat: In development for treatment of MYC-altered cancers

Fimepinostat Overview

CURIS

Mechanism #2

The PI3K component

Enhances

In development for patients with MYC-altered cancers

Profile			
Value Proposition	 First-in-class drug candidate with demonstrated anti- cancer activity as a monotherapy in MYC-altered patients in Phase 1 and Phase 2 trials Composition-of-matter IP extends into 2032 		
Population	 Patients with MYC-altered cancer (>50% of all cancers are effected by MYC)³ 		
Product Candidate Description	 Potent and orally bioavailable dual inhibitor of HDAC and PI3K enzymes¹ Favorable safety profile in over 200 patients 		

MYC transcription²

Mechanism #1

The HDAC component

Suppresses

HDACi

HOH

PI3Ki



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

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

Fimepinostat + venetoclax appear highly synergistic in preclinical models



Fimepinostat + Venetoclax As Combination Therapy Partners

Active single-agents in DLBCL

Fimepinostat = 23% ORR with 13.6 month DOR¹ Venetoclax = 18% ORR²

Highly synergistic combination

• Combination index of < 0.1 at multiple doses³

High unmet need

NCCN: Double-hit lymphoma (DHL) is poor outcome group FDA: DHL is high unmet need

Regulatory path

- Potential for accelerated approval in DHL or other orphan indications
- Potential for full approval with randomized controlled trial

1) 14 PR/CR out of 60 patients in Ph1 & Ph2 (23% ORR)

- 2) Davids et al. JCO. 2017. 35:826
- 3) Booher et al. ASH 2016 (poster #4184)
- 4) Data from Curis preclinical study

Fimepinostat + Venetoclax Appear Highly Synergistic in Preclinical Studies

(DH DOHH-2 DLBCL model)⁴



Phase 1 combination study designed to demonstrate safety of combination

Patient Population

- Patients with R/R DLBCL, including DH/DE Lymphoma
- 8 Study Sites (US only)

Treatment

Fimepinostat: Oral daily (5 days on, 2-days off) Venetoclax: Oral daily (with rapid dose ramp-up)

Objective

- Safety/tolerability during dose escalation
- Efficacy during expansion



Preliminary Phase 1 Tolerability Data Readout

- Generally well tolerated
- No drug-drug interaction that required dose modification of either agent



Targeted Programs in Heme Malignancies

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

CA-4948 Overview



In development for patients with MYD88/TLR-altered disease

	Profile			
Value Proposition	 First-in-class IRAK4 inhibitor in cancer Specific malignancies have overactivity of the myddosome/TLR pathway (dependent upon IRAK4) Composition-of-matter IP extends into 2035 	Designed to be best-in-class IRAK4 inhibitor ¹	Kinase IRAK4 IRAK1 IRAK2 IRAK3	Affinity K _d (nM) 23 12,000 >20,000 8,500
Population	Lymphoma: IRAK4-dependent pathway activated; Ibrutinib-treated patients (strong synergy) Leukemia: Tumors with splicing mutations that overexpress IRAK4	Potent suppressor	Control 10 1.0	5 μM Ρ-ΙΚΚα/β
Product Candidate Description	 Potent and orally bioavailable inhibitor of IRAK4 for treatment of MYD88-altered tumors and augmentation of BTK inhibition 	of signal transduction ²	Phospho-protein leve after treatment w	P-NF-KB P-ERK els in AML cells ith CA-4948

Mechanism of Action



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

- Waldenström's macroglobulinemia¹
- MCL, MZL, CLL

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

Potent preclinical anti-cancer activity in MYD88-altered DLBCL models

Anti-cancer activity in MYD88-altered DLBCL¹



Preclinical Anti-Cancer Activity

Potent as monotherapy

• Anti-cancer activity demonstrated in MYD88altered DLBCL

Strong Synergy

• Anti-cancer activity demonstrated to be highly synergistic with BTK inhibition

CA-4948 Phase 1 Study to date in R/R Lymphoma Preliminary clinical data demonstrate safety, PK, PD, and anti-cancer activity



- Safety/tolerability during dose escalation
- Efficacy during expansion







Dose Response Observed

5 of 6 patients see tumor reduction as dose increased to therapeutic levels (200mg-400mg)

* 3 patients are too early for evaluation; 1 patient considered not evaluable for efficacy due to dose limiting toxicity on day 4

CA-4948 Phase 1 Study in R/R Lymphoma

Dose response observed as study enrolls at therapeutic dose levels



<u>Dose Response Observed</u> increased tumor reduction observed as patient increased dose



Small Molecule Immune Checkpoint Inhibitor

CA-170: In development for treatment of VISTA/PDL1-expressing cancers

CA-170 Overview



Curis is the first to advance an oral small molecule checkpoint inhibitor into the clinic

Profile			
Value Proposition	 First-in-class oral inhibitor of VISTA Only anti-VISTA drug in the clinic Composition-of-matter IP through 2034 		
Population	 Patients with VISTA-expressing cancers, including Mesothelioma, NSCLC, and TNBC Patients whose disease progresses after treatment with immune checkpoint therapy 		
Product Description	 Orally available, small molecule targeting VISTA and PD-L1 immune checkpoints Favorable safety profile demonstrated in 59 patients² 		

CA-170 binds to the receptor-ligand interaction site



Dose dependent activation of VISTA or PDL1inhibited human T cells *ex-vivo*¹



1) Lazorchak et al. AACR 2016

2) Data from Ph1 (NCT02812875) study

IFN- γ production used as a marker for T cell activation

Summary



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Robust Pipeline	CA-4948:	first-in-class suppressor of the TLR Pathway There are no drugs currently approved that block the entire TLR pathway	
	CA-170*:	first-in-class suppressor of VISTA There are no drugs currently approved for VISTA inhibition	
Potential Upcoming Milestones	 Further safety data in fimepinostat-venetoclax combination study Initiation of CA-4948 Phase 1 study in combination with BTK inhibitor Initiation of CA-4948 Phase 1 study in AML/MDS 		

*Based on initial data no further patients will be enrolled in the study. We are currently evaluating future studies for CA-170.

Curis Leadership Team























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