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 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

Mission
Work relentlessly to develop innovative and differentiated therapeutics that improve the lives of cancer patients

Strategy
Select the right targets
Design the right drugs
Study the right patients
### 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*

### 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 cash equivalents of $26.3M as of Nov 30, 2020
Evolution of Curis

Progressing through Clinical Studies on the Path to Potential Registration

2019

Initial Clinical Data

- Report initial Ph1 data for CA-4948 in NHL
- Evaluate new published research in IRAK4-L expression and the potential opportunity for CA-4948 in AML/MDS

2020

Expand Clinical Opportunities

- Report expanded Ph1 data for CA-4948 study in NHL and identify Recommended Phase 2 Dose (RP2D)
- Initiate a Ph1 study of CA-4948 in AML/MDS including patients expressing IRAK4-L and report initial Ph1 data
- Acquire exclusive option to license the leading VISTA monoclonal antibody program (CI-8993) and initiate a Ph1 study

2021

Registrational Strategy

- Initiate Combination Study of CA-4948 and ibrutinib in NHL and evaluate potential paths for registration
- Report expanded Ph1 data for CA-4948 study in AML/MDS and identify Recommended Phase 2 Dose (RP2D)
- Initiate the clinical and non-clinical research collaboration with the NCI under the CRADA for CA-4948
- Report initial clinical data for CI-8993 Ph1 study targeting VISTA in solid tumors
**Pipeline**

*All Curis programs are novel, first-in-class*

<table>
<thead>
<tr>
<th>Indication</th>
<th>Pre-Clinical</th>
<th>Clinical</th>
<th>Marketed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heme Malignancies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CA-4948*</td>
<td>MYD88/TLR-altered Lymphoma (NHL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRAK4</td>
<td>IRAK4L-expressing Leukemia (AML/MDS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fimepinostat HDAC/PI3K</td>
<td>MYC-altered Cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Immune Checkpoint Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-8993**</td>
<td>VISTA-expressing Cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VISTA</td>
<td>PDL1/TIM3-expressing Cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CA-327*</td>
<td>PDL1/TIM3-expressing Cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDL1/TIM3</td>
<td>PDL1/VISTA-expressing Cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CA-170*</td>
<td>PDL1/VISTA-expressing Cancers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDL1/VISTA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Erivedge</strong>*</td>
<td>Basal Cell Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hedgehog</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* IP licensed from Aurigene
** Option to license IP from ImmuNext
*** IP licensed to Genentech (Curis receives royalty income)
IRA4K Targeted Program in NHL

CA-4948: In development for treatment of cancers driven by NF-κB and the TLR/Myddosome
### CA-4948 Overview

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

<table>
<thead>
<tr>
<th><strong>Profile</strong></th>
<th></th>
</tr>
</thead>
</table>
| **Value Proposition** | • First-in-class IRAK4 inhibitor in cancer  
• Specific malignancies in Lymphoma are characterized by overactivity of NF-κB and the TLR/myddosome (which is dependent upon IRAK4)  
• Specific malignancies in Leukemia are characterized by spliceosome mutations that cause an overexpression of IRAK4-L (the oncogenic isoform of IRAK4)  
• Composition-of-matter IP extends into 2035 |
| **Target Patient Population** | Lymphoma: 100% of patients treated w/ibrutinib (IRAK4i combination with BTKi)  
Leukemia: >50% of AML/MDS patients (population which overexpresses IRAK4-L) |
| **Product Candidate Description** | • Potent and orally bioavailable inhibitor of IRAK4 for treatment of NF-κB driven lymphomas and IRAK4-L driven leukemia |

#### Designed to be best-in-class IRAK4 inhibitor

<table>
<thead>
<tr>
<th>Kinase</th>
<th>$K_d$ (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRAK4</td>
<td>23</td>
</tr>
<tr>
<td>IRAK1</td>
<td>12,000</td>
</tr>
<tr>
<td>IRAK2</td>
<td>&gt;20,000</td>
</tr>
<tr>
<td>IRAK3</td>
<td>8,500</td>
</tr>
</tbody>
</table>

#### In Lymphoma: Potent suppressor of NF-κB signal transduction

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

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1) Data from Curis preclinical study  
2) Booher et al. AACR 2017 (poster #1168)  
3) Smith et al. Nat Cell Biol 2019
CA-4948

**Novel Mechanism of Action for Addressing NF-κB**

*Pathway is Oncogenic*

*Pathway activates NF-κB*

*Pathway is dependent upon BTK*

BTK and TLR are parallel pathways and primary independent activators of NF-κB

1) IMBRUVICA Package Insert. Rev 08/2018
4) Smith et al. Nat Cell Biol 2019

**Pathway is Oncogenic**

**Pathway activates NF-κB**

**Pathway is dependent upon IRAK4**

---

In Nov 2020, the NCI selected CA-4948 and entered into a CRADA agreement with Curis to conduct non-clinical and clinical studies of CA-4948 as a potential anti-cancer agent that works via suppression of the TLR Pathway.
CA-4948 in Lymphoma

**Trial Design**

**Baseline Characteristics of Ph1 Patients**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (N=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>26 (84%)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (16%)</td>
</tr>
<tr>
<td>Median Age</td>
<td>69yrs</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma (DLBCL)</td>
<td>14 (45%)</td>
</tr>
<tr>
<td>Transformed follicular lymphoma (t-FL/DLBCL)</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Waldenström’s Macroglobulinemia (WM)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Other Lymphoma*</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Prior Therapies</td>
<td></td>
</tr>
<tr>
<td>Median prior lines of therapy</td>
<td>4 prior lines</td>
</tr>
<tr>
<td>BTK inhibitor, n (%)</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>CAR-T, n (%)</td>
<td>5 (16%)</td>
</tr>
<tr>
<td>ASCT , n (%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Other</td>
<td>13 (42%)</td>
</tr>
<tr>
<td>MYD88 Status</td>
<td></td>
</tr>
<tr>
<td>Positive, n (%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Negative, n (%)</td>
<td>18 (58%)</td>
</tr>
<tr>
<td>Unknown, n (%)</td>
<td>11 (35%)</td>
</tr>
</tbody>
</table>

*includes Lymphoplasmacytic (n=2), Mantle Cell (n=2), Marginal Zone (n=2), High Grade MYC-BCL6 (n=1)

**Study Objectives**

- **Primary:** Safety and tolerability
- **Secondary:** Pharmacokinetic (PK) profile, preliminary anti-cancer activity

**Study Population**

- Relapsed/Refractory disease
- Histopathologically confirmed B-cell NHL, including WM/LPL
- Age ≥ 18 years
- ECOG performance status of ≤ 1

**Dosing**

- Oral, QD or BID continuous dosing
- 21-day cycles

**Dose Levels, 3+3 Design**

- QD: 50, 100mg
- BID: 50, 100, 200, 300 or 400mg
CA-4948 in Lymphoma

Two Potential Biomarkers Identified

Is NF-κB activity driven by the TLR/myddosomal axis?

**MYD88 Mutation**
Genetic alteration of MYD88 at baseline causes constitutive activation of the myddosome and is a driver of NF-κB activity

This potential predictive biomarker may support patient enrichment by identifying patients with excessive myddosome activity (who may therefore be good candidates for IRAK4 inhibition)

Is NF-κB is active?

**NF-κB phospho-p50**
Positive expression of NF-κB phospho-p50 indicates that the NF-κB complex is active

This potential biomarker may support patient selection and provide evidence that CA-4948 is hitting the direct target (IRAK4) and inhibiting the downstream target (the NF-κB complex)

---

1) IMBRUVICA Package Insert. Rev 08/2018
CA-4948 in Lymphoma

Early Biomarker Data from Phase 1 patients

**NF-κB phospho-p50**

NF-κB phospho-p50 protein expression at baseline (indicator of NF-κB activity) correlates with patient outcomes.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Best Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-1002</td>
<td>+86% PD</td>
</tr>
<tr>
<td>018-2004</td>
<td>+156% PD</td>
</tr>
<tr>
<td>001-4002</td>
<td>+7% PD</td>
</tr>
<tr>
<td>002-4004</td>
<td>+75% PD</td>
</tr>
<tr>
<td>012-4004</td>
<td>+125% PD</td>
</tr>
<tr>
<td>012-5006</td>
<td>+190% PD</td>
</tr>
<tr>
<td>013-6001</td>
<td>+98% PD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient</th>
<th>Best Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-1001</td>
<td>-35% SD</td>
</tr>
<tr>
<td>02-1001</td>
<td>-23% SD</td>
</tr>
<tr>
<td>02-3003</td>
<td>+22% SD</td>
</tr>
<tr>
<td>012-5007</td>
<td>-34% SD</td>
</tr>
<tr>
<td>002-6007</td>
<td>+25% SD</td>
</tr>
<tr>
<td>002-6008</td>
<td>+16% SD</td>
</tr>
<tr>
<td>15-1001</td>
<td>+66% PD</td>
</tr>
</tbody>
</table>

Note: data included for all patients for whom pre/post samples were available as of Nov 23, 2020

**p-p50 Biomarker May Support Patient Selection**

- Patients whose tumors do not exhibit NF-κB activity may not be amenable to NF-κB downregulation
  - 7 of 7 patients testing negative at baseline experienced disease progression
  - 2 of these patients were dosed at 200mg BID
- Patients whose tumors do exhibit NF-κB activity may be amenable to NF-κB downregulation
  - 6 of 7 patients testing positive for p-p50 at baseline achieved stable disease or tumor shrinkage
  - 1 of these patients (012-5007) was dosed at 300mg BID

**MYD88 Biomarker May Support Patient Enrichment**

- Both patients whose tumor tested positive for MYD88 mutation saw tumor reduction
- Observed tumor reduction is consistent with our thesis that patients with MYD88-mutated tumors should benefit from IRAK4 inhibition

**Phospho-p50 Expression in Pre/Post Tumor Biopsies Also Provides Evidence that CA-4948 is Hitting the Target (IRAK4) and Downregulating NF-κB Activity**

After treating the patient with CA-4948, their tumor no longer expresses NF-κB phospho-p50

This clinical study is ongoing, more data are needed to confirm these potential biomarkers.
Demonstrated Anti-Cancer Activity
Objective Response observed at 300mg BID (RP2D)

Demonstrated Dose Response
Tumor burden decreased with each increase in dose

Note:
This WM patient is one of the two patients in the Ph1 study who tested positive for MYD88

Data cut-off: 23Nov2020
CA-4948 in Lymphoma

In Updated Ph1 Data, 300mg BID (RP2D) Offered Best Balance of Tolerability and Anti-Cancer Activity

- Clear Single Agent Anti-Cancer Activity at RP2D
  Tumor reduction 6 of 7 pts in a heavily pretreated population (4 prior lines of therapy)

- Durable Tolerability Profile at RP2D
  Patients receiving 300mg BID have remained on therapy for extended periods of time (1 to 2 years)

Data cut-off: 23Nov2020
CA-4948 in Lymphoma

In Updated Ph1 Data, 300mg BID (RP2D) Offered Best Balance of Tolerability and Anti-Cancer Activity

- Clear Single Agent Anti-Cancer Activity at RP2D
  Tumor reduction 6 of 7 pts in a heavily pretreated population
  (4 prior lines of therapy)

- Durable Tolerability Profile at RP2D
  Patients receiving 300mg BID have remained on therapy for extended periods of time (1 to 2 years)

Patients Dosed at Recommended Ph2 Dose
(300mg BID)

[Graph showing percentage reduction in tumor burden over days on study]

-data cut-off: 23 Nov 2020

(dotted line indicates ongoing treatment)
CA-4948 in Lymphoma

2021 Plan: Initiate Clinical Study in Combination Therapy (CA-4948 + ibrutinib)

Mean Tumor Volume (mm$^3$) ± SEM

Days of Treatment

- **Anti-Cancer Activity in Monotherapy and Combination Therapy** in MYD88-altered DLBCL preclinical model (OCI-Ly10)

- **Mechanism of Action Supports Combination**
  - CA-4948 potentially offers a novel mechanism for reducing NF-$\kappa$B activity by targeting the TLR/myddosome (a parallel and complementary pathway to BTK)

- **Clear Single Agent Anti-Cancer Activity**
  - Monotherapy anti-cancer activity demonstrated in both preclinical models and initial Ph1 data

- **Clear Synergy with ibrutinib**
  - CA-4948 and ibrutinib show clear synergy in preclinical models
  - Next Step: initiate clinical study of CA-4948 and ibrutinib

Bocher et al. Waldenstrom Roadmap Symposium 2019
CA-4948 in Lymphoma (planned combination study)

**Trial Design**

**Study Objectives**
- **Primary:** Safety and tolerability of CA-4948 in combination with ibrutinib
- **Secondary:** Pharmacokinetic (PK) profile, preliminary anti-cancer activity

**Study Population**
- Relapsed/Refractory disease
- Histopathologically confirmed B-cell NHL, including WM/LPL
- Age ≥ 18 years
- ECOG performance Status of ≤ 1

**Dosing**
- CA-4948 – Oral twice daily
- ibrutinib – Oral daily at labeled dose
- 21-day cycles
- 3+3 escalation design for CA-4948 (1st cohort will be 200mg BID)

**Additional Patient Cohorts to be Studied in Planned Expansion**
- BTK-naïve, Marginal Zone Lymphoma (MZL)
- BTK-naïve, ABC-DLBCL
- BTK-naïve, Primary CNS Lymphoma (PCNSL)
- Patients with adaptive resistance to ibrutinib
IRAK4 Targeted Program in AML/MDS

CA-4948: In development for treatment of cancers driven by IRAK4-L
CA-4948 in AML/MDS

Landscape of Disease Targets in AML/MDS

- Non-targeted therapies administered in monotherapy have historically provided limited clinical benefit, especially in relapsed/refractory patients

- Targeted therapies (e.g., FLT3, IDH) have been limited by the size of their respective target patient populations

- IRAK4-L is a novel target in AML/MDS and has been shown to be preferentially expressed in >50% of the AML/MDS patient population

<table>
<thead>
<tr>
<th>Disease Driver</th>
<th>% of Patient Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRAK4-L</td>
<td>&gt; 50%&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>FLT3</td>
<td>25-30%&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>TET2</td>
<td>10-20%&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>IDH2</td>
<td>9-13%&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>IDH1</td>
<td>6-10%&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>CEBPA</td>
<td>~10%&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

1) Smith et al. Nat Cell Biol 2019
3) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6142505/
CA-4948 in AML/MDS

IRAK4-L is a Novel Target in AML/MDS

Specific Genetic Mutations Drive the 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

Blocking IRAK4-L appears to reduce the formation of leukemia colonies in preclinical studies

CA-4948 Directly Targets IRAK4

Direct inhibition of the protein associated with disease (IRAK4) may offer accelerated regulatory path

CA-4948 treatment appears to reduce leukemic blasts in patient-derived xenografts

Smith et al. Nat Cell Biol. 2019

Choudhary et al. AACR 2017
CA-4948 in AML/MDS

Trial Design

Study Objectives

Primary: Maximum tolerated dose and recommended Phase 2 dose
Secondary: Pharmacokinetic (PK) profile, preliminary anti-cancer activity

Study Population

- Relapsed/Refractory disease
- Histopathologically confirmed AML or High-Risk MDS
- Age ≥ 18 years
- ECOG performance Status of ≤ 2

Dosing

- Oral
- 28-day cycles
- 3+3 escalation design (200mg BID, 300mg BID, and 400mg BID)

Baseline Characteristics of Ph1 Patients

<table>
<thead>
<tr>
<th></th>
<th>Overall (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>5 (83%)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Median Age (range)</td>
<td>72 (32-84)</td>
</tr>
<tr>
<td>Median Prior Therapies (range)</td>
<td>3 (1-4)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Acute Myelogenous Leukemia (AML)</td>
<td>4 (67%)</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome (MDS)</td>
<td>2 (33%)</td>
</tr>
</tbody>
</table>

Data cut-off: 23 Nov 2020
CA-4948 in AML/MDS

Monotherapy Anti-Cancer Activity Observed in Early Ph1 Data

- **1st** patient dosed in Q3 2020
- Consistent reduction of Marrow Blasts across population (6 patients)
- 2 patients have achieved Marrow CR

<table>
<thead>
<tr>
<th></th>
<th>Blasts Baseline</th>
<th>Blasts Best Resp</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML 005-2003</td>
<td>32%</td>
<td>26%</td>
<td>-19%</td>
</tr>
<tr>
<td>AML 005-2002</td>
<td>39%</td>
<td>25%</td>
<td>-36%</td>
</tr>
<tr>
<td>AML 003-1002</td>
<td>24%</td>
<td>9%</td>
<td>-63%</td>
</tr>
<tr>
<td>hrMDS 003-1003</td>
<td>4%</td>
<td>2%</td>
<td>-50%</td>
</tr>
<tr>
<td>hrMDS 003-1001</td>
<td>11%</td>
<td>2%</td>
<td>-82%</td>
</tr>
<tr>
<td>AML 005-2001</td>
<td>23%</td>
<td>1%</td>
<td>-96%</td>
</tr>
</tbody>
</table>

Marrow CR

Note: To achieve Marrow CR, a patient’s blast count must be elevated at baseline (>5%) and, after treatment, decrease by ≥ 50% from baseline into the normal range (≤5%)

Data cut-off: 23Nov2020
VISTA Targeted Program in Solid Tumors

CI-8993: In development for treatment of cancers driven by VISTA-mediated Immune Suppression
**CI-8993 Overview**

**In Development for VISTA Expressing and Infiltrated Cancers**

<table>
<thead>
<tr>
<th><strong>Profile</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Value Proposition</strong></td>
</tr>
<tr>
<td>* First-in-class monoclonal antibody antagonist of VISTA</td>
</tr>
<tr>
<td>* Composition-of-matter IP extends into 2034</td>
</tr>
<tr>
<td><strong>Target Patient Population</strong></td>
</tr>
<tr>
<td>* Patients with VISTA-expressing cancers (incl. Mesothelioma, NSCLC, and TNBC)</td>
</tr>
<tr>
<td>* Patients receiving PD1/PDL1 or CTLA4 antibody therapy (or those who have already received it and have developed resistance to it)</td>
</tr>
<tr>
<td><strong>Product Description</strong></td>
</tr>
<tr>
<td>* Monoclonal antibody developed by ImmuNext/Janssen in partnership with Randy Noelle’s lab at Dartmouth (the co-discoverer of VISTA)</td>
</tr>
</tbody>
</table>
CI-8993 Target Background

VISTA is an Important Checkpoint Regulator

RESEARCH ARTICLE SUMMARY

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

Mohamed A. Eltanbouly, Yanding Zhao, Elizabeth Nowak, Jiannan Li, Evelin Schaafuma, Isabelle Le Mercier, Sabrina Coeraz, 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

Eltanbouly et al. Science. 2020

Integration of VISTA with other well-established negative checkpoint regulators of T cell activation

Quiescence • Anergy • Exhaustion

CTLA-4 • PD-1

Activation • Priming • Effector function

Eltanbouly et al. Science. 2020
Role of VISTA in Immune Suppression in the Tumor Microenvironment (TME)

1. Normal Immune Suppression

Blocking PD-1 activates T cells

2. Temporary Immune Activation

VISTA re-suppresses T cells

3. VISTA-mediated Immune Suppression

Blocking VISTA re-activates T cells

4. Alleviation of Immune Suppression

T cells Activated after PD1 Treatment

T cells Suppressed by VISTA after PD1 Treatment

T cells Re-Activated after VISTA Treatment

blocking PD1 causes up to 5x increase in VISTA expression


2 Data from ImmuNext preclinical studies
CI-8993 Preclinical Data

*Preclinical anti-cancer activity demonstrated in both monotherapy & combination therapy*

**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 Clinical Plan

Phase 1 dose escalation study design

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
• Anti-cancer activity 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 anti-cancer activity (0.5 – 2.0mg/kg) was never reached

Curis Design for Ph1 Study Design 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 is now familiar with managing CRS; NCCN guidelines were issued in 2018
• FDA cleared the study IND which outlined our plan for managing CRS and enabling escalation to therapeutic dose levels
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**

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

1) Qian et.al. Clin Cancer Res. 2012. 18: 4104
2) Sun et.al. Mol Cancer Ther. 2017. 6: 285

**Mechanism #1**
The HDAC component Suppresses MYC transcription²

**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)
Fimepinostat Overview

Clinical Anti-Cancer Activity in Patients with MYC-Altered Cancers in Ph1 and Ph2 Studies

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 Ph1 and Ph2 clinical data

Currently evaluating assays, biomarkers, and potential companion diagnostics in research collaboration with DarwinHealth to help identify specific patient populations for potential future clinical development.
**Summary**

<table>
<thead>
<tr>
<th>Investment Thesis</th>
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<tr>
<td>Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need</td>
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<table>
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<tr>
<th>Robust Pipeline</th>
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<tbody>
<tr>
<td>CA-4948: first-in-class inhibitor of IRAK4 in oncology</td>
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<tr>
<td>There are no drugs currently approved for IRAK4 inhibition in oncology</td>
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<tr>
<td>CI-8993: first-in-class antagonist of VISTA</td>
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<tr>
<td>There are no drugs currently approved for VISTA inhibition</td>
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<th>Potential Catalysts</th>
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<tr>
<td>1H 2021: Initiate combination study of CA-4948 and ibrutinib in NHL patients</td>
</tr>
<tr>
<td>2H 2021: Report expanded data in CA-4948 Ph1 study in AML/MDS patients</td>
</tr>
<tr>
<td>2H 2021: Report initial data in CI-8993 dose escalation Ph1 study</td>
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</table>
Curis

Leadership Team

Rachel Blasbalg  
Head, Human Resources

James Dentzer  
President & CEO

Christine Guertin  
Head, Regulatory

Robert Martell  
Head, R&D

Mark Noel  
Head, Intellectual Property

Reinhard von Roemeling  
Head, Clinical Development

Raul Soikes  
Head, Portfolio Management

Nancy Soohoo  
General Counsel

William Steinkrauss  
Chief Financial Officer