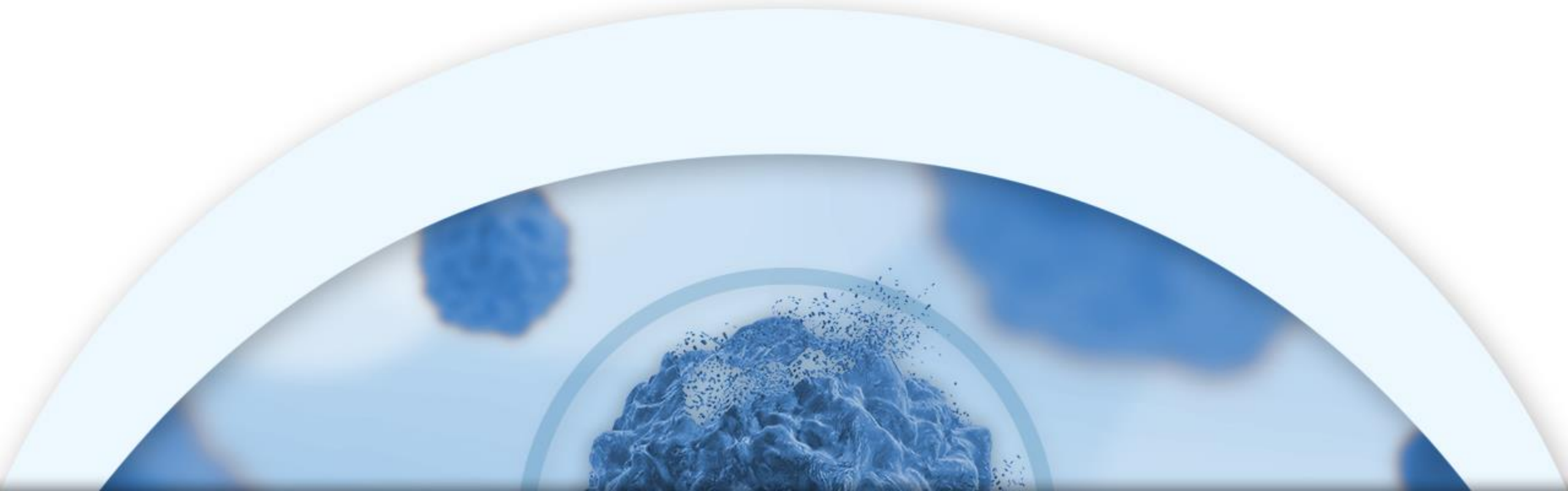




Corporate Presentation

NASDAQ: CRIS

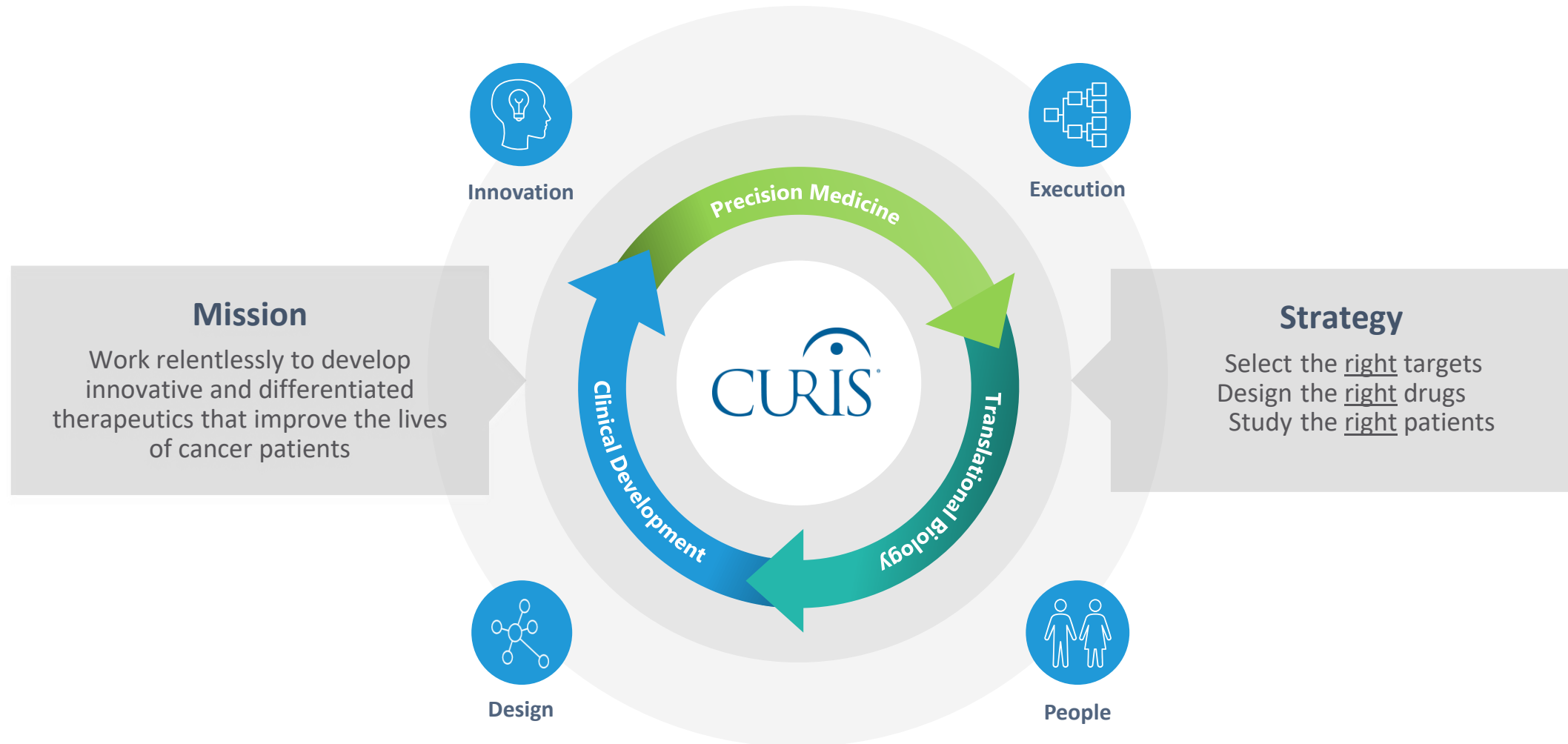


Cautionary Note Regarding Forward Looking Statements

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 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



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	<p>CA-4948: first-in-class inhibitor of IRAK4 in oncology <i>There are no drugs currently approved for IRAK4 inhibition in oncology</i></p> <p>CI-8993: first-in-class antagonist of VISTA <i>There are no drugs currently approved for VISTA inhibition</i></p>
Corporate	<ul style="list-style-type: none">• 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• Pro forma cash and investments of approximately \$185M* as of Nov 30, 2020

*Pro Forma Cash = \$26.3M as reported + \$159.1M in proceeds from December Public Offering

Progressing through Clinical Studies on the Path to Potential Registration



Pipeline

All Curis programs are novel, first-in-class

		PRE-CLINICAL	CLINICAL				MARKETED
		Proof of Principle	Safety	Dose Optimization	Clinical Activity	Pivotal	Commercial
<i>Heme Malignancies</i>							
CA-4948* IRAK4	MYD88/TLR-altered Lymphoma (NHL)						
CA-4948* IRAK4	IRAK4L-expressing Leukemia (AML/MDS)						
Fimepinostat HDAC/PI3K	MYC-altered Cancers						
<i>Immune Checkpoint Inhibitors</i>							
CI-8993** VISTA	VISTA-expressing Cancers						
CA-327* PDL1/TIM3	PDL1/TIM3-expressing Cancers						
CA-170* PDL1/VISTA	PDL1/VISTA-expressing Cancers						
<i>Basal Cell Carcinoma</i>							
Erivedge*** Hedgehog	Basal Cell Carcinoma						

A large, circular, light-blue microscopic image of a cell cluster is centered behind the text. The cluster has a textured, irregular surface with many small, dark blue dots scattered across it, possibly representing individual cells or molecules. The background of the slide is white with several out-of-focus, light-blue circular shapes scattered around, giving a sense of depth and a scientific or biological theme.

IRAK4 Targeted Program in AML/MDS

CA-4948: In development for treatment of cancers driven by IRAK4-L

CA-4948 Overview

First-in-Class Inhibitor of IRAK4 in Oncology



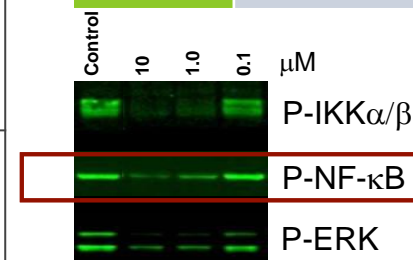
In Nov 2020, the NCI selected CA-4948, Curis's first-in-class IRAK4 inhibitor, and entered into an agreement ("CRADA") with Curis to conduct both clinical and non-clinical studies of CA-4948 in oncology

Profile

Value Proposition	<ul style="list-style-type: none"> 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	<p>Lymphoma: 100% of patients treated w/ibrutinib (IRAK4i combination with BTKi)</p> <p>Leukemia: >50% of AML/MDS patients (population which overexpresses IRAK4-L)</p>
Product Candidate Description	<ul style="list-style-type: none"> Potent and orally bioavailable inhibitor of IRAK4 for treatment of NF-κB driven lymphomas and IRAK4-L driven leukemia

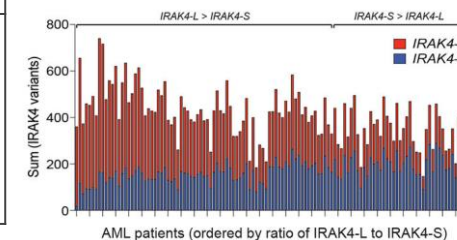
Kinase	Affinity K _d (nM)
IRAK4	23
IRAK1	12,000
IRAK2	>20,000
IRAK3	8,500

Highly specific and targeted IRAK4 inhibitor¹



Phospho-protein levels in AML cells after treatment with CA-4948

In Lymphoma:
Potent suppressor of NF- κ B signal transduction²



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

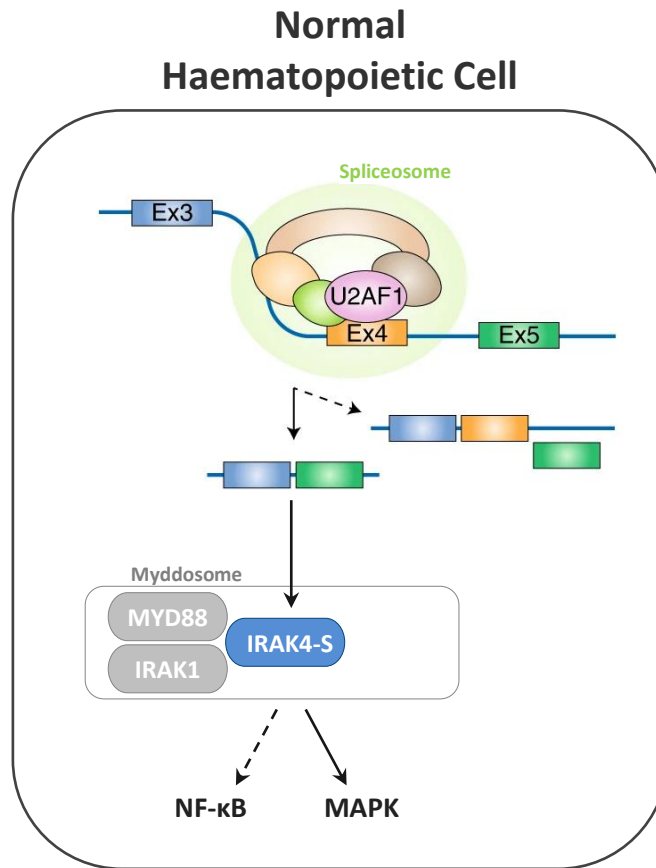
1) Data from Curis preclinical study

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

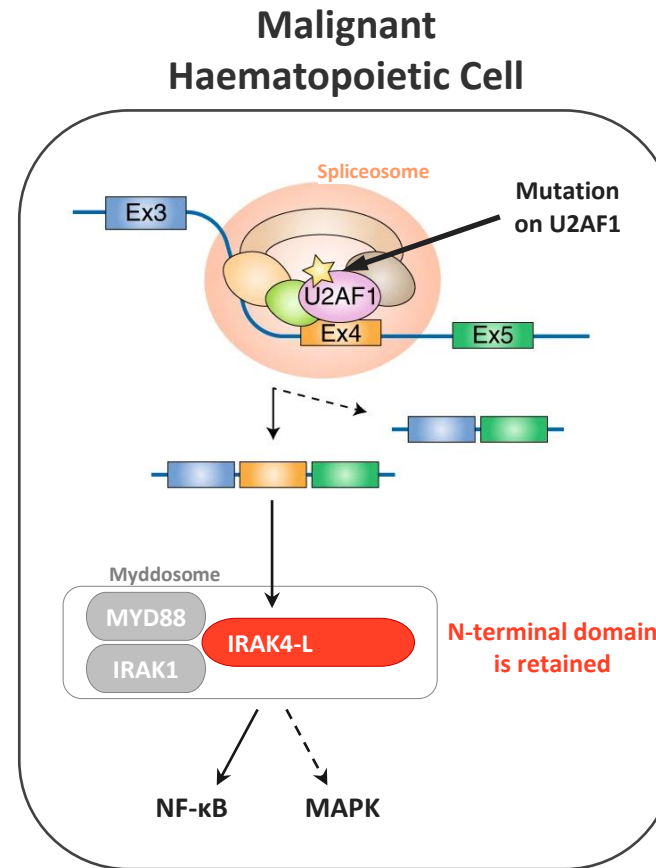
3) Smith et al. Nat Cell Biol 2019

CA-4948 in AML/MDS

IRAK4-L is a Novel Target in AML/MDS



Guillamot et al. Nat Cell Biol. 2019

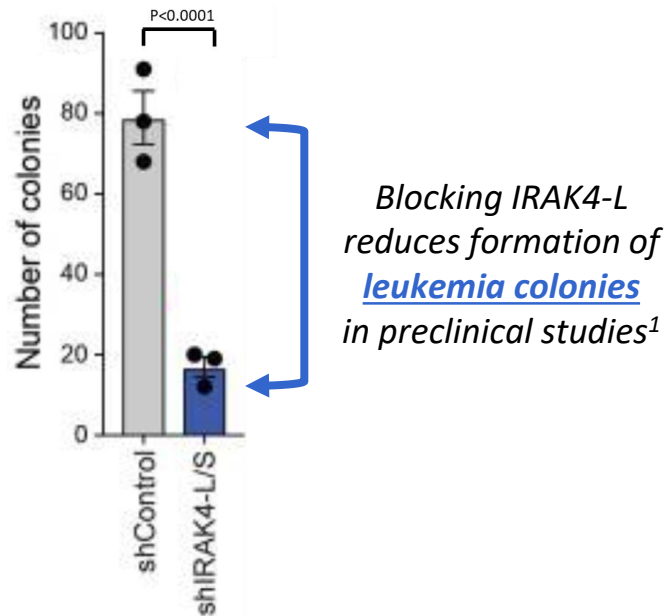


Guillamot et al. Nat Cell Biol. 2019

*specific genetic mutations
(incl. U2AF1 and SF3B1)
drive the expression of IRAK-L,
the long isoform of IRAK4*

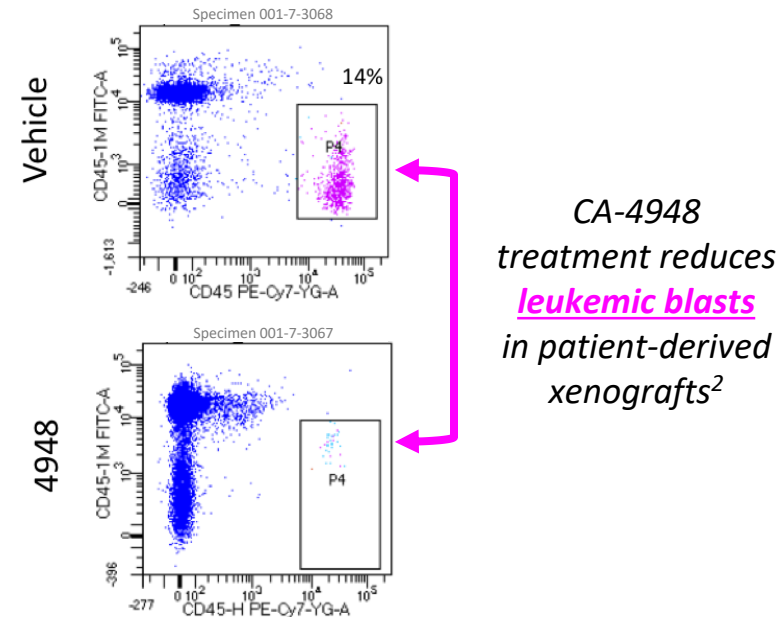
Targeting IRAK-L Demonstrates Anti-Cancer Activity in Preclinical Models

IRAK4-L is Oncogenic



IRAK4-L knockdown models demonstrate genetic link to oncogenic immune signaling in AML/MDS¹

CA-4948 Targets IRAK4-L



IRAK4-L inhibition with CA-4948 demonstrates anti-cancer activity consistent with knockdown models²

1) Smith et al. Nat Cell Biol 2019

2) Choudhary et al. AACR 2017

Landscape of Disease Targets in AML/MDS

<u>Disease Driver</u>	<u>% of Patient Population</u>
IRAK4-L	> 50% ¹
FLT3	25-30% ²
TET2	10-20% ³
IDH2	9-13% ⁴
IDH1	6-10% ⁴
CEBPA	~10% ³

- 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

1) Smith et al. Nat Cell Biol 2019

2) Saygin, et al. J Hematol Oncol. 2017 Apr 18

3) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6142505/>

4) DiNardo et al. N Engl J Med 2018

Trial Design

Data cut-off: 23Nov2020

Baseline Characteristics of Ph1 Patients	Overall (N=6)
Male (%)	5 (83%)
Female (%)	1 (17%)
Median Age (range)	72 (32-84)
Median Prior Therapies (range)	3 (1-4)
Histology	
Acute Myelogenous Leukemia (AML)	4 (67%)
Myelodysplastic Syndrome (MDS)	2 (33%)

Study Objectives

Primary: Maximum tolerated dose and recommended Phase 2 dose

Secondary: Pharmacokinetic (PK) profile, preliminary anti-cancer activity

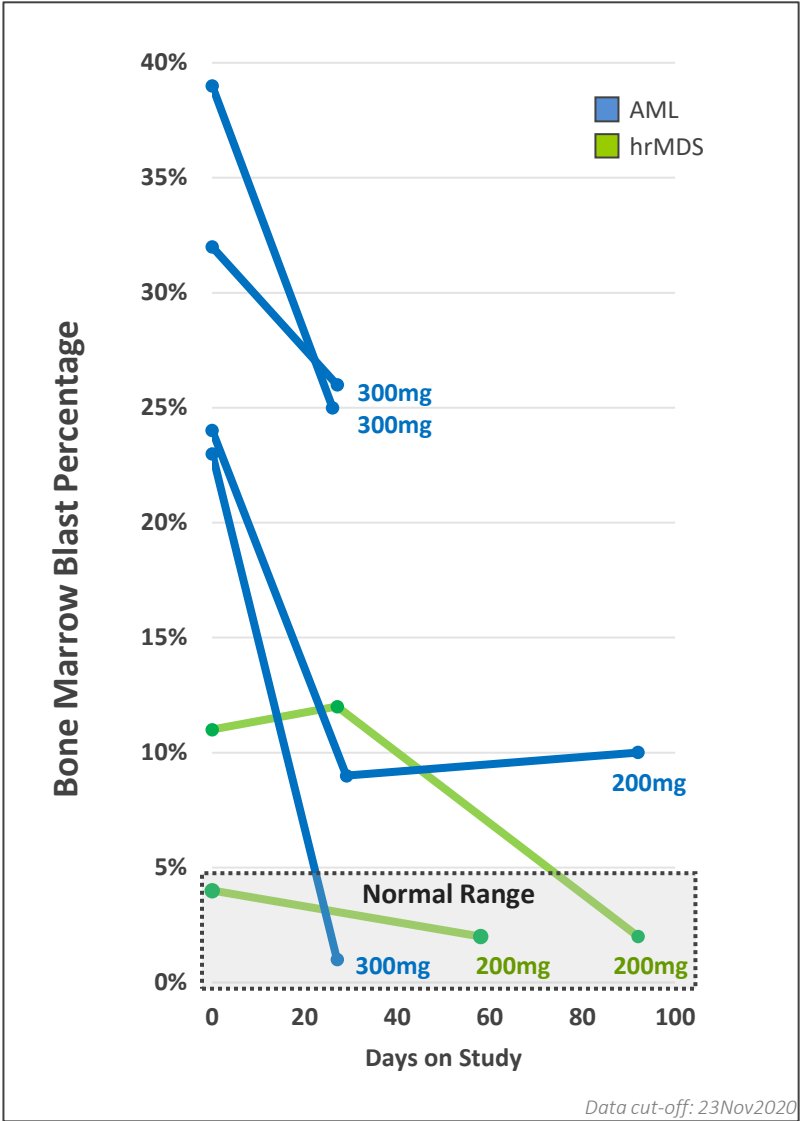
Study Population

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

Dosing

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

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

		Blasts Baseline	Blasts Best Resp	Change	
AML	005-2003	32%	26%	-19%	
AML	005-2002	39%	25%	-36%	
AML	003-1002	24%	9%	-63%	
hrMDS	003-1003	4%	2%	-50%	
hrMDS	003-1001	11%	2%	-82%	Marrow CR
AML	005-2001	23%	1%	-96%	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%)

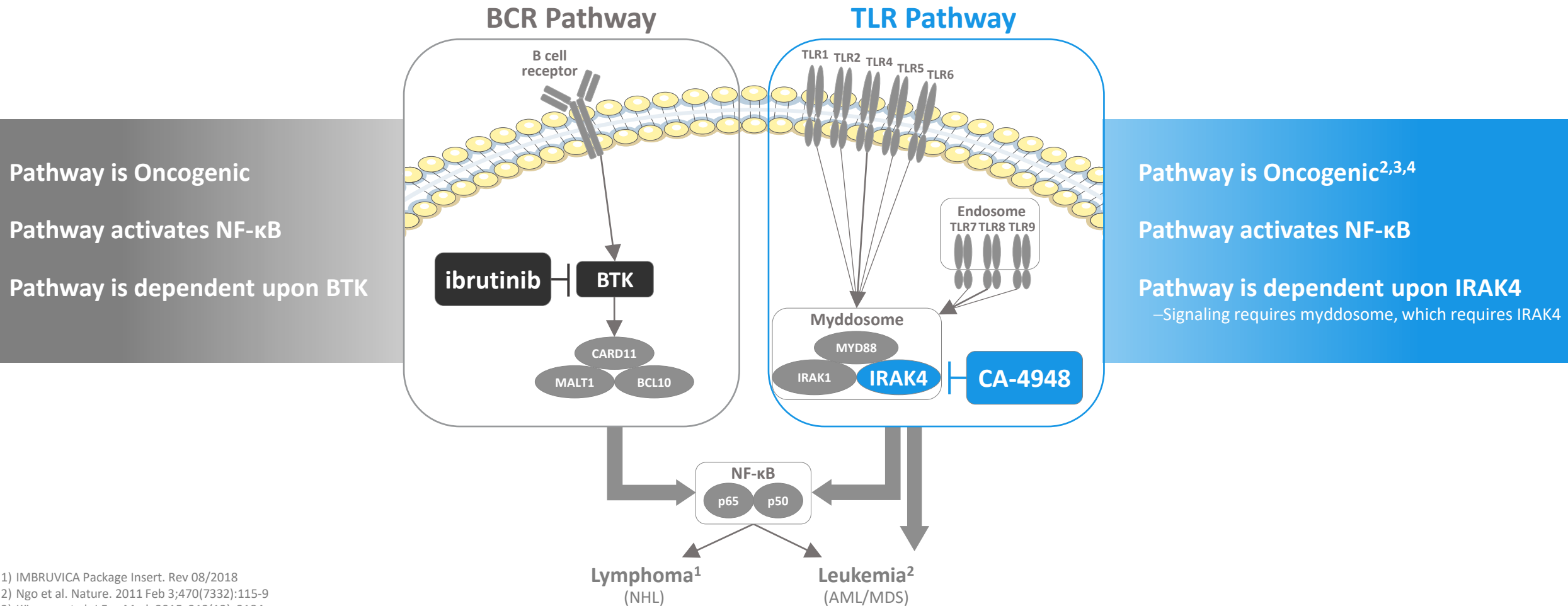
A large, circular, light-blue microscopic image of a cell cluster is centered behind the text. The cluster has a textured, irregular surface with many small, dark blue dots scattered across it, possibly representing individual cells or molecules. The background of the slide is white with several out-of-focus, light-blue circular shapes scattered around.

IRAK4 Targeted Program in NHL

CA-4948: In development for treatment of cancers driven by NF- κ B and the TLR/Myddosome

Novel Mechanism of Action for Addressing NF- κ B

BCR and TLR are parallel pathways and primary independent activators of NF- κ B



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

Data cut-off: 23Nov2020

Baseline Characteristics of Ph1 Patients	Overall (N=31)
Male	26 (84%)
Female	5 (16%)
Median Age	69yrs
Histology	
Diffuse large B-cell lymphoma (DLBCL)	14 (45%)
Transformed follicular lymphoma (t-FL/DLBCL)	6 (19%)
Waldenström's Macroglobulinemia (WM)	4 (13%)
Other Lymphoma*	7 (23%)
Prior Therapies	
Median prior lines of therapy	4 prior lines
BTK inhibitor, n (%)	6 (19%)
CAR-T, n (%)	5 (16%)
ASCT, n (%)	7 (23%)
Other	13 (42%)
MYD88 Status	
Positive, n (%)	2 (6%)
Negative, n (%)	18 (58%)
Unknown, n (%)	11 (35%)

*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

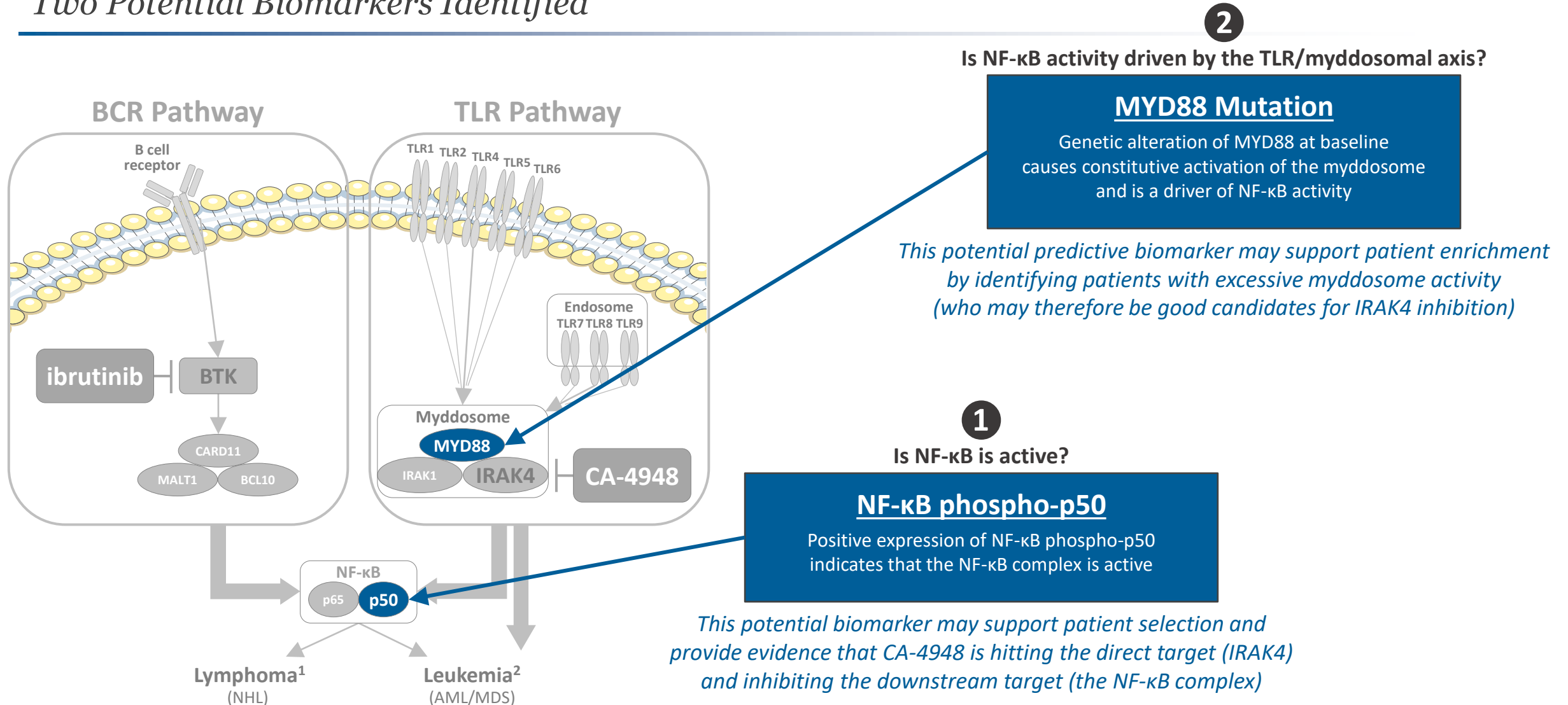
Dose Levels, 3+3 Design

QD: 50, 100mg

BID: 50, 100, 200, 300 or 400mg

CA-4948 in Lymphoma

Two Potential Biomarkers Identified



1) IMBRUVICA Package Insert. Rev 08/2018

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

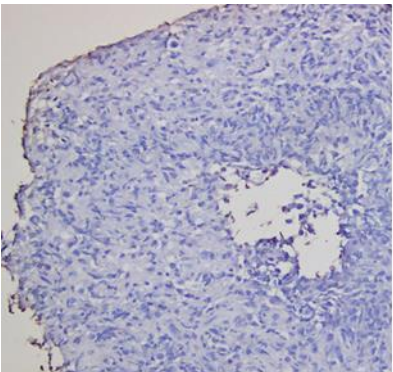
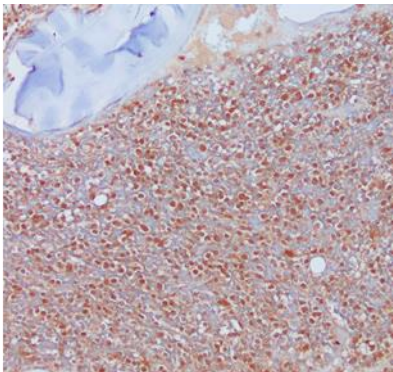
CA-4948 in Lymphoma

Early Biomarker Data from Phase 1 patients

This clinical study is ongoing, more data are needed to confirm these potential biomarkers

NF-κB phospho-p50

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

NEGATIVE at baseline		POSITIVE at baseline	
NFκB phospho-p50 expression before treatment with CA-4948		NFκB phospho-p50 expression before treatment with CA-4948	
			
Patient	Best Response	Patient	Best Response
12-1002	+86% PD	19-1001	-35% SD
018-2004	+156% PD	02-1001	-23% SD
001-4002	+7% PD	02-3003	+22% SD
002-4004	+75% PD	012-5007	-34% SD
012-4004	+125% PD	002-6007	+25% SD
012-5006	+190% PD	002-6008	+16% SD
013-6001	+98% PD	15-1001	+66% PD

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

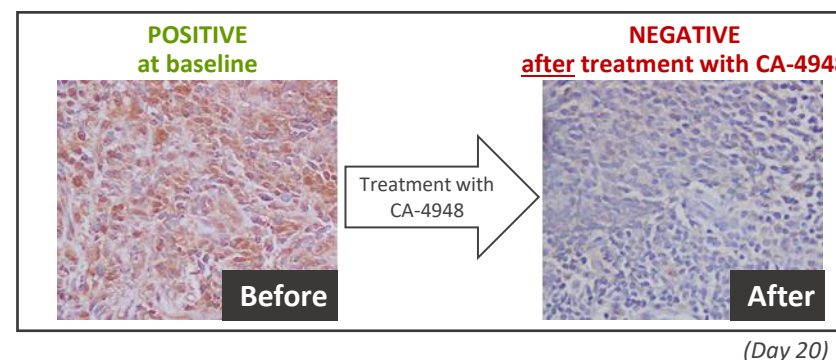
- Patients whose tumors do not exhibit NF-κB activity may not be amenable to NF-κB downregulation
7 of 7 patients testing negative at baseline experienced disease progression
2 of these patients were dosed at 200mg BID
- Patients whose tumors do exhibit NF-κB activity may be amenable to NF-κB downregulation
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

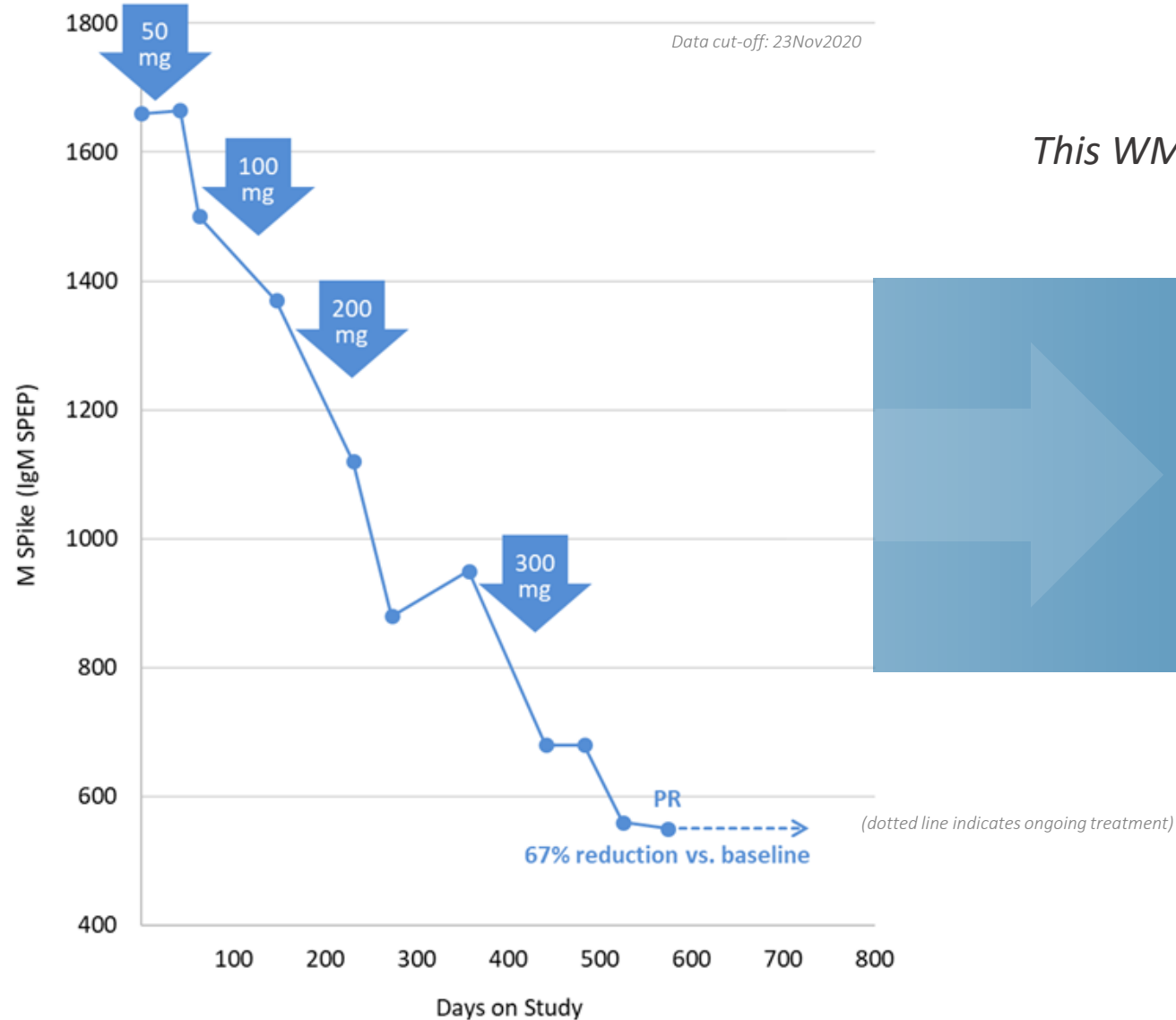
Phospho-p50 Expression in Pre/Post Tumor Biopsies Also Provides Evidence that CA-4948 is Hitting the Target (IRAK4) and Downregulating NF-κB Activity

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



CA-4948 in Lymphoma

Anti-Cancer Activity and Dose Response in a Patient with Waldenströms Macroglobulinemia (WM)



Note:

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

Demonstrated Anti-Cancer Activity

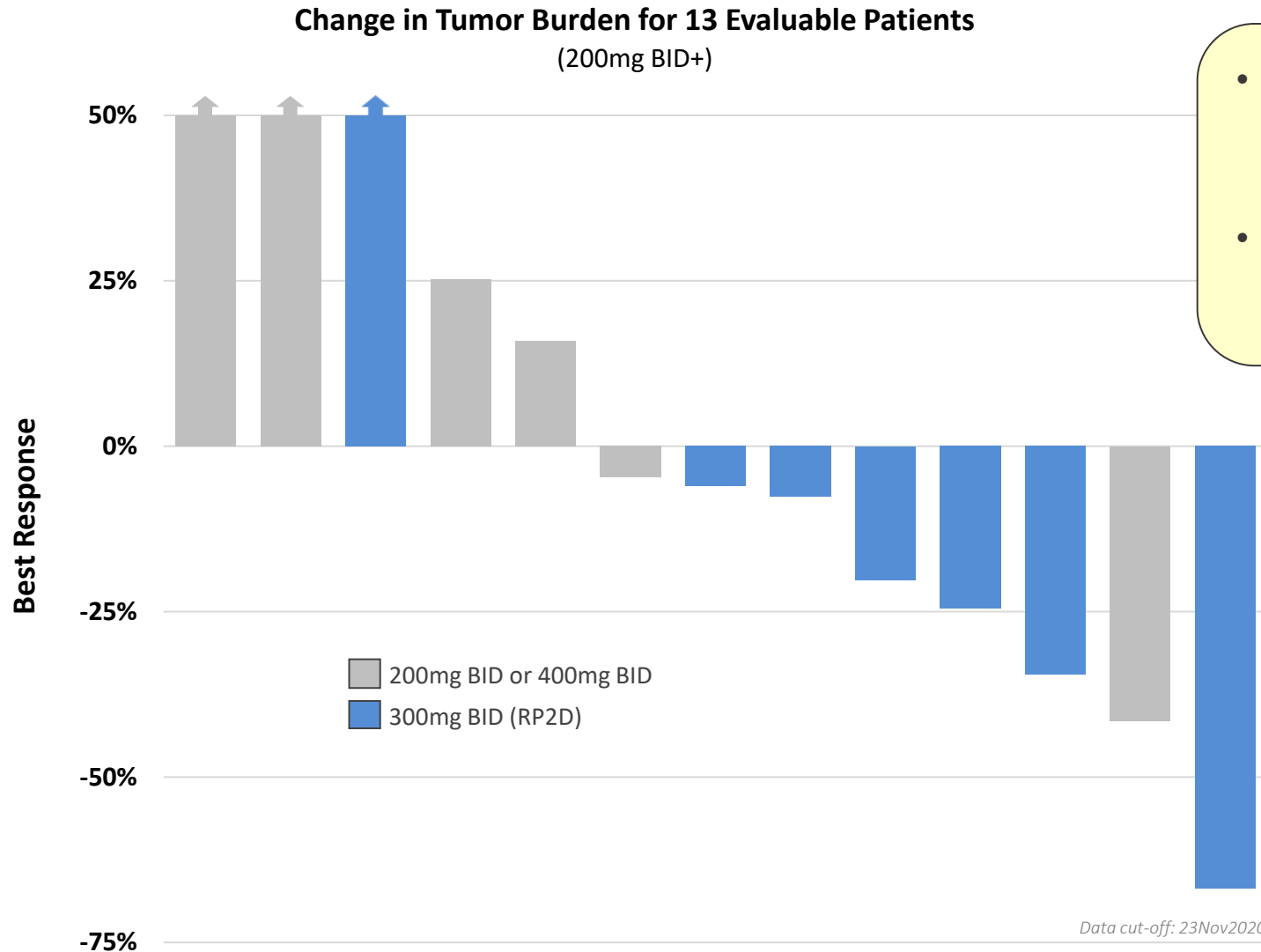
Objective Response observed at 300mg BID (RP2D)

Demonstrated Dose Response

Tumor burden decreased with each increase in dose

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**

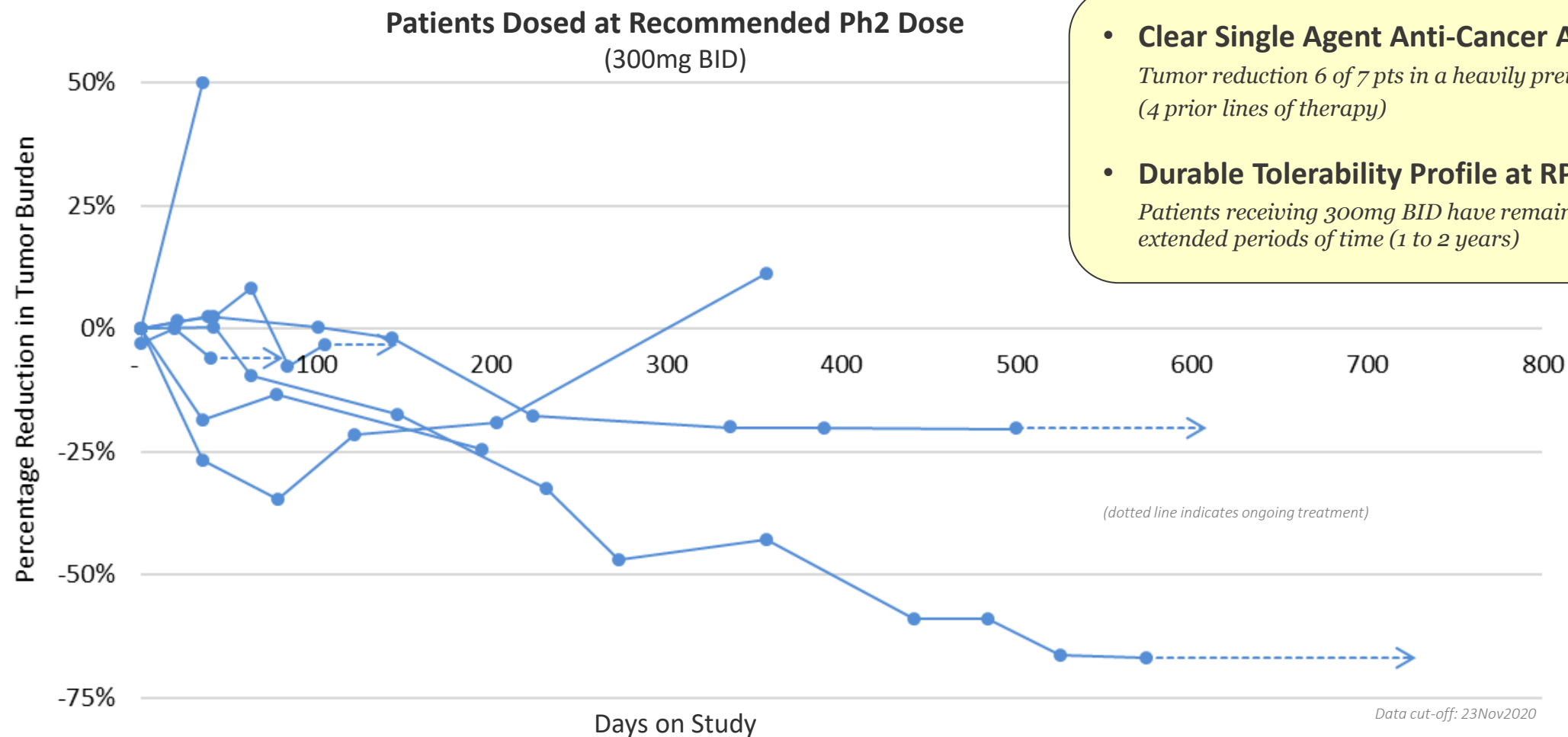
*Tumor reduction 6 of 7 pts in a heavily pretreated population
(4 prior lines of therapy)*

- **Durable Tolerability Profile at RP2D**

*Patients receiving 300mg BID have remained on therapy for
extended periods of time (1 to 2 years)*

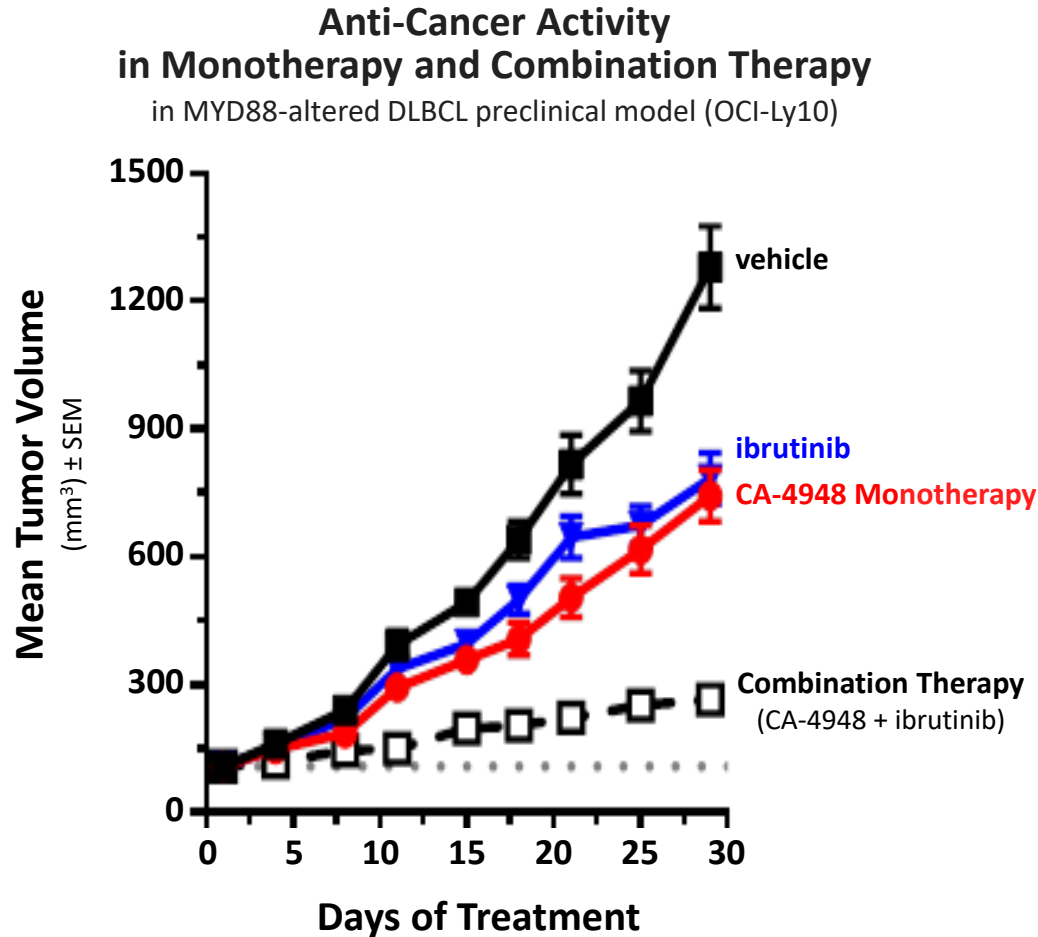
CA-4948 in Lymphoma

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



CA-4948 in Lymphoma

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



Booher et al. Waldenstrom Roadmap Symposium 2019

Mechanism of Action Supports Combination

- CA-4948 potentially offers a novel mechanism for reducing NF- κ B activity by targeting the TLR/myddosome (a parallel/complementary pathway to the BCR/BTK pathway)

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

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

A circular inset image showing a microscopic view of a tumor. The tumor is a dense, irregular mass of cells with a blueish-grey color. It is surrounded by a lighter, more granular area, possibly representing the surrounding tissue or the tumor's interface with the environment. The entire image is set against a background of blurred, light blue circular shapes.

VISTA Targeted Program in Solid Tumors

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

In Development for VISTA Expressing and Infiltrated Cancers

Profile	
Value Proposition	<ul style="list-style-type: none">• First-in-class monoclonal antibody antagonist of VISTA• Composition-of-matter IP extends into 2034
Target Patient Population	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Monoclonal antibody developed by ImmuNext/Janssen in partnership with Randy Noelle’s lab at Dartmouth (the co-discoverer of VISTA)

CI-8993 Target Background

VISTA is an Important Checkpoint Regulator

RESEARCH ARTICLE SUMMARY

T CELLS

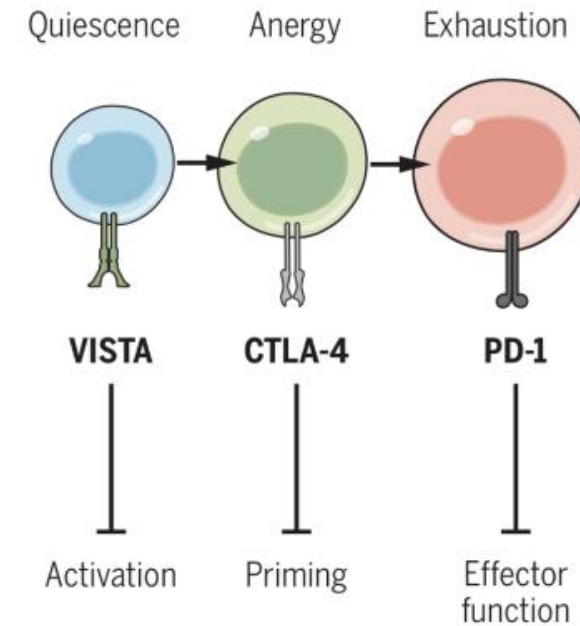
VISTA is a checkpoint regulator for naïve T cell quiescence and peripheral tolerance

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

ElTanbouly et al. Science. 2020

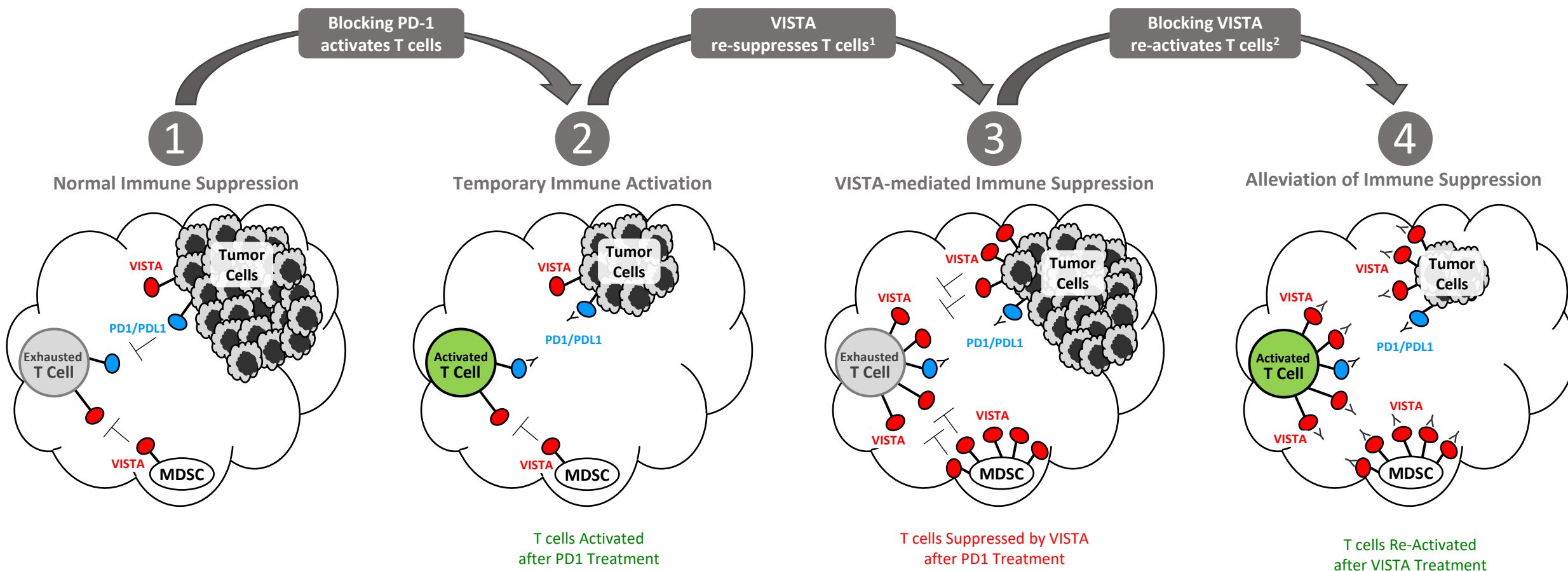
Integration of VISTA with other well-established negative checkpoint regulators of T cell activation



ElTanbouly et al. Science. 2020

CI-8993 Target Background

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



blocking PD1 causes up to 5x increase in VISTA expression¹

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

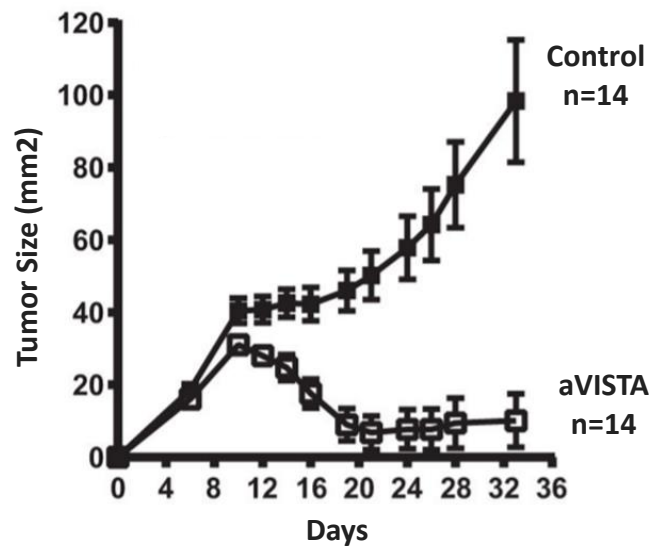
² Data from ImmuNext preclinical studies

CI-8993 Preclinical Data

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

Monotherapy

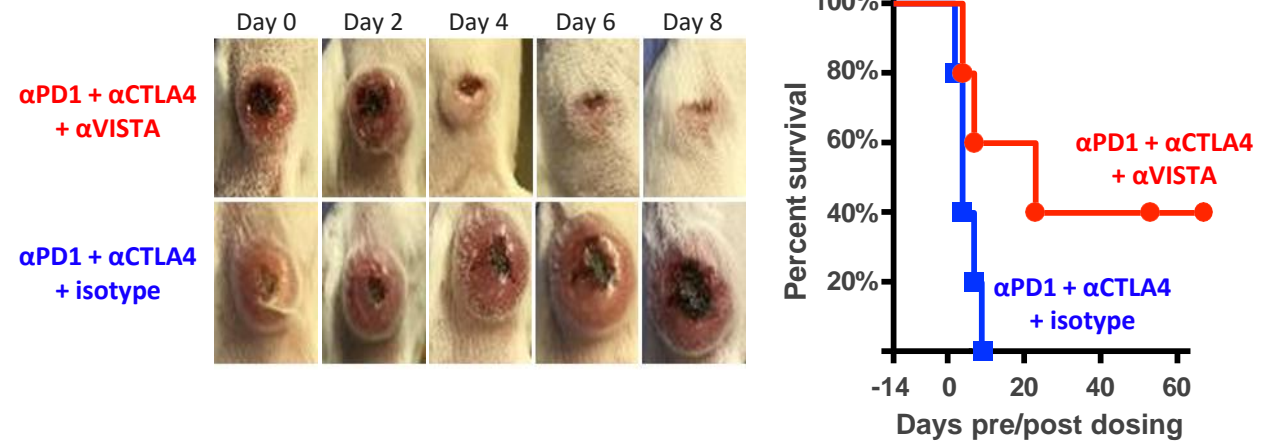
Anti-VISTA inhibited tumor growth in B16ova melanoma model¹



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

Combination Therapy

Anti-VISTA inhibited xenograft growth in checkpoint resistant CT26 model²

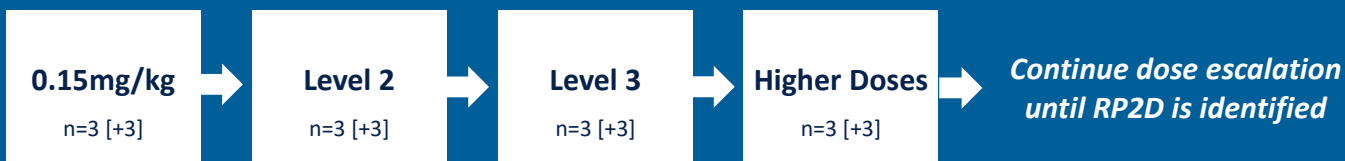


² J. Lines, IEBMC Conference 2019

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

Summary

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

Leadership Team





End of Corporate Presentation

NASDAQ: CRIS

