

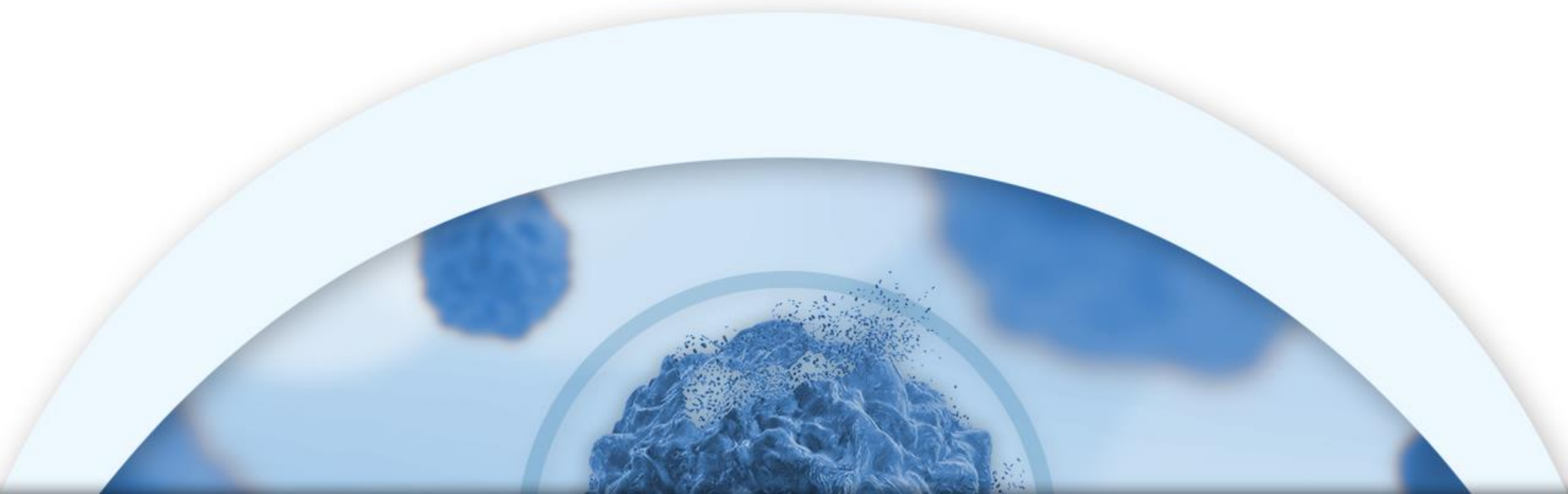


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Dec 2020 Key Opinion Leader Event

*NASDAQ: CRIS*

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A circular inset image showing a microscopic view of a cell, likely a yeast cell, with a textured, blue-tinted surface. The cell is centered in the background of the slide.

## CEO Introduction

*James Dentzer*

## *Agenda for Today's Event*

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### **Introduction**

James Dentzer  
CEO, Curis

### **CA-4948: NHL Phase 1 Study Update**

Robert Martell, M.D., Ph.D.  
Head of R&D, Curis

### **AML/MDS Landscape and CA-4948 Pre-Clinical Data**

Amit Verma, M.D.  
Professor of Medicine-Oncology, Albert Einstein College of Medicine  
Director, MDS Program, Montefiore Medical Center

### **CA-4948: AML/MDS Phase 1 Study Update**

Robert Martell, M.D., Ph.D.  
Head of R&D, Curis

### **Closing Remarks**

James Dentzer  
CEO, Curis

### **Q&A**

*Disclosure: Dr. Verma has received research funding and payments for scientific advisory services from Curis, Inc.*

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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.

A circular inset image showing a microscopic view of a cell cluster, likely a tumor spheroid, with a blue and white color scheme. The cluster is composed of numerous small, interconnected cells, with some areas appearing more dense and others more porous. The image is centered on the slide and partially overlaid by a white horizontal bar containing the title and author information.

## CA-4948 NHL Phase 1 Study Update

*Robert Martell, M.D., Ph.D.*

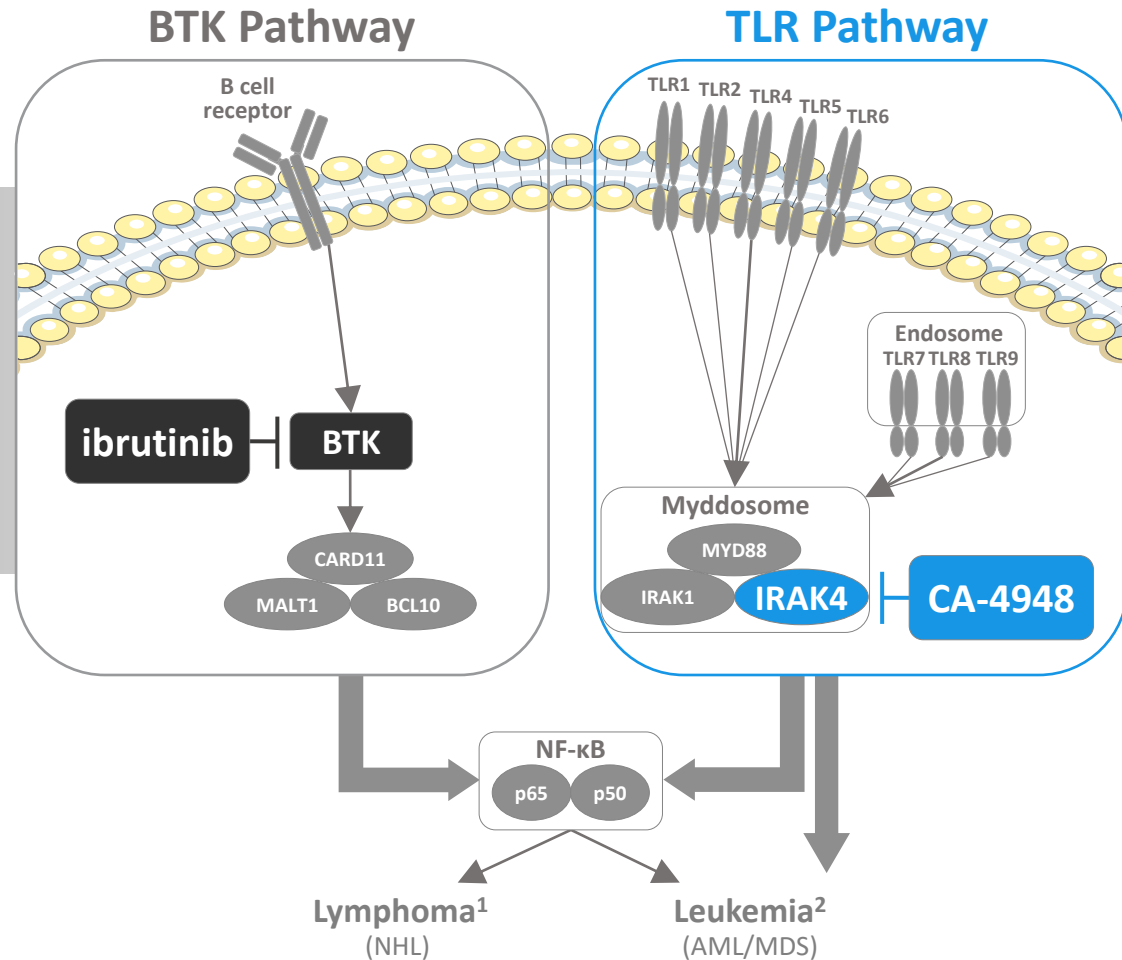
# CA-4948

## Novel Mechanism of Action for Addressing NF-κB



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

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



Pathway is Oncogenic

Pathway activates NF-κB

Pathway is dependent upon BTK

Pathway is Oncogenic<sup>2,3,4</sup>

Pathway activates NF-κB

Pathway is dependent upon IRAK4

–Signaling requires myddosome, which requires IRAK4

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-BCL<sub>6</sub> (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

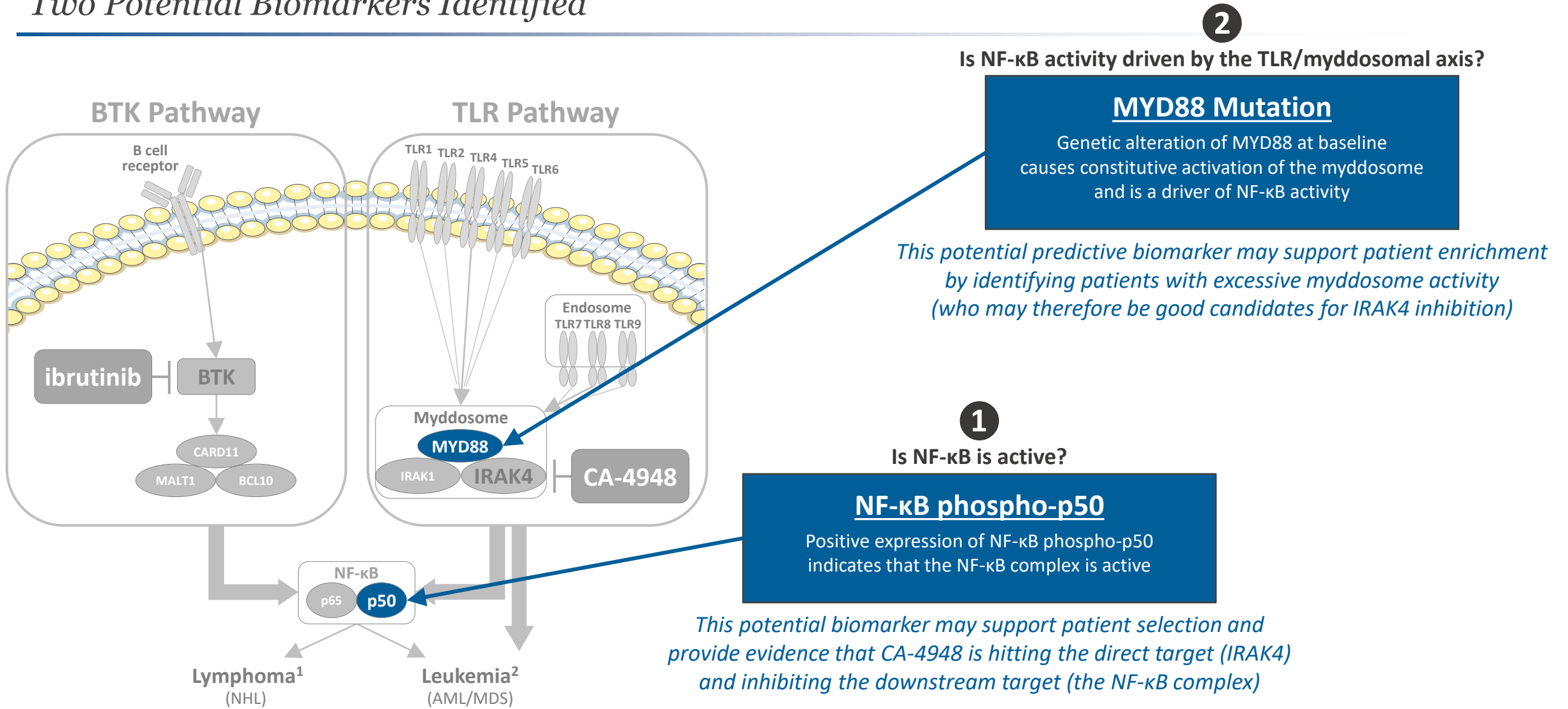
### Dose Levels, 3+3 Design

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



## 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

### 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

POSITIVE at baseline	NEGATIVE after treatment with CA-4948
Before	After

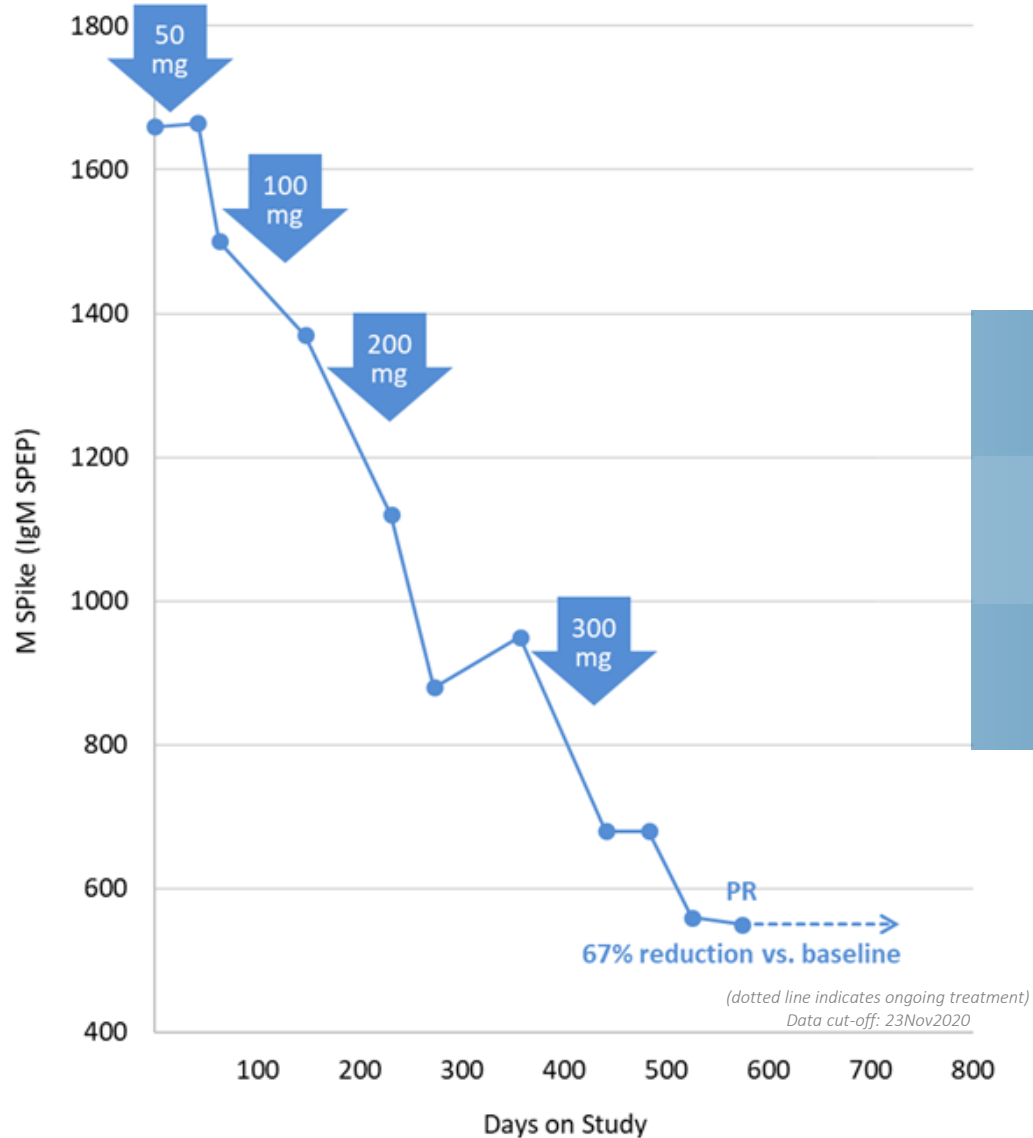
Treatment with CA-4948

(Day 20)

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

# CA-4948 in Lymphoma

## Anti-Cancer Activity and Dose Response in a Patient with Waldenström's Macroglobulinemia (WM)



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

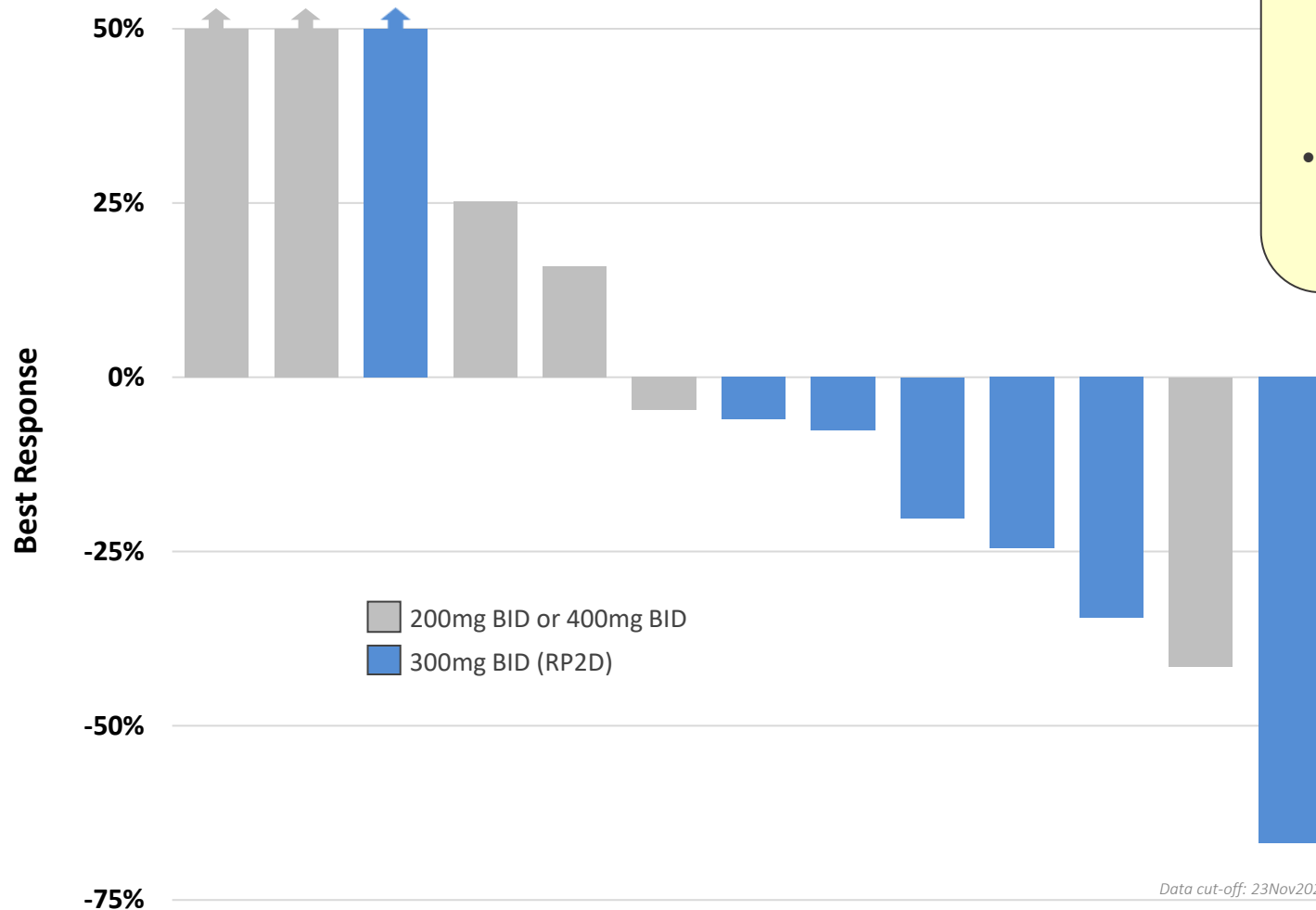
**Demonstrated Anti-Cancer Activity**  
*Objective Response observed at 300mg BID (RP2D)*

**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*

**Change in Tumor Burden for 13 Evaluable Patients**  
(200mg BID+)

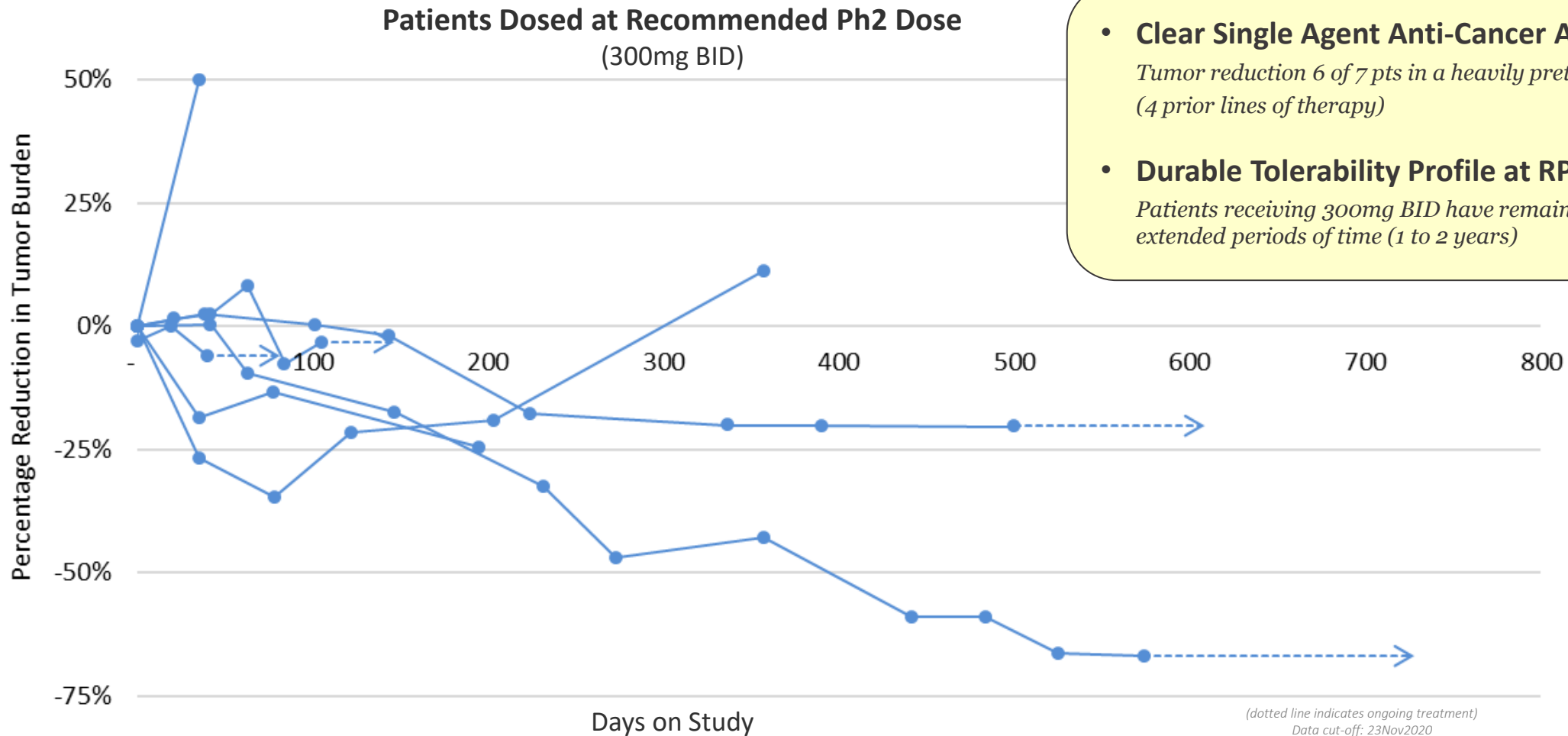


- **Clear Single Agent Anti-Cancer Activity at RP2D**  
*Tumor reduction 6 of 7 pts in a heavily pretreated population (4 prior lines of therapy)*
- **Durable Tolerability Profile at RP2D**  
*Patients receiving 300mg BID have remained on therapy for extended periods of time (1 to 2 years)*

*Data cut-off: 23Nov2020*

# CA-4948 in Lymphoma

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

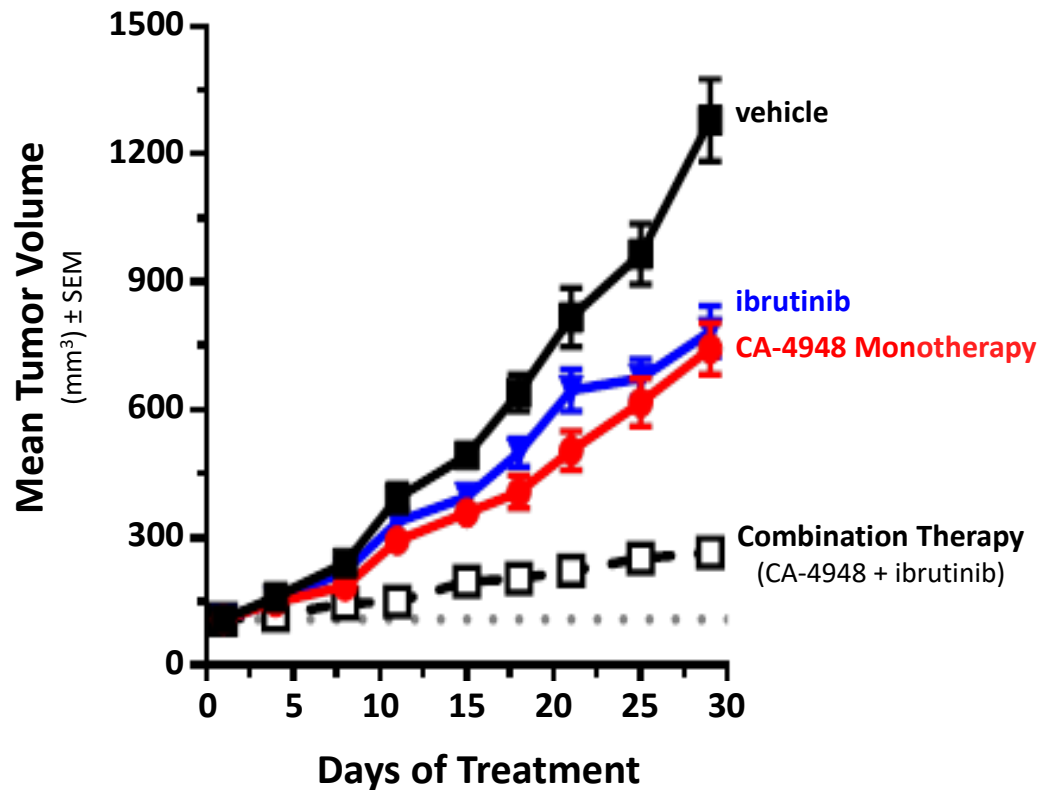


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*Tumor reduction 6 of 7 pts in a heavily pretreated population (4 prior lines of therapy)*
- **Durable Tolerability Profile at RP2D**  
*Patients receiving 300mg BID have remained on therapy for extended periods of time (1 to 2 years)*

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

## Anti-Cancer Activity in Monotherapy and Combination Therapy

in MYD88-altered DLBCL preclinical model (OCI-Ly10)



Booher et al. Waldenstrom Roadmap Symposium 2019

## 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

A circular inset image showing a microscopic view of a cell cluster. The cells are blue and have a textured, porous appearance, with some smaller particles or debris scattered around them. The image is centered on the slide and partially obscured by a white horizontal bar.

## IRAK4 in AML/MDS

*Amit Verma, M.D.*

## Overview of AML/MDS Disease and Available Treatment Options

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

### Patient Prognosis

- AML
- high-risk MDS (hrMDS)
- low-risk MDS (lrMDS)

### Current Available Treatments

- Chemotherapy
- Hypomethylating Agents (HMA)
- Targeted Therapy
- Stem Cell Transplant

### Front Line vs. Relapsed/Refractory Setting

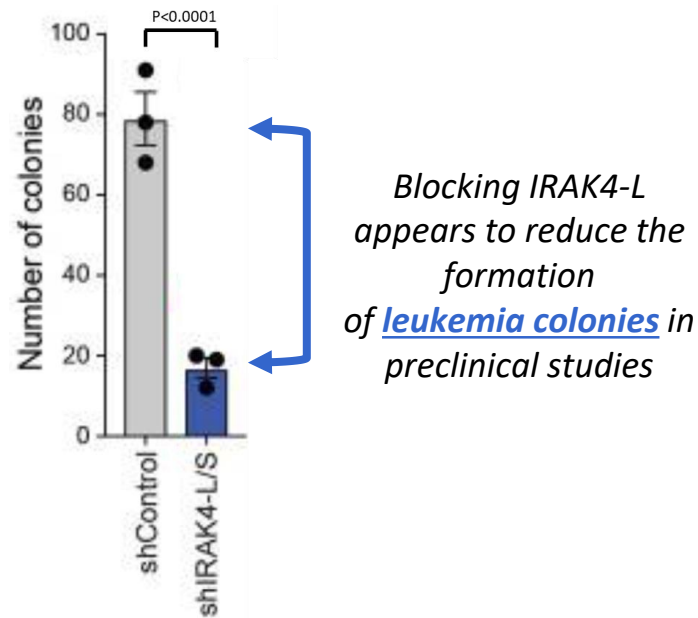
## *IRAK4-L is a Novel Target in AML/MDS*

### 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

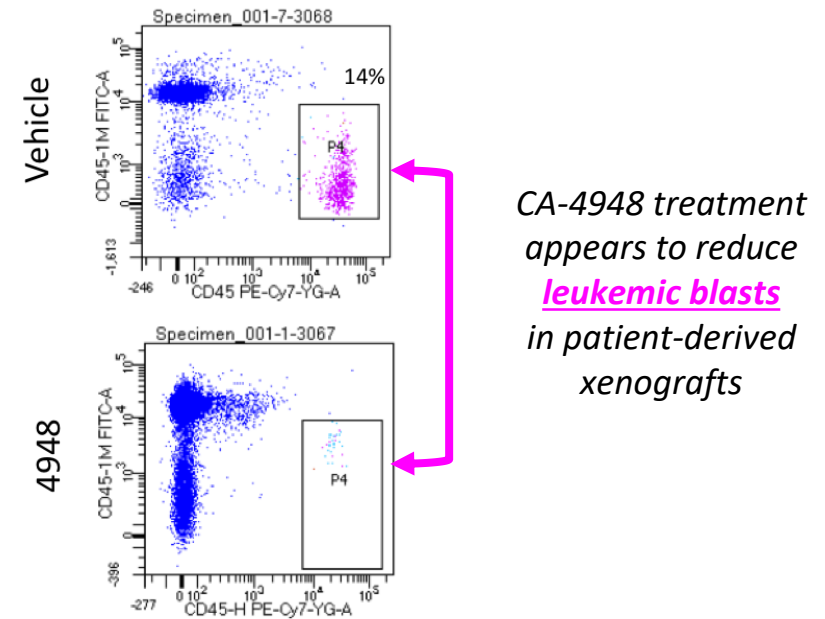
IRAK4-L provides a genetic link to oncogenic immune signaling in AML/MDS



Smith et al. Nat Cell Biol. 2019

#### CA-4948 Directly Targets IRAK4

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



Choudhary et al. AACR 2017



A circular inset image showing a microscopic view of a cell cluster, likely a tumor spheroid, with a blue and white color scheme. The cluster is composed of many small, interconnected cells, with some areas appearing more dense and others more porous. The background of the slide is a light blue gradient with several larger, out-of-focus circular shapes of varying shades of blue.

## CA-4948 AML/MDS Phase 1 Study Update

*Robert Martell, M.D., Ph.D.*

## 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

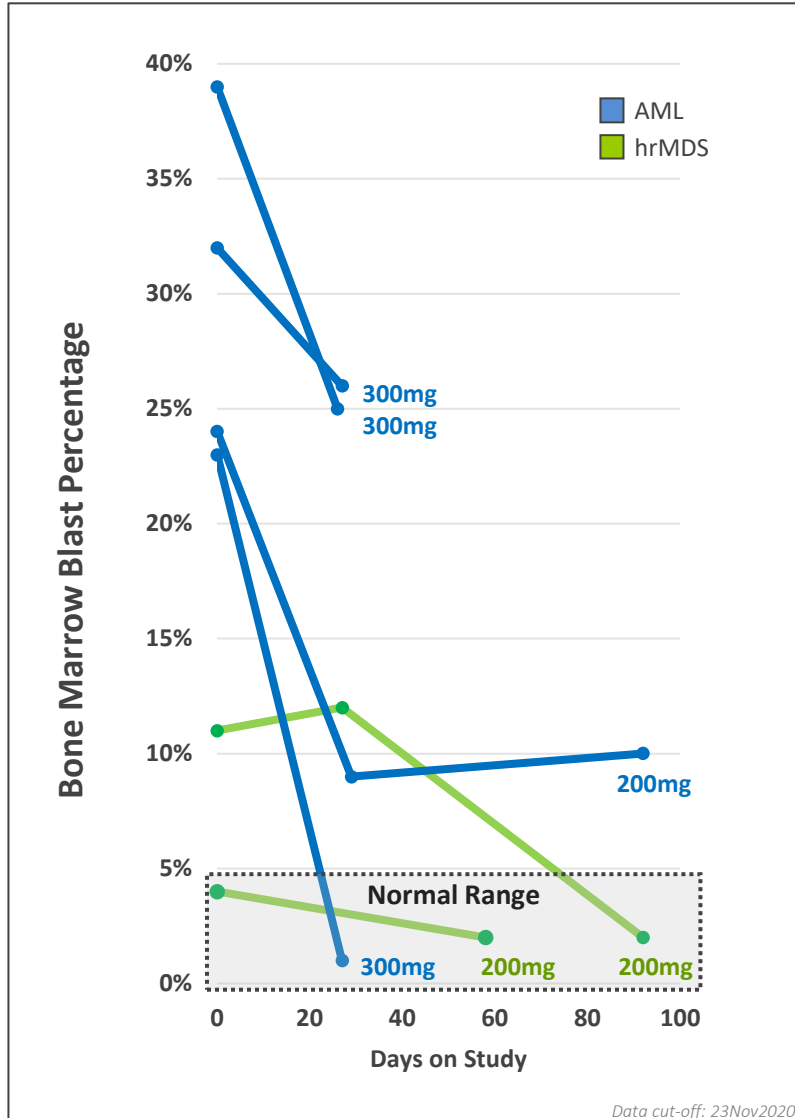
- Relapsed/Refractory disease
- Histopathologically confirmed AML or High-Risk MDS
- Age  $\geq$  18 years
- ECOG performance Status of  $\leq$  2

### Dosing

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

# CA-4948 in AML/MDS

## Monotherapy Anti-Cancer Activity Observed in Early Ph1 Data



- 1<sup>st</sup> 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%	<b>Marrow CR</b>
AML	005-2001	23%	1%	-96%	<b>Marrow CR</b>

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

A circular inset image showing a microscopic view of a cell, likely a yeast cell, with a textured, blue-tinted surface. The cell is centered in the background of the slide.

## Closing Discussion

*James Dentzer*



Q&A





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End of Presentation

*NASDAQ: CRIS*

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