



TARGETING CANCER

New Science. New Cancer Therapies. New Hope.

Company Overview – May 28 2021

#### FORWARD-LOOKING STATEMENTS



This presentation contains forward-looking statements (including within the meaning of §21E of the U.S. Securities Exchange Act of 1934, as amended, and § 27A of the U.S. Securities Act of 1933, as amended). Forward-looking statements, which generally include statements regarding goals, plans, intentions and expectations, are based upon current beliefs and assumptions of Oncternal Therapeutics, Inc. ("Oncternal") and are not guarantees of future performance. Statements that are not historical facts are forward-looking statements, and include statements regarding the expected timing for achieving key milestones, including initiating ROR1 CAR-T studies and completing and announcing results of clinical trials of Oncternal's other product candidates, the anticipated market potential, duration of patent coverage, ability to obtain and maintain favorable regulatory designations, and potential accelerated approval pathways for Oncternal's product candidates and preclinical programs, and Oncternal's anticipated cash runway.

All forward-looking statements are subject to risks and uncertainties, including risks and uncertainties inherent in Oncternal's business, including risks associated with the clinical development and process for obtaining regulatory approval of Oncternal's product candidates such as potential delays in the commencement, enrollment and completion of clinical trials; the risk that results seen in a case study of one patient likely will not predict the results seen in other patients in the clinical trial; the risk that interim results of a clinical trial do not predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues, and as more patient data become available; and other risks described in Oncternal's filings with the U.S. Securities and Exchange Commission ("SEC"). Except as required by applicable law, Oncternal undertakes no obligation to revise or update any forward-looking statement. All forward-looking statements in this presentation are current only as of the date on which the statements were made. Additional factors that could cause actual results to differ materially from those expressed in the forward-looking statements are discussed in Oncternal's filings with the SEC.

Cirmtuzumab, TK216 and Oncternal's CAR-T targeting ROR-1 are investigational product candidates or preclinical programs that have not been approved by the U.S. Food and Drug Administration for any indication.

This presentation includes certain information obtained from trade and statistical services, third-party publications, and other sources. Oncternal has not independently verified such information and there can be no assurance as to its accuracy.

## **Corporate Highlights**



#### CIRMTUZUMAB: POTENTIALLY FIRST-IN-CLASS MONOCLONAL ANTIBODY TARGETING ROR1

- Ongoing clinical studies in MCL, CLL and breast cancer, and preclinical studies in additional cancer indications
- Interim Phase 1/2 results for cirmtuzumab + ibrutinib in MCL compare favorably to historical single-agent ibrutinib data
- Dialogue with FDA regarding potential accelerated approval study design in MCL

## ROR1 CAR-T CELL THERAPY: AGREEMENTS WITH SHANGHAI PHARMA, KAROLINSKA INSTITUTET AND LENTIGEN

In development to treat hematological malignancies and solid tumors

#### **TK216: TARGETED ETS INHIBITOR**

- Two durable complete responses in patients with metastatic relapsed/refractory Ewing sarcoma in ongoing Phase 1/2
- Additional opportunities in ETS-driven tumor indications

#### **MULTIPLE DATA CATALYSTS EXPECTED IN NEXT 12 MONTHS**

- Clinical data updates expected in MCL, CLL, breast cancer and Ewing sarcoma
- ROR1 CAR-T cell therapy expected to reach clinic in 1H 2022

#### **EXPERIENCED MANAGEMENT AND BOARD OF DIRECTORS**

## **Experienced Team**





James Breitmeyer, MD, PhD CEO, Founder, Director









**Richard Vincent** CFO







**Chase Leavitt** General Counsel



**Tang Capital** Management





**David Hale** Co-founder, Board Chairman



Michael Carter, MD, Ch.B., F.R.C.P. Director



Daniel Kisner, MD Director



**Bill LaRue** Director































Caliper Caliper





Raj Krishnan PhD CTO **GILEAD** 





Salim Yazji, MD CMO





**Gunnar Kaufmann, PhD** CSO



Scripps Research



Rosemary Mazanet, MD, PhD Director









Xin Nakanishi, PhD Director









Charles Theuer, MD, PhD Director













Johnson Johnson

Robert Wills, PhD

Director

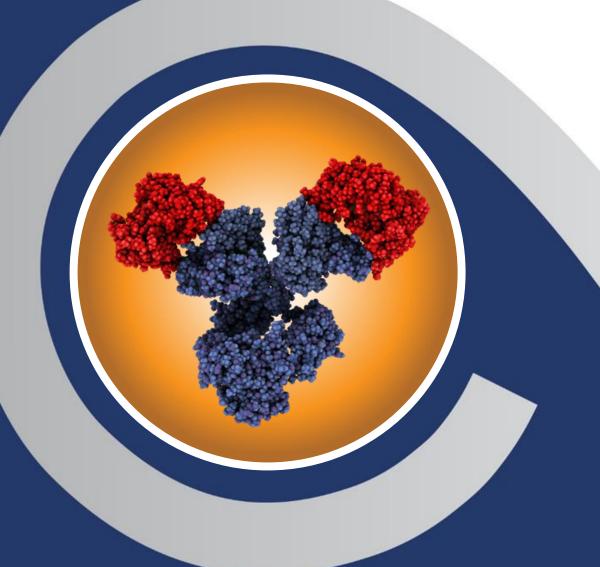


## **Robust Pipeline – Novel Product Candidates in Multiple Indications**



Produ	uct Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Modality
	Cirmtuzumab	Mantle Cell Lymphoma (MCL)					
Cirr		Chronic Lymphocytic Leukemia (CLL)					
		Breast Cancer				KC	OR1 mAb
		Ewing Sarcoma					1
	TK216	Acute Myeloid Leukemia (AML)				ETS oncoprotei	in inhibitor
		Prostate Cancer				210 oncoproce	
DO.	ROR1 CAR-T	Heme Cancers					
RU		Solid Tumors				ROR1 CAR-T cell t	herapy





## **CIRMTUZUMAB**

ROR1 monoclonal antibody

# ROR1 (Receptor Tyrosine Kinase-Like Orphan Receptor 1) Compelling Tumor-Specific Target



- Expressed on most B-cell malignancies, including
  - Mantle cell lymphoma (MCL), diffuse large B-cell lymphoma (DLBCL), chronic lymphocytic leukemia (CLL)
- Expressed on many solid tumors
  - Increased ROR1 expression associated with more aggressive tumors, shorter PFS and OS
- ROR1 activity associated with aggressive phenotype
  - Invasion, metastasis, stem cell-like behavior, and resistance to treatment
- Subject of recent large pharma acquisitions
  - ROR1-ADCs: Merck (VelosBio), Boehringer (NBE)
- Oncternal ROR1 pipeline differentiated and advancing
  - Therapeutic antibody and cell therapy programs

## ROR1 Expressed on Multiple Solid and Liquid Tumors

MCL	95%
CLL	95%
Uterus	96%
Lymphoma	90%
Prostate	90%
Skin	89%
Pancreatic	83%
Adrenal	83%
Lung	77%
Breast	75%
Testicular	73%
Colon	57%
Ovarian	54%

Zhang 2012 AJP

Green 2008 Trends Cell Biol. 2008; Matsuda T 2001 Mech Dev.; Fukuda 2008 PNAS; Hudecek 2010 Blood; Zhang 2012 Am J Pathology; Zhang 2014 PNAS

## **Two Development Programs at Oncternal Target ROR1**







#### **Background**

- High-affinity IgG1 humanized ROR1 mAb
- Patent coverage through 2033
- Supported by ~\$14M non-dilutive CIRM grant and Pharmacyclics product donation
- Cirmtuzumab is the mAb used in VLS-101 ADC
  - VelosBio spun out in 2018, acquired by Merck in 2020 for \$2.75B

#### **Development status**

- MCL: lead indication. P2 with ibrutinib (data: ASCO 2021)
  - Orphan Drug Designations for MCL and CLL
- CLL: P2 with ibrutinib (data: ASCO 2021); P1b with venetoclax
- HER-2 negative breast cancer: P1b with paclitaxel
- Investigating additional ROR1-expressing indications



#### **Background**

- CAR utilizing cirmtuzumab scFv for targeting
- ROR1 expression on many tumor types
- Potential safety and efficacy advantages
- VLS-101 data at ASH 2020 reported no off-tumor ROR1 organ toxicities

#### **Development status**

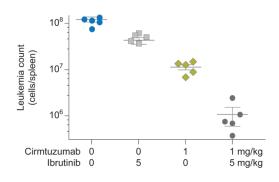
- Collaborations with Shanghai Pharma (China) and Karolinska Institutet. Manufacturing with Lentigen
- First-in-human dosing expected 1H 2022

# Extensive Preclinical Research Supports Evaluation As Combination Therapy, Multiple Tumor Indications and Potential Safety Advantage



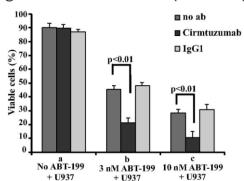
#### **Synergism with Targeted Agents**

- Synergistic with ibrutinib in CLL + MCL
  - ROR1-Wnt5a pathway not inhibited by ibrutinib

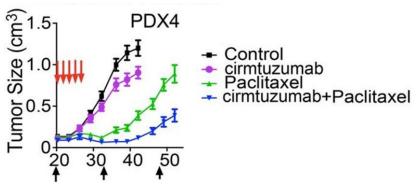


Yu 2017 Leukemia

Synergistic with venetoclax (ABT-199)

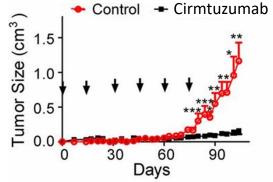


## Supporting Preclinical Data in Solid Tumors



Cirmtuzumab and paclitaxel are at least additive against TNBC PDX growth, and eliminate tumor forming cells

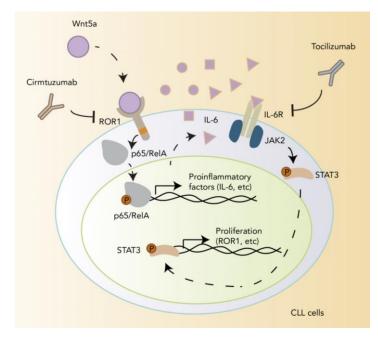
Zhang 2019 PNAS



Anti-tumor activity in PDX models of ovarian cancer *Zhang 2014 PNAS* 

## ROR1 Antagonism Suppresses Inflammation in CLL

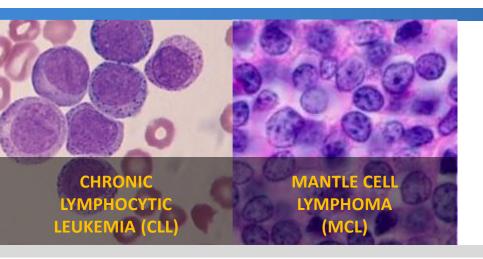
- Cirmtuzumab blocks pro-inflammatory NF-kB signaling pathway in CLL cells
  - Potential explanation for safety profile observed in patients



Chen 2019 Blood

### Phase 1/2 Study of Cirmtuzumab and Ibrutinib in Patients with MCL and CLL





#### **CIRLL** Study:

- Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma
- MCL enrollment recently expanded
- Dialogue with FDA regarding potential accelerated approval study design in MCL

#### STUDY DESIGN

#### PART 1 (in CLL & MCL)

#### **DOSE-FINDING COHORT**

- Cirmtuzumab at 2/4/8 & 16 mg/kg and 300 & 600 mg per dose
- Ibrutinib added after one month (420 mg CLL, 560 mg MCL qd po)

**Enrolled** 

PART 2 (in CLL & MCL)

## DOSE-EXPANSION COHORT

 Confirm Recommended Dosing Regimen (RDR) of cirmtuzumab (600 mg) + ibrutinib at approved dose (420 mg CLL, 560 mg MCL)

MCL Phase 2 enrolling
CLL enrolled

#### PART 3 (in CLL)

#### **RANDOMIZED EFFICACY**

- Cirmtuzumab + ibrutinib vs ibrutinib
- Primary endpoint: Complete Response rate

Enrolled

- Funded by CIRM
- Collaboration with UC San Diego and CIRM
- Ibrutinib from
   Pharmacyclics/Abbvie

## CIRLL Trial Cirmtuzumab + Ibrutinib: Best Overall Response in MCL and CLL Data Update at ASCO 2021



## High response rates and durable responses observed in both MCL and CLL

	MCL evaluable=18	CLL evaluable=34
ORR, n (%)	15 (83.3)	32 (94.1)
CR, n (%)	7 (38.9)	5 (14.7)
PR, n (%)	8 (44.4)	27* (79.4)
SD, n (%)	2 (11.1)	2 (5.9)
PD, n (%)	1 (5.6)	0
Clinical Benefit Rate, n (%)	17 (94.4)	34 (100)
Median Duration of response in months (95% CI)	NE (11.93, NE)	NE

Data cut: 16APR2021; Evaluable MCL Part 1 & 2 patients (n=34); Patients were considered evaluable for response if they had 1-dose of cirmtuzumab and had 1-post baseline tumor assessment; CR- complete remission, PR- partial remission, SD- stable disease, PD- progressive disease; ORR- number and percent of patients that achieved CR or PR; Clinical benefit rate- number and percent of patients that achieved CR, PR or SD; NE- not estimable; \*includes 1 partial remission with lymphocytosis

Oncternal Data 19MAY2021

Note: Rule et al., 2017 Br J Haem: ORR 66% and CR rate 20% for ibrutinib in MCL population with similar number of prior lines of therapy (pooled analysis across three third-party clinical studies).

## R/R MCL: Tumor Reduction and Progression-Free Survival Cirmtuzumab + Ibrutinib Data Update at ASCO 2021

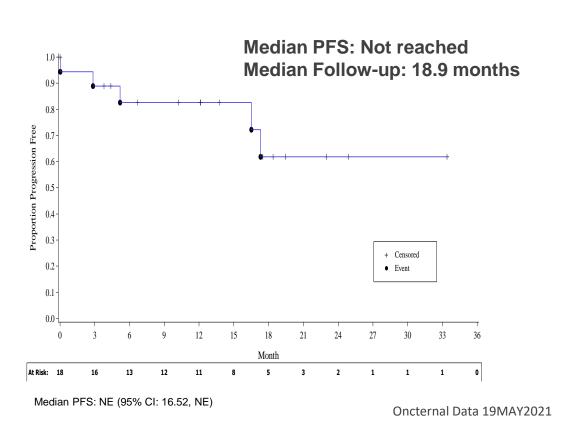


### 83% ORR and median PFS not reached in MCL

### **Best Tumor Reduction (SPD cm<sup>2</sup>)**

## -20 -30 -40 % Change in SPD PR -50° -60 12.5 -70 -80 -90

### **Progression-Free Survival**



Data cut: 16APR2021; Evaluable MCL Part 1 & 2 patients (n=18); Patients were considered evaluable for response if they had 1-dose of cirmtuzumab and had 1-post baseline tumor assessment; SPD= sum of product of diameters; Number under bars represent baseline SPD; NE=not estimable

Note: Rule et al., 2017 Br J Haem: median PFS 12.8 months for ibrutinib in MCL population with similar number of prior lines of therapy (pooled analysis across three third-party clinical studies).

# R/R MCL: Clinical Response in Subgroups Cirmtuzumab + Ibrutinib Data Update at ASCO 2021



# Responses rates are favorable in patients with high-risk factors associated with difficult to treat disease, including prior ibrutinib (4CR/4PR)

	All MCL evaluable=18	Ki-67 ≥30% n=9	>1 prior systemic regimen n=9
Overall Response Rate (ORR), n (%)	15 (83.3)	8 (88.9)	8 (88.9)
CR, n (%)	7 (38.9)	3 (33.3)	5 (55.6)
PR, n (%)	8 (44.4)	5 (55.6)	3 (33.3)
SD, n (%)	2 (11.1)	0	1 (11.1)
PD, n (%)	1 (5.6)	1 (11.1)	0
Clinical Benefit Rate, n (%)	17 (94.4)	8 (88.9)	9 (100)
Median Duration of Response in months (95% CI)	NE (11.93, NE)	13.84 (8.66, NE)	NE (8.66, NE)
Median Time to First Response in months (95% CI)	2.79 (2.66, 2.79)	2.79 (2.66, 2.79)	2.77 (1.84, 2,82)
Median Time to CR in months (95% CI)	2.79 (1.84, 8.20)	2.79 (2.66, 11.02)	2.79 (1.84, 8.20)

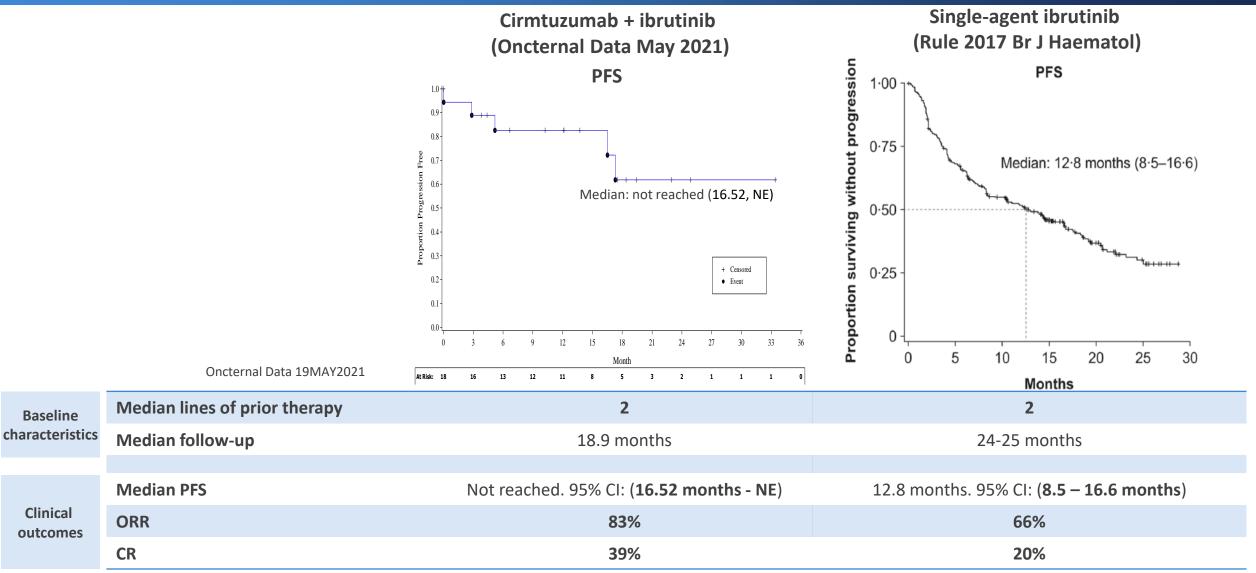
Data cut: 16APR2021; CR- complete remission, PR- partial remission, SD- stable disease, PD- progressive disease; ORR- number and percent of patients that achieved CR or PR; Clinical benefit rate- number and percent of patients that achieved CR, PR or SD; NE- not estimable; Time to response analyses- Part 1 first scans were done at day 28, Part 2 first scans were done at 3 months

Oncternal Data 19MAY2021

Note: Rule et al., 2017 Br J Haem: median PFS 12.8 months for ibrutinib in MCL population with similar number of prior lines of therapy (pooled analysis across three third-party clinical studies).

## Cirmtuzumab + Ibrutinib Interim Clinical Results in MCL (ASCO 2021) Compare Favorably to Historical Single-Agent Ibrutinib Data





Note: Data presented are from separate studies and such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of the combination of cirmtuzumab and ibrutinib compared to single-agent ibrutinib; NE= not estimable

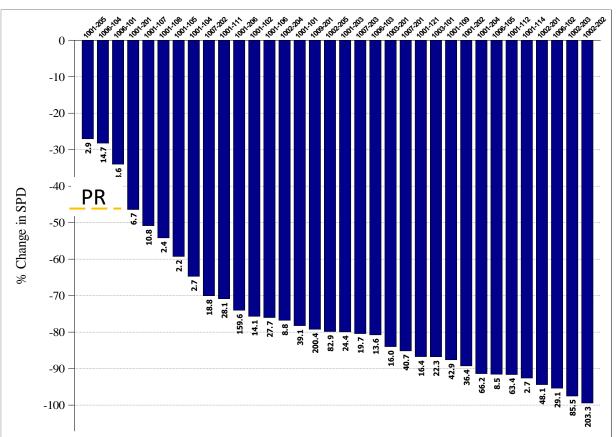
## **CLL: Tumor Reduction and Progression-Free Survival**

Cirmtuzumab + Ibrutinib Data Update at ASCO 2021



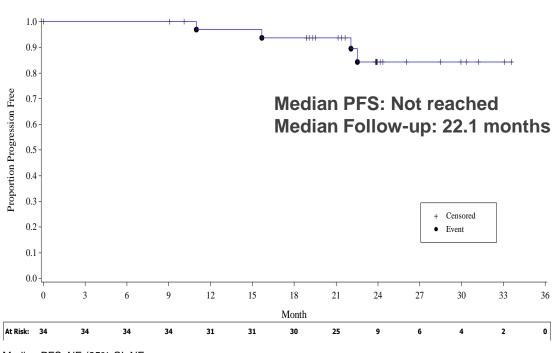
### 94% ORR and median PFS not reached in CLL

## Best % Tumor Reduction CLL Parts 1 & 2



## Data cut: 16APR2021; Evaluable CLL Part 1 & 2 patients (n=34); Patients were considered evaluable for response if they had 1-dose of cirmtuzumab and had 1-post baseline tumor assessment; SPD= sum of product of diameters; Number under bars represent baseline SPD; NE= not estimable

## Progression-Free Survival CLL Parts 1 & 2



Median PFS: NE (95% CI: NE

Oncternal Data 19MAY2021

## **CIRLL Trial Cirmtuzumab + Ibrutinib: Summary**

#### **Data Update at ASCO 2021**



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#### MCL:

- Clinical activity compares favorably to published singleagent ibrutinib data\*
  - ORR 83% (15/18)
  - CR rate 39% (7/18)
  - CRs durable for 8-30+ months
  - Clinical benefit 94% (17/18)
  - Median PFS and OS not reached, regardless of prior number of therapies, after a median follow-up of 18.9 months
- Encouraging clinical activity in high-risk sub-populations
  - Ki-67 levels ≥30% (n=9): **89%** ORR (3 CR, 5 PR)
  - > 1 prior systemic therapy (n=9): 89% ORR (5 CR, 3 PR)
  - Prior ibrutinib (n=4): **100%** ORR (2 CR, 2 PR)
  - Prior SCT or CAR-T (n=6): 100% ORR (4 CR, 2 PR)

#### CLL/SLL:

- The combination of cirmtuzumab plus ibrutinib is a welltolerated and active regimen in CLL
  - Updated Part 1 & 2 results:
    - ORR 94% (32/34)
    - CR rate 15% (5/34); 3 with clinical CR
    - Clinical Benefit 100% (34/34)
    - One patient achieved CR durable for >17 months off all therapy
    - Median PFS and OS not reached after median follow-up of 22.1 months
  - Updated randomized cohort (Part 3) results to be presented 2H 2021
- No additional toxicity when cirmtuzumab is combined with ibrutinib
- The combination of cirmtuzumab plus ibrutinib has been well tolerated, with treatment emergent adverse events and hematologic abnormalities consistent with, or slightly lower than those reported for ibrutinib alone
  - There have been no dose-limiting toxicities and no serious adverse events attributed to cirmtuzumab alone

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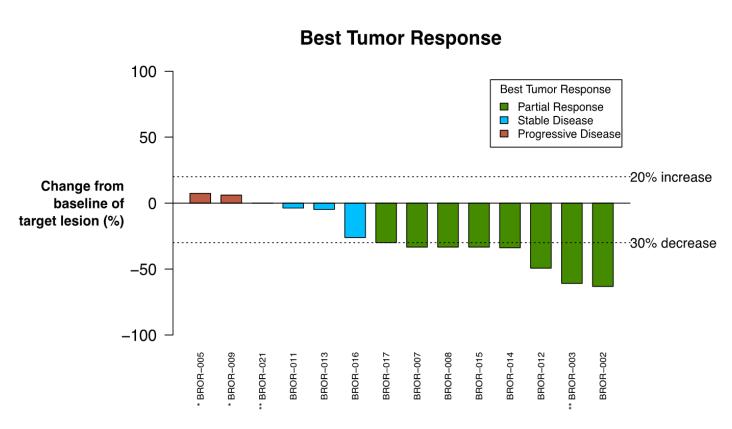
<sup>\*</sup>Historical data with single-agent ibrutinib in MCL population with similar distribution of prior lines of therapy reported overall ORR 66% and CR rate 20% (Rule et al. 2017 Br J Haem); such data may not be directly comparable due to differences in study protocols, conditions and patient populations.

# HER2-negative Breast Cancer: Cirmtuzumab + Paclitaxel Interim Data Presented at AACR: ORR 57%



- Investigator sponsored trial at UC San Diego, Barbara Parker & Rebecca Shatsky
- Patients with HER2 negative, metastatic or locallyadvanced unresectable breast cancer
- Cirmtuzumab 600 mg/month + paclitaxel weekly at 80 mg/m2 IV
- 15 patients, median of 6 prior therapies for metastatic disease
  - 4/15 patients had triple negative breast cancer
- Adverse events (AEs) were consistent with known safety profile of paclitaxel alone
- 100% of tumors expressed ROR1
  - (8/8 fresh or archival tissue)
- 57% objective response rate
  - Similar to previous interim data reported
  - 8 PRs among 14 evaluable patients
  - One PR durable for 52 weeks, ~6 months on cirmtuzumab alone
  - 4 additional patients had stable disease

Shatsky 2021 AACR ClinicalTrials.gov Identifier: NCT02776917



<sup>\*</sup> BROR-05 and BROR-09 had stable disease with targeted lesion response, overall response was PD due to new or worsening non-targeted lesions. \*\* BROR-03 and BROR-21 were still on treatment as of 2/26/2021. BROR-01 was not included in the graph due to progressive disease symptoms 3 weeks after treatment initiation requiring study discontinuation before first imaging assessment.

### Historical reported weekly paclitaxel ORR ~30%(1)

(1) Weekly paclitaxel ORR: 21% - Miller 2007 NEJM, 32-42% - Seidman 2008 JCO, 32% - Kim 2017 Lancet Oncol, 29% - Schmid 2019 JCO. Disclaimer: Results not based on head-to-head clinical studies. The results from historical trials not directly comparable and do not imply a clinical benefit of cirmtuzumab + paclitaxel over paclitaxel alone.

## Cirmtuzumab Consolidation for Treatment of CLL Patients with Detectable MRD on Venetoclax



- Investigator-sponsored, single-center two-stage study to determine the efficacy of cirmtuzumab in patients with measurable disease on venetoclax for at least 1 year who have detectable disease (MRD > 0.01% in the blood or marrow)
- Following 6 months of cirmtuzumab + venetoclax, patients are assessed for MRD in the blood/marrow.

#### Screening

0.01%)

Dx of CLL/SLL
At least 1 year of venetoclax
Detectable MRD in blood or marrow (>

Cirmtuzumab 600 mg IV day 1, 15, 29, then q28d (7 total infusions)



Primary Endpoint
uMRD in marrow
at end of
combination
therapy

Venetoclax 400 mg PO daily

<u>Primary Feasibility Endpoint:</u>
Undetectable MRD (uMRD) rate
after Cirmtuzumab + Venetoclax

<u>Secondary and Exploratory</u> <u>Endpoints:</u> Safety, time to next treatment, gene expression changes

#### Main inclusion criteria:

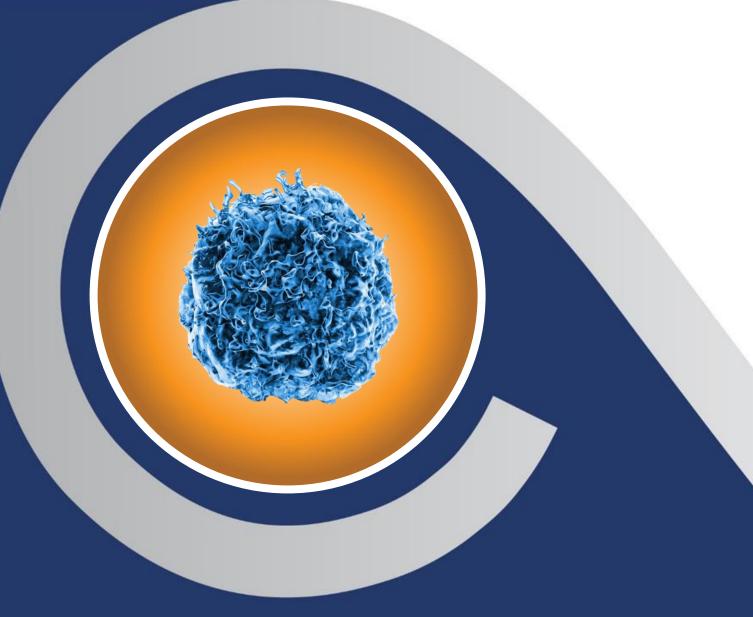
- CLL or SLL
- Detectable CLL (> 0.01% CLL cells in the blood or marrow)
- Must have received at least 12 months of venetoclax. (may be receiving venetoclax at the time of screening and study entry.)

#### **Statistical Considerations**

- Success rate of 25% uMRD considered compelling.
- Success rate of < 5% would be considered not compelling.
- n =16, 80% power to reject  $H_0$ ,  $\alpha$  < 5%

ClinicalTrials.gov Identifier: NCT04501939

uMRD = Undetectable Minimal Residual Disease





**ROR1 CAR-T Program** 

## **CAR-T Cell Therapy Targeting ROR1 Addresses Two Common Challenges**



### Current CAR-T Cell Therapy Weaknesses

#### **Treatment failures**

- Resistance to CAR-T therapy, frequently due to mutations, downregulation or loss of the non-essential target antigen
  - For example: CD19, BCMA

#### Safety concerns

 CAR-T cell therapy safety issues related to activation by normal cells expressing the target antigen

## Strengths of Targeting ROR1

### Potential for fewer antigen negative relapses

- ROR1 expression associated with aggressive tumor phenotype
- ROR1 mutation or loss might render cancer cells less aggressive and susceptible to chemotherapy

#### **Potential safety advantages**

- No crossreactivity of cirmtuzumab to normal human tissues in IND-enabling studies
- No serious adverse events related to cirmtuzumab-only observed in clinical studies
- ROR1 ADC VLS-101 no unusual organ toxicity\*



## **ROR1 CAR-T: Program Overview**

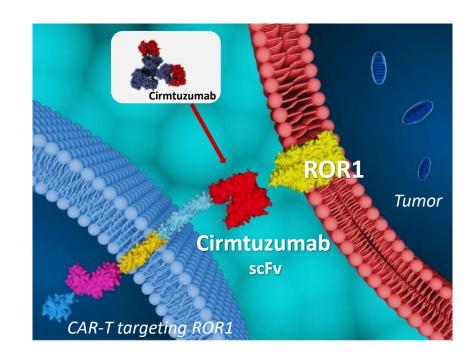


#### **DEVELOPMENT STATUS**

- Utilizing cirmtuzumab scFv as targeting component
- Preclinical data in hematologic and solid tumor models
- IND-enabling activities initiated
- Karolinska Institutet R&D collaboration for ROR1-targeting CAR-T and CAR-NK cell therapies
- Agreement with Lentigen for lentivirus production and manufacturing
- Shanghai Pharma collaboration for clinical trials

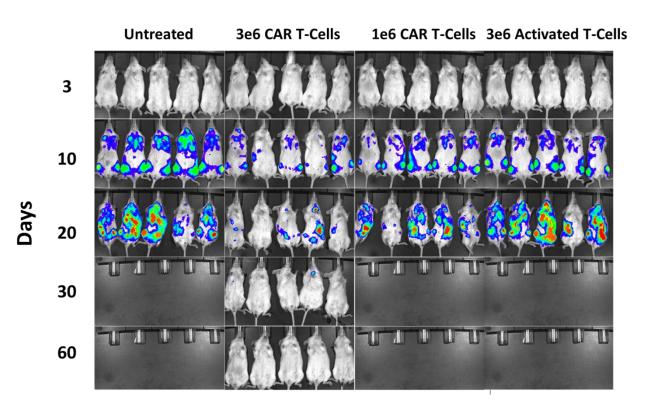
#### **OPPORTUNITY**

- Selective targeting strategy across multiple tumor indications based
- First human proof-of-concept in hematological cancers, then expansion into solid tumors

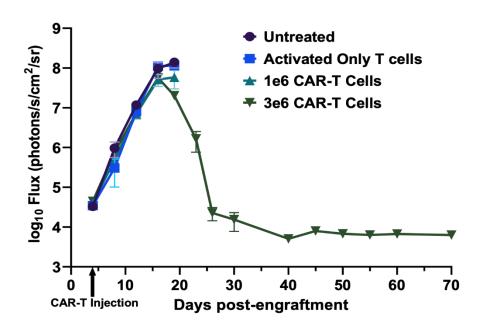


### **ROR1 CAR-T Cells Showed Potent Anti-Tumor Activity In CLL Preclinical Model**





Bioluminescence imaging of mice inoculated with MEC1-ROR1 cells and with ROR1 CAR T-cells. Animals treated with CAR-T cells had reduced disease burden compared to controls.



Bioluminescence imaging of MEC1-ROR1 cells following treatment with ROR1 CAR-T cells. Mice treated with 3e6 CAR-T reduced the leukemic burden to background levels by day 30 and controlled disease for remainder of study. Animals in the control groups (untreated, ATC or lower 1e6 dose) had to be sacrificed on day 20.

## **Oncternal's Two-Pronged CAR-T Cell Therapy Development Strategy**



Demonstrate safety and efficacy of ROR1 CAR-T cell therapy in humans

- Demonstrate evidence of clinical safety and activity
- Reduce technology risk: autologous, heme indication susceptible to CAR-T cell therapy
- SPH collaboration for clinical trials
- If successful, rapidly initiate clinical development in U.S. or Europe



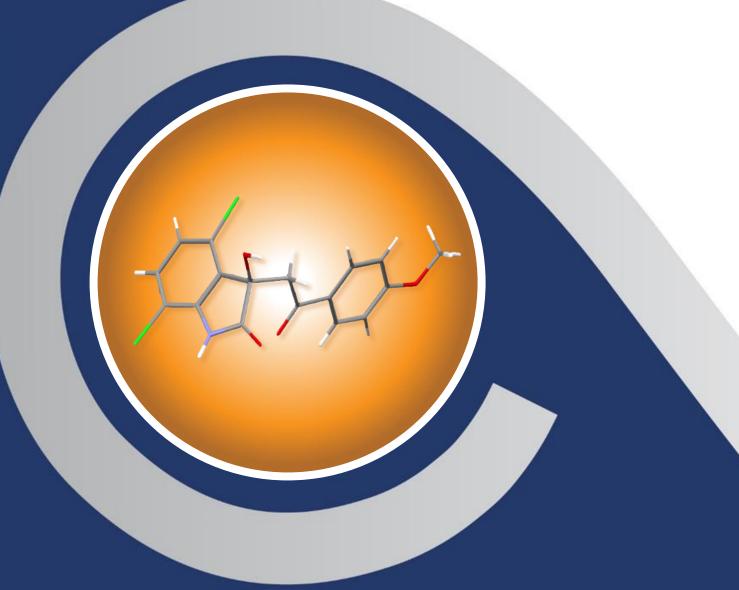


Develop next-generation cell therapies targeting ROR1

- Introduce cutting-edge cell therapy technologies
- Partnerships
- Allogeneic CAR-T and CAR-NK
- Solid tumors







**TK216** 

Targeted ETS Oncoprotein Inhibitor

## **TK216: First-in-Class Targeted ETS Oncoprotein Inhibitor**



#### **OPPORTUNITY**

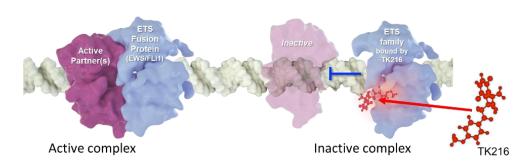
- Fast-to-market strategy in Ewing sarcoma (>95% ETS+)
  - Rare Pediatric Disease Designation, Orphan Drug Designation and Fast Track Status granted by FDA; Potentially Pediatric Voucher eligible
- Significant market potential in other cancers with ETS alterations
- COM patent coverage through 2037

#### **MECHANISM OF ACTION**

- Novel small molecule inhibitor of ETS family oncoproteins
  - Designed to prevent/disrupt formation of transcriptionally-active protein complex
- ETS transcription factors regulate many target genes implicated in cancer development and progression

#### **DEVELOPMENT STATUS**

 Encouraging activity in ongoing expansion cohort for relapsed/refractory Ewing sarcoma. ETS = E26 Transformation-Specific oncogene family



# Unmet Medical Need Relapsed / Refractory Ewing Sarcoma



- Nearly all Ewing sarcoma driven by translocations of ETS family oncogenes (EWS-FLI1 85-90%, EWS-ERG ~10%)
  - ETS transcription factors regulate many genes implicated in cancer development and progression
- Orphan disease, second most common pediatric bone tumor
  - U.S. incidence ~430 p.a.<sup>(1)</sup>
  - U.S. prevalence ~4,000 <sup>(1)</sup>
- Median age at diagnosis 15 years
- No standard second-line treatment and poor prognosis
  - Metastatic EWS: 5-year OS ~30%
  - Recurrent EWS: 5-year OS ~10-15%



ETS = E26 Transformation-Specific oncogene family

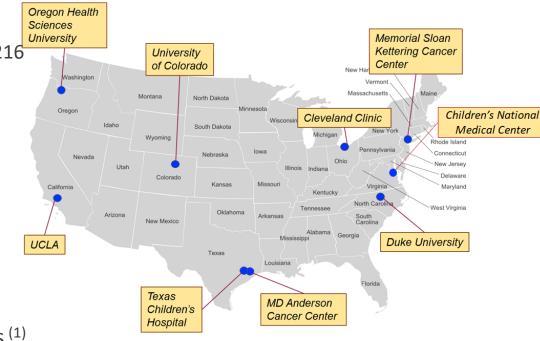
# Phase 1/2 Study of TK216 in Patients with Relapsed/Refractory Ewing Sarcoma: Early Evidence of Clinical Activity, Enrolling Expansion Cohort



3+3 dose and schedule escalation cohorts completed

Total 68 patients with relapsed/refractory Ewing sarcoma treated with TK216

- Median number of prior theories: 3 (range: 1, 9)
- Recommended Phase 2 dose (RP2D) established:
   TK216 200 mg/m²/day for 14 days + vincristine 0.75 mg/m² day 1
- <u>Safety</u>: generally well-tolerated, with dose limiting toxicity of manageable myelosuppression and no obvious off-target toxicity
- <u>PK</u>: drug plasma levels at RP2D exceeded those associated with anti-cancer activity in preclinical models
- Activity at RP2D: 45% disease control rate among 31 evaluable patients (1)
  - 2 durable complete responses (one surgical CR): no evidence of disease at 24+ months and 14+ months on study
- Enrollment in Phase 2 expansion cohort is ongoing



## **TK216 Demography & Baseline Characteristics**

#### **Interim Data Presented at ASCO 2021**



	All Patients n=68	Cohort 9 & Expansion (RP2D) n=39
Median Age (years)	27.0 (11.0, 77.0)	27.0 (11.0, 77.0)
Male, n (%)	43 (63.2)	25 (64.1)
ECOG* 0-1, n (%)	52 (96.3)	29 (93.5)
Median time from diagnosis to study start (years)	3.4 (0.4, 18.0)	3.4 (0.4, 18.0)
Prior surgery, n (%)	53 (77.9)	32 (82.1)
Prior radiotherapy, n (%)	57 (83.8)	34 (87.2)
Median number of prior systemic treatments	3.0 (1.0, 9.0)	3.0 (1.0, 8.0)
Metastases at study entry, n (%)	67 (98.5)	39 (100)
Bone only	6 (8.8)	2 (5.1)
• Lung only	31 (45.6)	21 (53.8)
Bone and Lung only	10 (14.7)	8 (20.5)
Other location	20 (29.4)	8 (20.5)

Data Cut: 16APR2021; \*ECOG (Eastern Cooperative Oncology Group) performance score was evaluated in 54 and 31 all treated and Cohort 9 & Expansion patients, percentage is based on number of patients with ECOG evaluated; Median estimates are shown with (min, max)

## Population: Heavily pre-treated and high disease burden

## TK216 Overall Best Clinical Response and PFS in R/R Ewing Sarcoma

**Interim Data Presented at ASCO 2021** 

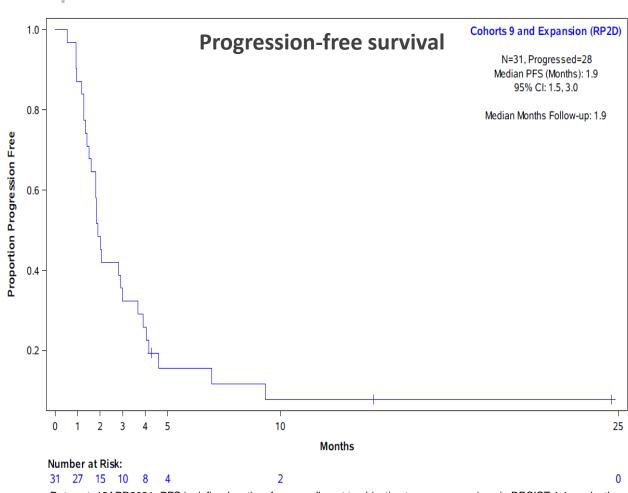


## Notable responses and disease control observed at the RP2D

#### **Overall Best Clinical Response**

	•	
	All Patients evaluable=54	Cohort 9 & Expansion (RP2D) evaluable=31
Overall Response Rate (ORR), n (%)	3 (5.6)	3 (9.7)
CR*, n (%)	2 (3.7)	2 (6.5)
PR**, n (%)	1 (1.9)	1 (3.2)
SD, n (%)	13 (24.1)	11 (35.5)
PD, n (%)	38 (70.4)	17 (54.8)
Disease Control Rate (DCR), n (%)	16 (29.6)	14 (45.2)
Median Duration of SD (95% CI)	1.8 (1.4, 3.7)	1.9 (1.4, 3.7)

Data cut: 16APR2021; Patients were considered evaluable for response if they completed 1-cycle of treatment and had 1-post baseline tumor assessment; CR- complete response, PR- partial response, SD- stable disease, PD- progressive disease; ORR- number and percent of patients that achieved CR or PR; DCR- number of patients that achieved CR, PR or SD; \* Two confirmed CRs with no PD at data cut; \*\* Unconfirmed PR observed in target lesion at Cycle 4 then PD observed at Cycle 6 in non-target lesions



Data cut: 16APR2021; PFS is defined as time from enrollment to objective tumor progression via RECIST 1.1, or death from any cause, which ever occurs first; Evaluable patients were used for PFS analyses

# Case Study: First Sustained Complete Response with TK216 in Patient with Metastatic Relapsed/Refractory Ewing Sarcoma



#### **Patient background**

- 19-year-old male. Initially diagnosed with metastatic Ewing sarcoma involving the clavicle and lungs
- Prior treatment included VDC/IE, surgery, radiation, irinotecan/ temozolomide, bevacizumab, pazopanib
- Progressing with enlarging lung metastases when enrolled in TK216 clinical trial
- Enrolled in Phase 1 study of TK216 at MSKCC in 2019

#### **Treatment and outcome**

- Received TK216 in final dose-finding cohort (200 mg/m²/day)
- Resolution of target lesions after two cycles of single-agent TK216
  - Treatment well tolerated, with minimal myelosuppression
  - Vincristine added starting in third cycle
- Residual non-target 7 mm lung lesion excised after 6 cycles of therapy, leading to surgical complete remission
- Treatment ongoing, no evidence of disease at >24 months on study



2 cycles single-agent TK216

All target lesions resolved



**Baseline** 

## Case Study: Second Complete Response with TK216 in Patient with **Metastatic Relapsed/Refractory Ewing Sarcoma**



After 2 cycles

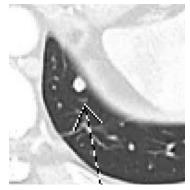
- Patient: 51-year-old with Ewing sarcoma diagnosed June 2018
  - 10-cm tumor near the right kidney and multiple lung metastases
- **Extensive prior treatment:** 
  - Chemotherapy: VDC/IE, high-dose ifosfamide
  - Surgery: right nephrectomy and vascular reconstruction
- Recurrence prior to enrollment: Multiple new and enlarging lung lesions
- **TK216:** Enrolled at MD Anderson Cancer Center in January 2020
  - Treated at RP2D (TK216 200 mg/m²/day for 14 days + vincristine 0.75 mg/m² day 1)
  - Myelosuppression in Cycle 1, did not recur in Cycle 2 with growth factor support and no TK216 dose reduction
- **Clinical response:** 
  - Deep partial response after 2 cycles, with 90% reduction of target lesions
  - Complete response after 6 cycles of therapy
- Treatment ongoing, with no evidence of disease at >14 months on study

**Pretreatment** 



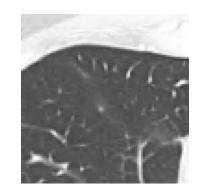


**ROI** #4









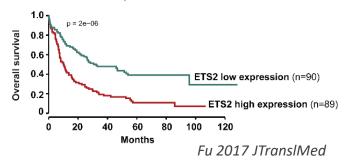
Pre-treatment: each lesion 10 mm After 2 cycles: one lesion 0 mm, one lesion 2 mm

## Additional Opportunities for TK216 in Cancers with ETS Alterations

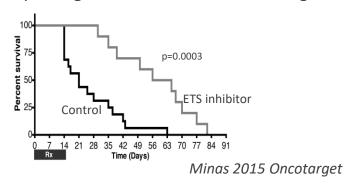


### **Acute Myeloid Leukemia (AML)**

- ETS family proteins overexpressed in ~30% AML cases
- ETS2 overexpression associated w/ shorter OS



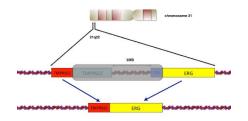
- Sensitivity of AML cell lines to TK216 was proportional to level of ETS overexpression
- ETS inhibition using TK216 precursor prolonged survival in EWS-FLI1 transgenic



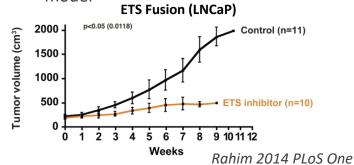
#### **Prostate Cancer**

55% of men with advanced prostate cancer carry ETS family gene fusion TMPRSS2-ERG associated with androgen resistance and poor clinical outcomes

TMPRSS2 and ERG are located on chromosome 21

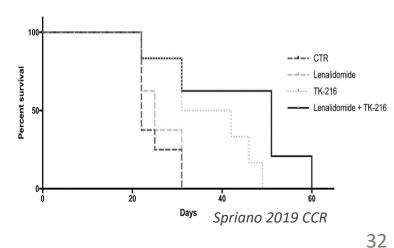


ETS inhibition using TK216 precursor demonstrated anti-tumor activity in human prostate cancer xenograft model



### **Diffuse Large B Cell** Lymphoma (DLBCL)

- ETS proteins overexpressed in DLBCL
- ETS family member genes are essential for activated B-cell-like (ABC) DLBCL and germinal center B-cell type (GCB) **DLBCL**
- Synergy with lenalidomide and venetoclax shown in preclinical models
- Single agent TK216 and combo therapy demonstrated potent anti-tumor activity in DLBCL xenograft model



ONCT Corporate Presentation May 28 2021





# BUSINESS & FINANCIALS

## **Financial Information**



Description	Ticker: ONCT (Nasdaq)
Cash & Cash Investments @ March 31, 2021	\$111M
Cash Runway into 2023	
Debt	\$0M
Capitalization:	
Common Shares Outstanding	49.4M
Options / Warrants in the Money @ Mar 31, 2021 <sup>(1)</sup>	7.7M
Fully Diluted	57.1M
Non-Dilutive Support	
<ul> <li>CIRM Grant for CIRLL Study</li> </ul>	~\$14M
<ul> <li>Ibrutinib CTM for CIRLL Study</li> </ul>	<b>Expanded Supply</b>
	Agreement

<sup>(1)</sup> Excludes out-of-the-money stock options and warrants totaling ~0.6M

## **Anticipated Pipeline Milestones**



### Cirmtuzumab

<ul> <li>MCL clinical data update for ongoing Phase 1/2*</li> </ul>	2Q 2021
<ul> <li>CLL clinical data update for ongoing Phase 1/2*</li> </ul>	2Q 2021
<ul> <li>HER2-negative breast cancer clinical data update for ongoing Phase 1b</li> </ul>	2Q 2021
<ul> <li>Preclinical data in additional ROR1-expressing tumors</li> </ul>	3Q 2021
<ul> <li>ROR1 CAR-T cell therapy first-in-human dosing</li> </ul>	1H 2022

### • TK216

<ul> <li>Ewing sarcoma Phase 1/2 expansion cohort data update*</li> </ul>	2Q 2021
<ul> <li>Preclinical data in additional ETS-driven tumors</li> </ul>	3Q 2021

<sup>\*</sup>ASCO 2021 data is included in press releases dated May 19, 2021

## **Corporate Highlights**



#### CIRMTUZUMAB: POTENTIALLY FIRST-IN-CLASS MONOCLONAL ANTIBODY TARGETING ROR1

- Ongoing clinical studies in MCL, CLL and breast cancer, and preclinical studies in additional cancer indications
- Interim Phase 1/2 results for cirmtuzumab + ibrutinib in MCL compare favorably to historical single-agent ibrutinib data
- Interim Phase 1b results for cirmtuzumab + paclitaxel in HER2<sup>neg</sup> breast cancer continue to show encouraging ORR
- Dialogue with FDA regarding potential accelerated approval study design in MCL

#### ROR1 CAR-T CELL THERAPY: AGREEMENTS WITH SHANGHAI PHARMA, KAROLINSKA INSTITUTET AND LENTIGEN

In development to treat hematological malignancies and solid tumors

#### **TK216: TARGETED ETS INHIBITOR**

- Two durable complete responses in patients with metastatic relapsed/refractory Ewing sarcoma in ongoing Phase 1/2
- Additional opportunities in ETS-driven tumor indications

#### MULTIPLE DATA CATALYSTS EXPECTED IN NEXT 12 MONTHS

- Clinical data updates expected in MCL, CLL, breast cancer and Ewing sarcoma
- ROR1 CAR-T cell therapy expected to reach clinic in 1H 2022

#### **EXPERIENCED MANAGEMENT AND BOARD OF DIRECTORS**