



TARGETING CANCER

New Science. New Cancer Therapies. New Hope.

#### FORWARD LOOKING STATEMENTS

This presentation includes 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 1932, 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," or the "Company") 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 completing and announcing results of clinical trials of the Company's product candidates, the anticipated market potential, duration of patent coverage, ability to obtain and maintain favorable regulatory designations and, potentially, accelerated approval pathways for the Company's product candidates and preclinical programs, and the Company's anticipated cash runway.

All forward looking statements are subject to risks and uncertainties, which include, but are not limited to: uncertainties associated with the clinical development and process for obtaining regulatory approval of Oncternal's product candidates, including potential delays in the commencement, enrollment and completion of clinical trials; inherent risks involved in the commercialization of any product, if approved; 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; the risk that unforeseen adverse reactions or side effects may occur in the course of developing and testing Oncternal's product candidates; risks associated with the COVID-19 pandemic, which may adversely impact our business operations and clinical trials, including delays in the enrollment of patients; the risk that the regulatory landscape that applies to the development programs for Company's product candidates may change over time; the risk that competitors may develop technologies or product candidates more rapidly than Oncternal, or that are more effective than Oncternal's product candidates, which could significantly jeopardize Oncternal's ability to develop and successfully commercialize its product candidates; the Company's dependence on the success of its product development programs; the risk that Oncternal may be unable to obtain sufficient additional capital to continue to advance the development of its product candidates and preclinical programs; the risk that the benefits associated with orphan drug designation may not be realized, including that orphan drug exclusivity may not effectively protect a product from competition and that such exclusivity may not be maintained; and the risk that, if an orphan designated product, including cirmtuzumab, receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

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 reports filed with the SEC by Oncternal, including its most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed 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.

**ONCT Corporate Presentation March 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
- 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 2H 2021 in China

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

## **Experienced Team**





James Breitmeyer, MD, PhD CEO, Founder, Director







**Richard Vincent** CFO







Raj Krishnan PhD









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



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



Daniel Kisner, MD



**Bill LaRue** Director



Director





















Edwina Baskin Bey, MD Acting CMO









**Gunnar Kaufmann, PhD** CSO







Rosemary Mazanet, MD, PhD Director









Xin Nakanishi, PhD Director







Charles Theuer, MD, PhD Director



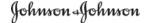










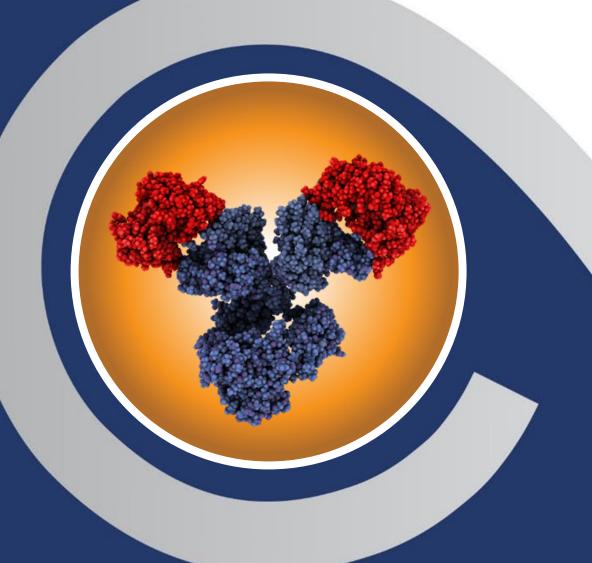


## **Robust Pipeline – Novel Product Candidates in Multiple Indications**



Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Modality	
	Mantle Cell Lymphoma (MCL)				ROR1 mAb		
Cirmtuzumab	Chronic Lymphocytic Leukemia (CLL)						
	Breast Cancer						
	Ewing Sarcoma				4		
TK216	Acute Myeloid Leukemia (AML)				ETS oncoprotei	n inhibitor	
	Prostate Cancer				ETS oncoprotes	Timbicol	
ROR1 CAR-T	Heme Cancers						
	Solid Tumors				ROR1 CAR-T cell to	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: ASH 2020)
  - Orphan Drug Designations for MCL and CLL
- CLL: P2 with ibrutinib (data: ASH 2020); 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**

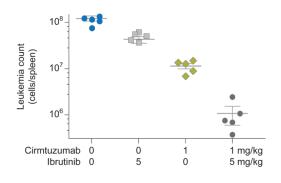
- Collaborations with Shanghai Pharma (China) and Karolinska Institutet. Manufacturing with Lentigen
- First-in-human dosing in China expected 2H 2021

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



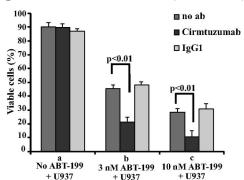
#### **Synergism with Targeted Agents**

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

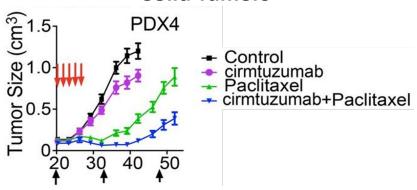


Yu 2017 Leukemia

Synergistic with venetoclax (ABT-199)

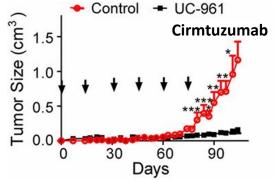


## Supporting Preclinical Data in Solid Tumors



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

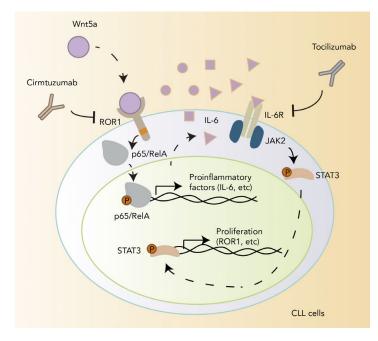
Zhang 2019 PNAS



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

## ROR1 Antagonism Suppresses Inflammation in CLL

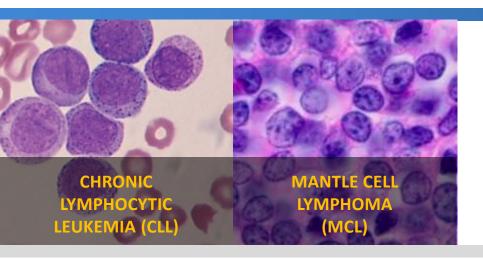
- Cirmtuzumab blocks pro-inflammatory NF-kB signaling pathway in CLL cells
  - Potential explanation for safety profile observed in patients



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

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## CIRLL Trial Cirmtuzumab + Ibrutinib: Best Overall Response in MCL and CLL Data Update at ASH 2020 – MCL ORR Increased to 87%



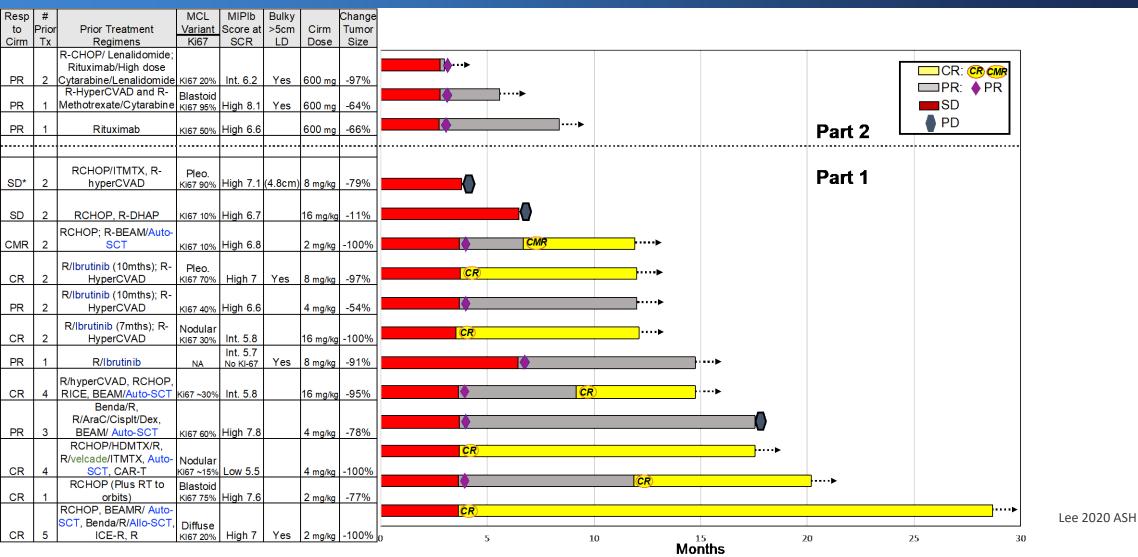
		Evaluable patients	Best ORR** (CR & PR)	CR	PR	Clinical Benefit (CR, PR, SD)
MCL	Part 1	12	<b>83%</b> 10/12	<b>58%</b> 7/12	<b>25%</b> 3/12	100%
	Part 2	3	100% 3/3	0	<b>100%</b> 3/3	100%
	Parts 1&2	34	<b>91%</b> 31/34	<b>3%</b> 1/34	<b>88%</b> 30/34 (26 PR, 4 PR-L)	100%
CLL	Part 3	15 Cirmtuzumab + Ibrutinib	<b>93%</b> 14/15	0	<b>93%</b> 14/15 (12 PR, 2 PR-L)	100%
		<b>7</b> ibrutinib	100% 7/7	0	100% 7/7	100%

<sup>\*</sup>Evaluable patients for efficacy are those who have completed treatment and have had the planned 3 month post cirmtuzumab + ibrutinib combination therapy imaging studies or had documented or clinical PD following 28 days of therapy. \*\*Includes both confirmed and unconfirmed best responses. For CLL: iwCLL criteria were used. For MCL, Cheson 2007/2014 was used. For MCL, data include one complete metabolic remission (CMR); blinded review of bone marrow biopsy was indeterminant for tumor involvement. Note: One Part 2 MCL patient (PR) met criteria for a CR with a morphologically normal marrow but with minimal marrow disease by flow. All ASH 2020 data presented herein as of Oct 30, 2020.

### MCL Patient Characteristics and Swimmer Plot

#### Cirmtuzumab + Ibrutinib Data Update at ASH 2020

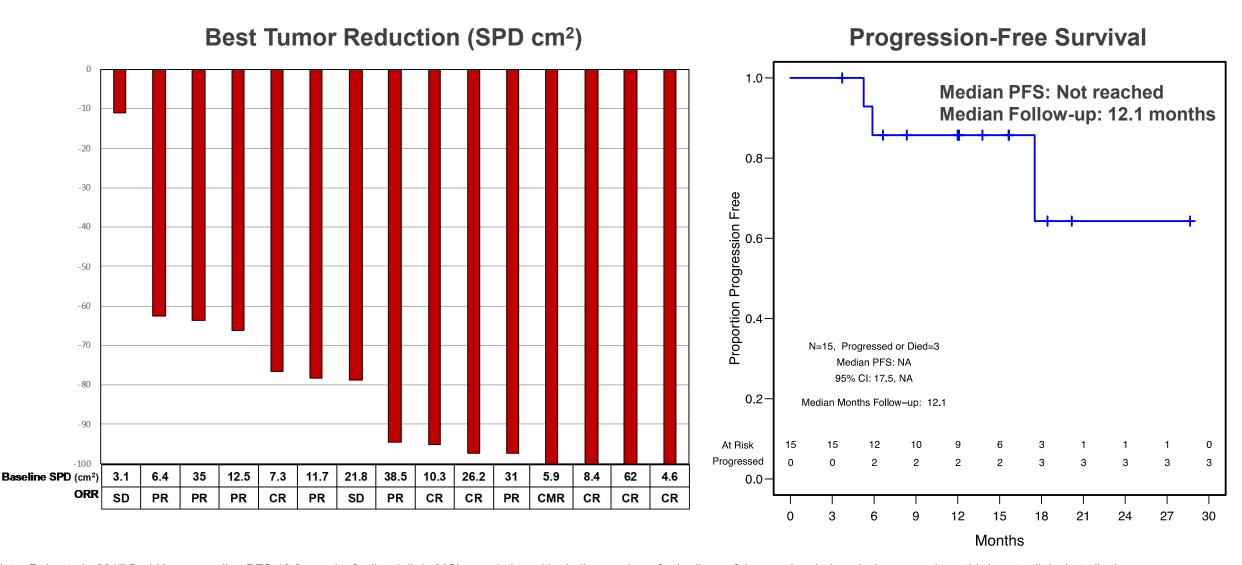




Note: Part 1 patients started Ibrutinib on Day 28, and Part 2 patients, on Day 0. Bars represent activity of patients on treatment to last response assessment; arrows indicate pt continues on treatment. Time to first response: 87% (13/15) CR/PR and 57% (4/7) CR occurred by the first evaluation after starting combined cirmtuzumab/ibrutinib.

# R/R MCL: Tumor Reduction and Progression-Free Survival Cirmtuzumab + Ibrutinib Data Update at ASH 2020





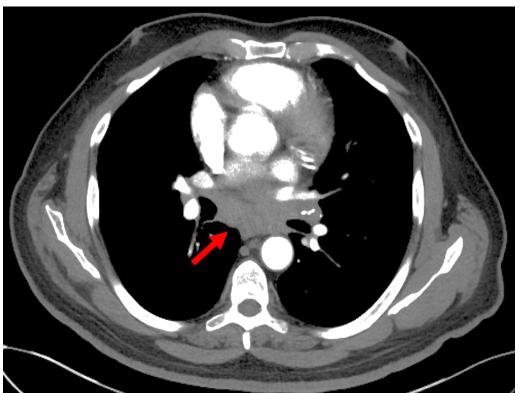
Note: Rule et al., 2017 Br J Haem: median PFS 12.8 months for ibrutinib in MCL population with similar number of prior lines of therapy (pooled analysis across three third-party clinical studies).

# Case Study: Durable Complete Response in Patient with R/R MCL in Clinical Trial of Cirmtuzumab and Ibrutinib

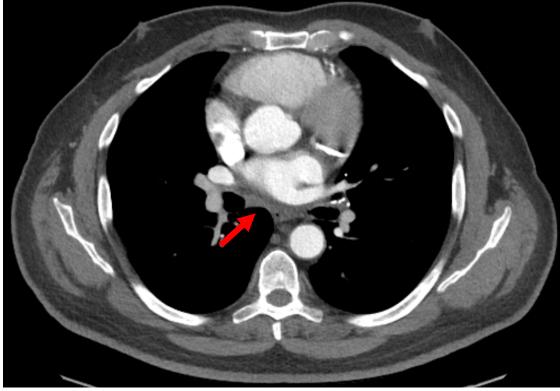


- 65-year-old male initially diagnosed in 2016 with MCL stage IV including involvement of bilateral orbits
- Initial treatment: radiation therapy and R-CHOP
- Recurred and enrolled onto Part 1 Cirmtuzumab/Ibrutinib study in 2019 at the 2mg/kg dose level
- High risk factors: Blastoid subtype; Ki-67: 75%; High MIPIb score 7.6
- After <4 mos treatment, achieved a PR and after 12 mos, a CR</li>
- Continues on therapy now >20 months and tolerating treatment well

#### **Pretreatment**



### <4 months Post Cirmtuzumab/Ibrutinib



Lee 2020 ASH

## **Cirmtuzumab + Ibrutinib Interim Clinical Results in MCL (ASH 2020) Compare Favorably to Historical Single-Agent Ibrutinib Data**

**Baseline** characteristics

Clinical

outcomes

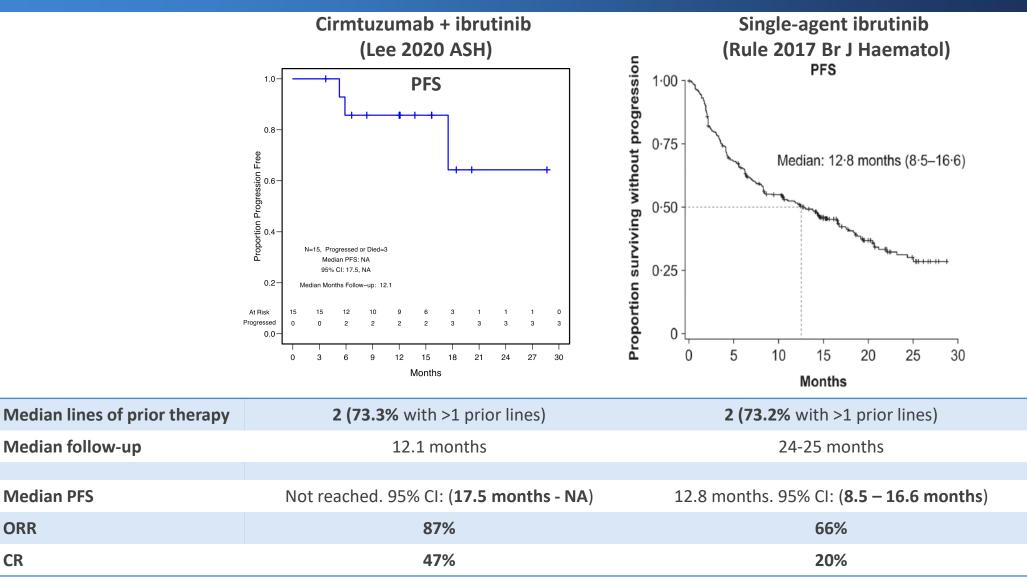
Median follow-up

**Median PFS** 

**ORR** 

CR



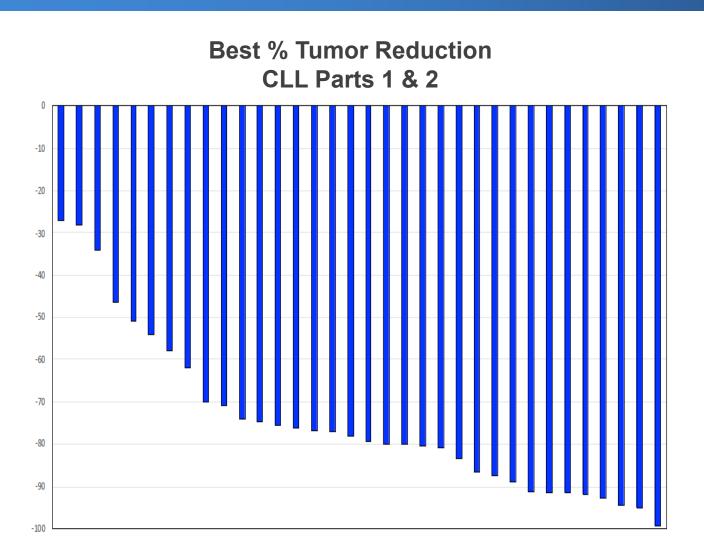


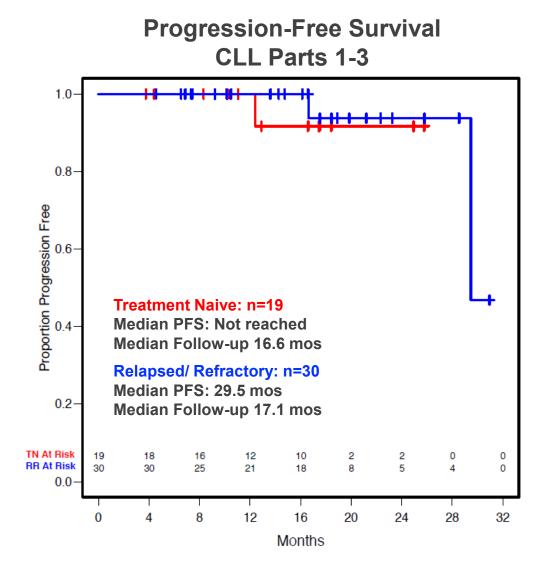
Note: Data presented are from separate studies and such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of the combination of cirmtuzumab and ibrutinib compared to single-agent ibrutinib. **ONCT Corporate Presentation March 2021** 

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

**Cirmtuzumab + Ibrutinib Data Update at ASH 2020** 







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

#### **Data Update at ASH 2020**



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#### MCL:

- Clinical activity compares favorably to published singleagent ibrutinib data\*
  - ORR 87% (12/15), CR rate 47% (7/15)
  - All CRs durable for 5 25+ months. No progressions reported after CR
  - Median PFS not reached after median follow-up of 12.1 months
- Encouraging clinical activity in high-risk sub-populations
  - Prior SCT or CAR-T (n=5): 100% ORR (4 CR, 1 PR)
  - Ki-67 levels ≥30% (n=9): **89%** ORR (4 CR, 4 PR)
  - Intermediate/high MIPI (n=14): 86% ORR (6 CR, 6 PR)
  - Prior ibrutinib (n=4): **100%** ORR (2 CR, 2 PR)

#### CLL/SLL:

- The combination of cirmtuzumab plus ibrutinib is a welltolerated and active regimen in CLL
  - ORR 92% (45/49), Clinical Benefit 100% (49/49)
  - One patient achieved CR durable for >17 months off all therapy
  - Median PFS for treatment-naïve CLL: not reached after median follow-up of 16.6 months
  - Median PFS for r/r CLL: 29.5 months after median follow-up of 17.1 months

- Adverse events reported for cirmtuzumab + ibrutinib -- typical for ibrutinib alone
  - No dose limiting toxicities or discontinuations due to cirmtuzumab
  - No Grade 3 or higher common adverse events attributed to cirmtuzumab alone

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Lee 2020 ASH

<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.

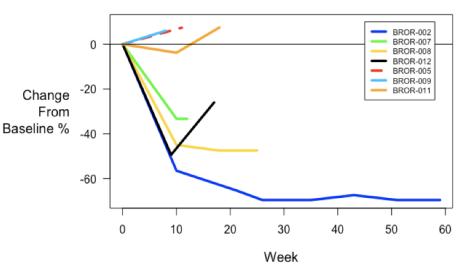
# HER2-negative Breast Cancer: Interim Phase 1 Data Cirmtuzumab + Paclitaxel Presented at SABCS 2019: ORR 57%



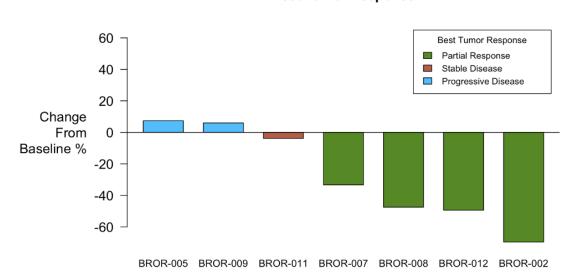
## % Tumor Volume Reduction by Week of Therapy

## Best Tumor Volume Response by Patient ORR = 57% (4/7)

#### Tumor Response by Week of Treatment



#### Best Tumor Response



### 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.

## HER2-negative breast cancer

## SABCS 2019 presentation of interim data

- Investigator sponsored trial at UC San Diego, Barbara Parker & Rebecca Shatsky
- Patients with HER2 negative, metastatic or locally-advanced unresectable breast cancer
- 600 mg cirmtuzumab monthly + 80 mg/m² paclitaxel weekly
- No DLTs or discontinuations
- Adverse events consistent with paclitaxel profile
- PK consistent with half-life of 30 days

Shatsky 2019 SABCS (data cutoff November 27, 2019)

## 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

Dx of CLL/SLL

At least 1 year of venetoclax

Detectable MRD in

blood or marrow (>

0.01%)

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



Venetoclax 400 mg PO daily

Primary Endpoint
uMRD in marrow
at end of
combination
therapy

#### <u>Primary Feasibility Endpoint:</u> Undetectable MRD (uMRD) rate

Undetectable MRD (uMRD) rate after Cirmtuzumab + Venetoclax

Secondary and Exploratory
Endpoints: Safety, time to next
treatment, gene expression
changes

#### Main inclusion criteria:

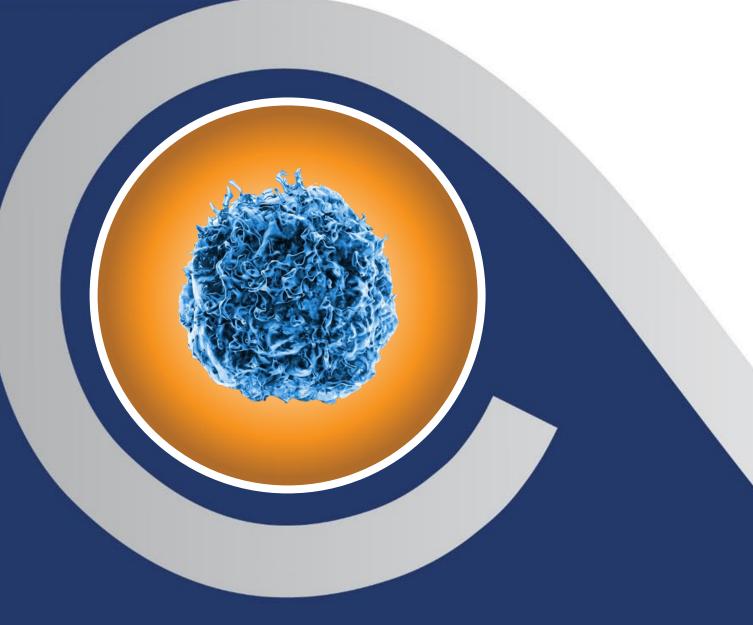
- CLL or SLL
- Detectable CLL (> 0.01% CLL cells in the blood or marrow)
- Must have received at least 12 months of venetoclax. (may be receiving venetoclax at the time of screening and study entry.)

#### **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



### 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**

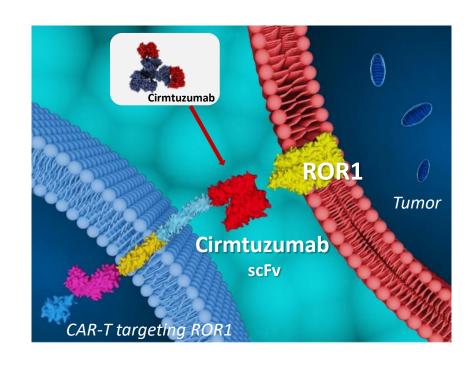


#### **DEVELOPMENT STATUS**

- 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 first-in-human study in China (2H 2021)

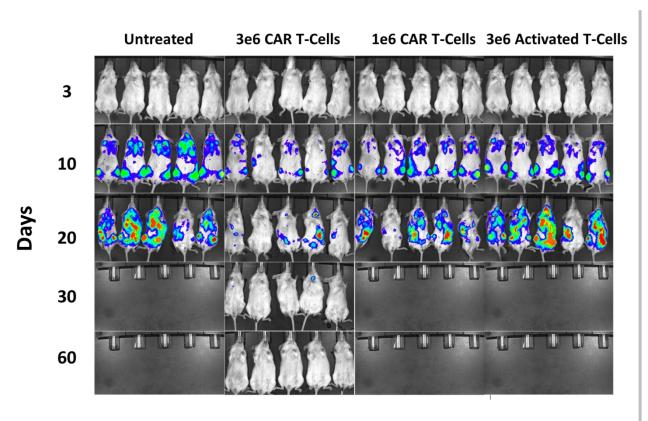
#### **OPPORTUNITY**

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

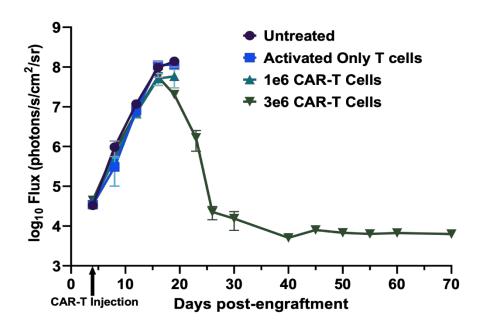


### **ROR1 CAR-T Cells Showed Potent Anti-Tumor Activity In CLL Preclinical Model**





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.

Prussak 2020 ASCO SITC

ONCT Corporate Presentation February 2021

## **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
- Target first-in-human dosing in China in 2H 2021: collaboration with SPH
- If successful, rapidly initiate clinical development in U.S. or Europe



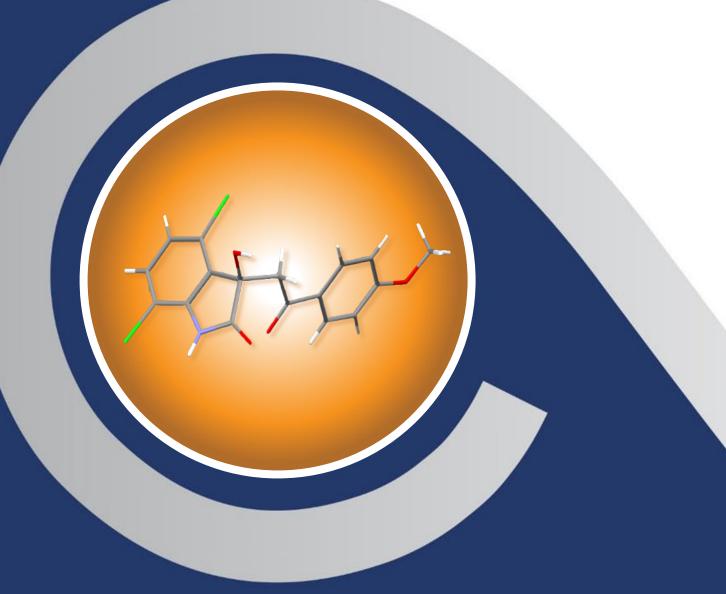


Develop next-generation cell therapies targeting ROR1

- 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

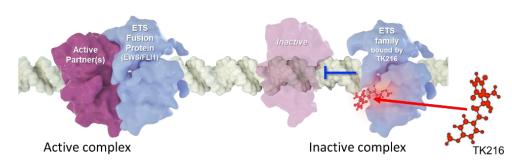
#### **MECHANISM OF ACTION**

- 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
  - 50 evaluable patients with relapsed/refractory Ewing sarcoma
  - Average of 4 prior therapies
  - 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: 43% disease control rate among 23 evaluable patients (1)
  - 2 durable complete responses (one surgical CR): no evidence of disease at 1.5+ years and 8+ months on study
  - 8 SD: median duration 100 days (range 49-213 days)
- Enrollment in expansion cohort is ongoing



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

#### **Interim Data Presented at CTOS 2020**

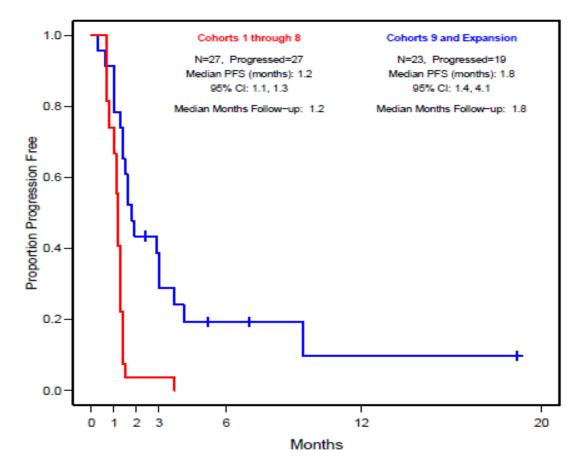


#### **Overall Best Clinical Response**

	Evaluable Patients N= 50	ORR	CR	PR	SD	Disease Control Rate CR+PR+SD
Dose Escalation Cohorts 1-6	21	0	0	0	1	4.8%
Schedule Escalation Cohorts 7-8	6	0	0	0	0	0
RP2D Cohort 9 & Expansion	23	2 (9%)	2 (9%)	0	8 (35%)	43%

Patients were considered evaluable for efficacy if they completed 2 planned cycles of treatment and follow-up tumor assessment studies or had documented or clinical PD following a complete first cycle of therapy

### **Progression-free survival**



# 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 lesion 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 months of therapy, leading to surgical complete remission
- Treatment ongoing, no evidence of disease at >1.5 years on study



2 cycles single-agent TK216

All target lesions resolved



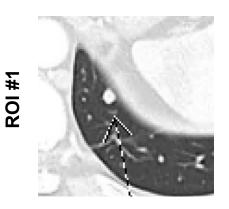
Baseline

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



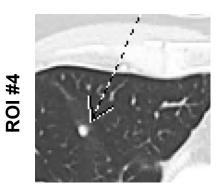
- Patient: 51-year-old with Ewing sarcoma diagnosed June 2018
  - 10-cm tumor near the right kidney and multiple lung metastases
- Extensive prior treatment:
  - Chemotherapy: vincristine/doxorubicin and ifosfamide (VAI), high-dose ifosfamide
  - Surgery: right nephrectomy and vascular reconstruction
- 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 and resolution of non-target lesions
  - · Complete response after 6 cycles of therapy
- Treatment ongoing, with no evidence of disease at >8 months on study

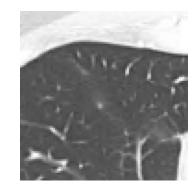
**Pretreatment** 



After 2 cycles







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

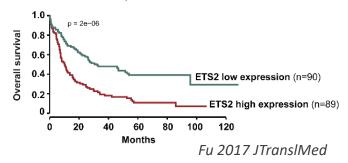
Data Cutoff 8/13/2020

## Additional Opportunities for TK216 in Cancers with ETS Alterations

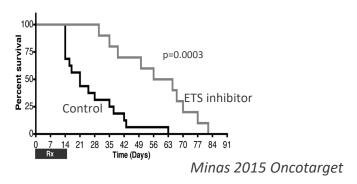


### **Acute Myeloid Leukemia (AML)**

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



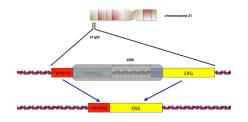
- Sensitivity of AML cell lines to TK216 was proportional to level of ETS overexpression
- ETS inhibition using TK216 precursor prolonged survival in EWS-FLI1 transgenic



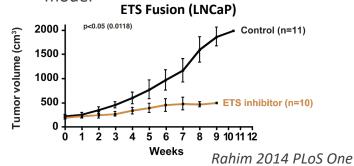
#### **Prostate Cancer**

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

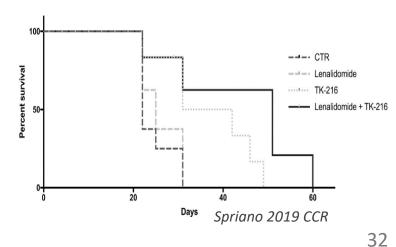


ETS inhibition using TK216 precursor demonstrated anti-tumor activity in human prostate cancer xenograft model



## **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 March 2021** 





BUSINESS & FINANCIALS

## **Financial Information**



Description	Ticker: ONCT (Nasdaq)
Cash & Cash Investments @ Dec. 31, 2020	\$117M
Cash Runway into 2023	
Debt	\$0.0M
Capitalization:	
Common Shares Outstanding	48.8M
Options / Warrants in the Money @ Dec. 31, 2020 <sup>(1)</sup>	4.1M
Fully Diluted	52.9M
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 ~4.1M

## **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>	2Q 2021
ROR1 CAR-T cell therapy first-in-human dosing in China	2H 2021
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>	2Q 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
- 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 2H 2021 in China

#### EXPERIENCED MANAGEMENT AND BOARD OF DIRECTORS