



# TARGETING CANCER

**New Science. New Cancer Therapies. New Hope.**

Company Overview – November 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 the submission of an Investigational New Drug application for ONCT-808 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.

Zilovertamab, ONCT-216, ONCT-808, and ONCT-534 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.

## **ZILOVERTAMAB (FORMERLY CIRMTUZUMAB): POTENTIALLY FIRST-IN-CLASS MONOCLONAL ANTIBODY TARGETING ROR1**

- Interim Phase 1/2 results for zilovetamab + ibrutinib in MCL compare favorably to historical single-agent ibrutinib data
- Ongoing FDA interactions regarding potential registration trial in patients with MCL

## **ONCT-808: AUTOLOGOUS CAR-T CELL THERAPY TARGETING ROR1**

- IND-enabling activities supported by Lentigen (lentivirus manufacturing) and Miltenyi Biotec (process development)
- Research collaborations for next-gen allogeneic CAR-T and CAR-NK cell therapies with Karolinska Institutet & Celularity

## **ONCT-216 (FORMERLY 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

## **ONCT-534 (FORMERLY GTX-534): DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

- Pre-clinical data in prostate cancer models suggest activity against tumors expressing androgen receptor splice variants

## **MULTIPLE DATA CATALYSTS**

- Clinical data updates in MCL, CLL, breast cancer and Ewing sarcoma
- Regulatory agreement on zilovetamab registration pathways
- ONCT-808 ROR1 CAR-T cell therapy IND submission planned in 1H 2022

# Experienced Team



**James Breitmeyer, MD, PhD**  
CEO, Founder, Director



**Richard Vincent**  
CFO



**Salim Yazji, MD**  
CMO



**Gunnar Kaufmann, PhD**  
CSO



**Raj Krishnan, PhD**  
CTO



**Chase Leavitt**  
General Counsel



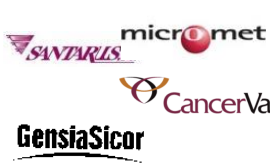
**Pablo Urbaneja**  
SVP, Corporate Development



**Steve Hamburger, PhD**  
SVP, Regulatory Affairs & Quality Assurance



**David Hale**  
Co-founder  
Board Chairman



**Michael Carter, MD**  
Director



**Jinzhu Chen, PhD**  
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**Daniel Kisner, MD**  
Director



**Rosemary Mazanet, MD, PhD**  
Director



**Bill LaRue**  
Director



**Xin Nakanishi, PhD**  
Director



**Charles Theuer, MD, PhD**  
Director



**Robert Wills, PhD**  
Director



# Robust Pipeline – Novel Product Candidates in Multiple Indications

Modality	Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3
ROR1 mAb	Zilovertamab (Cirmtuzumab)	Mantle Cell Lymphoma (MCL)				
		Chronic Lymphocytic Leukemia (CLL)				
		Breast Cancer				
ETS Oncoprotein inhibitor	ONCT-216 (TK216)	Ewing Sarcoma				
		Diffuse Large B Cell Lymphoma (DLBCL)				
		Prostate Cancer				
ROR1 Cell Therapy	ONCT-808 (Autologous CAR-T)	Hematological Malignancies				
	Allogeneic	Solid Tumors				
Dual-Action AR Inhibitor	ONCT-534	Prostate Cancer				

## **ZILOVERTAMAB: MONOCLONAL ANTIBODY TARGETING ROR1**

**ROR1 TARGETED CELL THERAPY PROGRAM**

**ONCT-216: TARGETED ETS INHIBITOR**

**ONCT-534: DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

**FINANCIAL INFO AND UPCOMING MILESTONES**




# 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**
  - Deep target expertise and experience

## ROR1 Expressed on Multiple Solid and Liquid Tumors



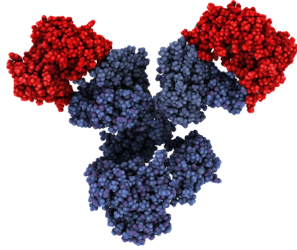
MCL	95%
CLL	95%
Uterus	96%
Lymphoma	90%
Prostate	90%
Skin	89%
Pancreatic	83%
Adrenal	83%
Lung	77%
Breast	75%
Testicular	73%
Colon	57%
Ovarian	54%

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

Zhang 2012 AJP

# Two Development Programs Targeting ROR1

## Zilovertamab ROR1 mAb



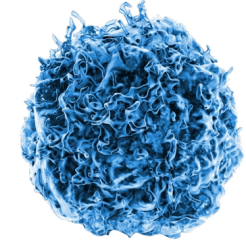
### Background

- High-affinity IgG1 humanized ROR1 mAb
- Binds to tumors but not normal adult tissues
- Patent coverage through 2033
- Supported by ~\$14M non-dilutive CIRM grant and ibrutinib product donation
- Zilovertamab is the mAb used in VLS-101 ADC
  - VelosBio spun out in 2018, acquired by Merck for \$2.75B

### Development status

- MCL: lead indication. P2 with ibrutinib (data: ASCO 2021)
  - FDA Orphan Drug Designations for MCL and CLL
- CLL: P2 with ibrutinib (data: ASCO 2021); P1b with venetoclax
- HER2-negative breast cancer: P1b with paclitaxel

## ROR1 CELL THERAPY PROGRAM



### Background

- ROR1 expression on many tumor types
- Potential safety and efficacy advantages
- VLS-101 ADC data at ASH 2020 reported no off-tumor ROR1 organ toxicities

### Development status

- ONCT-808 utilizing zilovertamab scFv selected as the lead autologous CAR-T product candidate
- Collaborations with Shanghai Pharma (China), Karolinska Institutet and Celularity Inc.
- Manufacturing with Lentigen and Miltenyi Biotec
- IND submission expected in 1H 2022

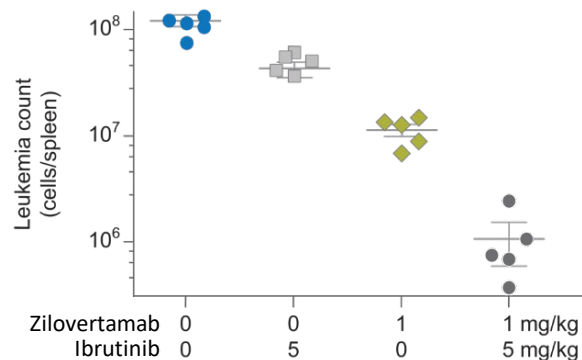


# Zilovertamab Extensive Preclinical Research

Potential as combination therapy, multiple tumor indications and safety advantage

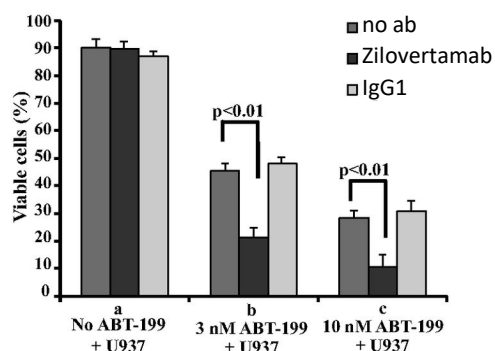
## Synergistic with Targeted Agents

- Synergistic with ibrutinib in CLL + MCL



Yu 2017 Leukemia

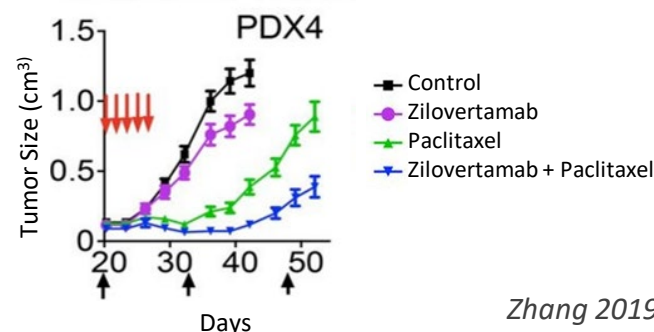
- Synergistic with venetoclax (ABT-199)



Rassenti 2017 PNAS

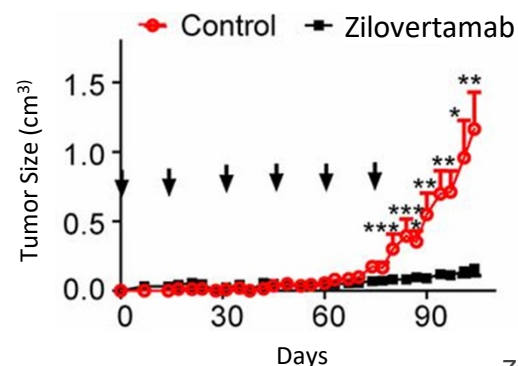
## Active in Solid Tumor Models

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



Zhang 2019 PNAS

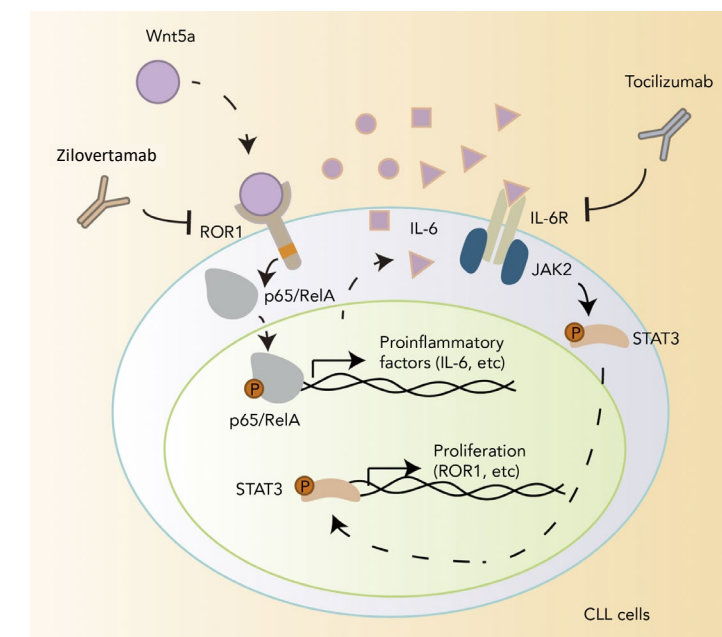
- Anti-tumor activity in PDX models of ovarian cancer



Zhang 2014 PNAS

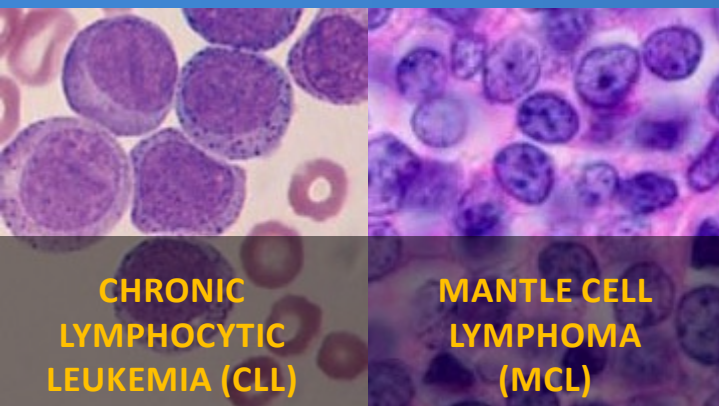
## Inhibits Inflammatory Pathway

- Zilovertamab blocks pro-inflammatory JAK/STAT signaling pathway in CLL cells
- Mechanism for potential safety advantage observed in patients



Chen 2019 Blood

# CIRLL Trial (CIRM-0001) – Phase 1/2 Study of Zilovertamab and Ibrutinib in Patients with MCL and CLL



- ✓ Encouraging interim clinical data in MCL and CLL presented at ASCO 2021
- ✓ Opened new treatment cohort in MCL patients who are refractory to prior BTK inhibitor treatment, or who had an inadequate response to ibrutinib
- ✓ Ongoing dialogue with FDA about potential registrational study in MCL

## STUDY DESIGN

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

**DOSE-FINDING COHORT**

- Zilovertamab at 2, 4, 8 & 16 mg/kg and 300 & 600 mg doses evaluated
- Ibrutinib added after one month

*Enrolled*

**PART 2 (in CLL & MCL)**

**DOSE-EXPANSION COHORT**

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

*MCL Phase 2 enrolling  
CLL enrolled*

**PART 3 (in CLL)**

**RANDOMIZED EFFICACY**

- Zilovertamab + ibrutinib vs. ibrutinib
- Primary endpoint: Complete Response rate

*Enrolled*

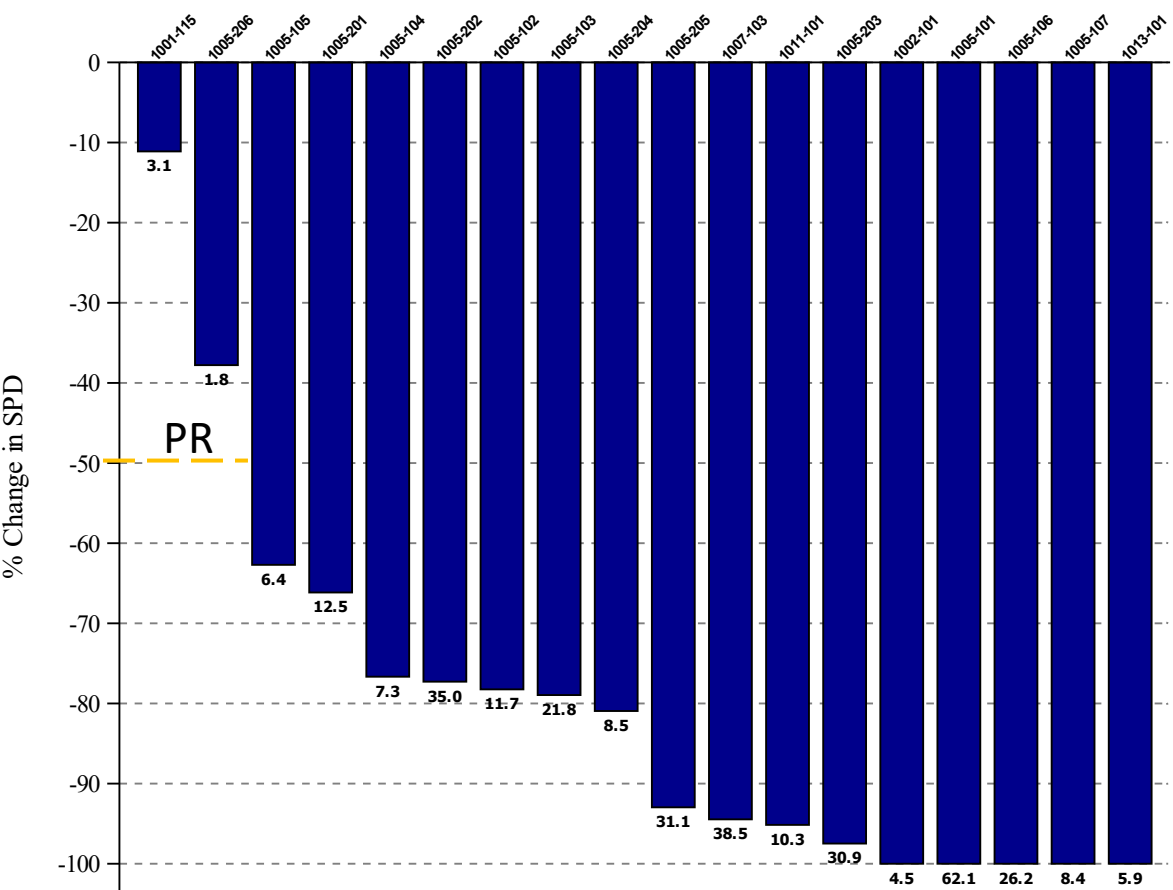
- Ibrutinib from Pharmacyclics/AbbVie
- Collaboration with UC San Diego and CIRM

*ClinicalTrials.gov Identifier: NCT03088878*

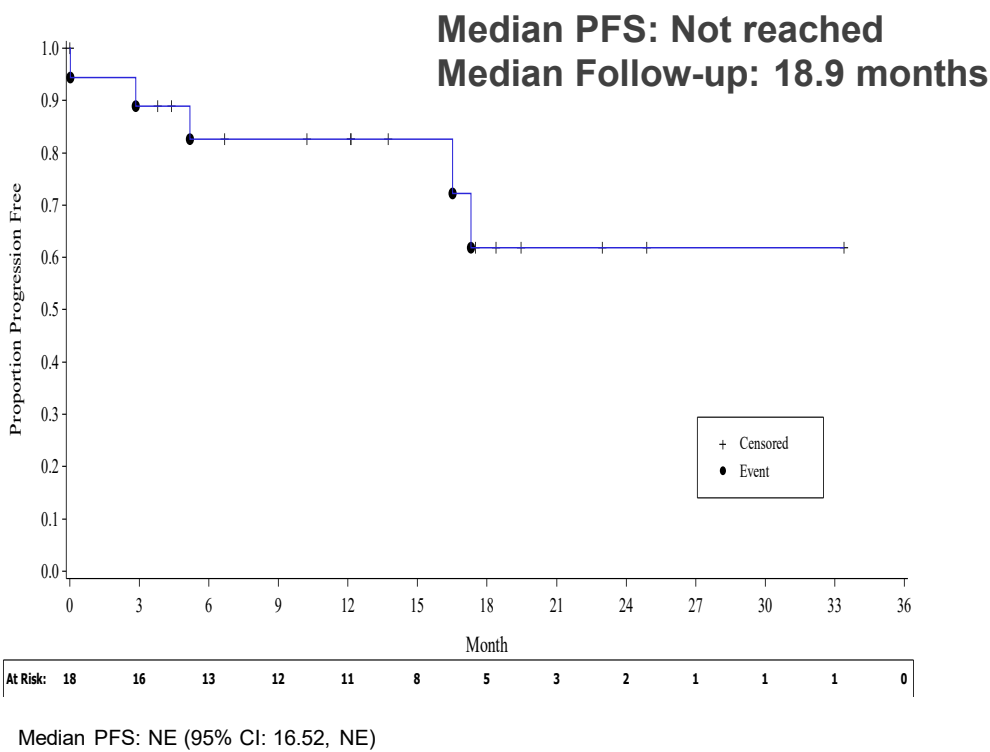
**CIRLL** = Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma  
**CIRM** = California Institute for Regenerative Medicine

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

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



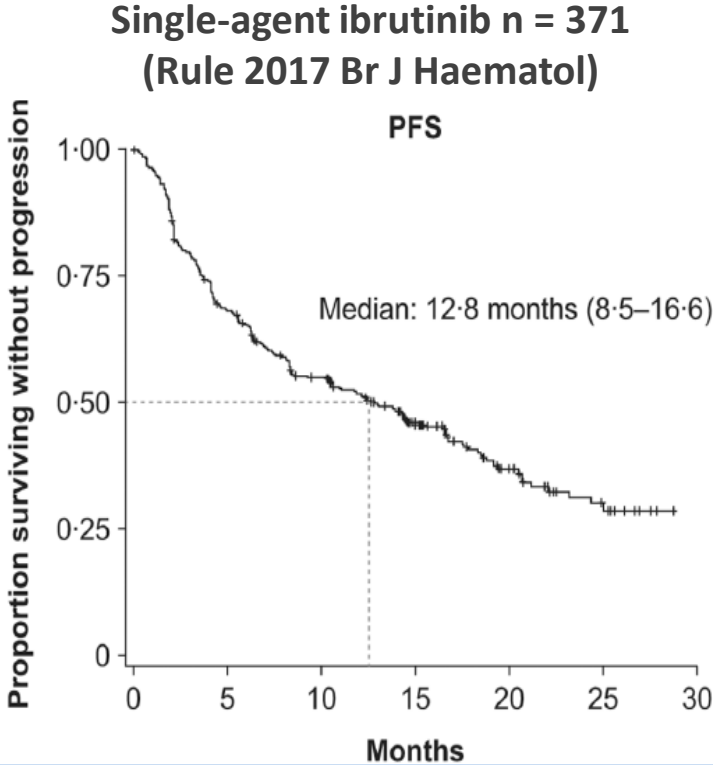
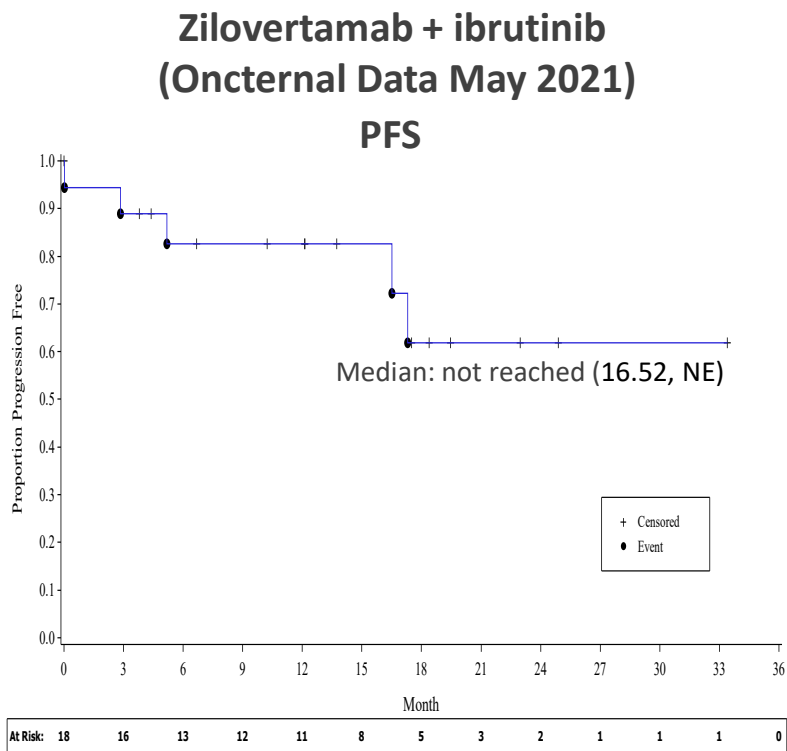
Progression-Free Survival



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

# R/R MCL: Compares Favorably to Historical Single-Agent Ibrutinib Data

## Zilovertamab + Ibrutinib Data Update at ASCO 2021

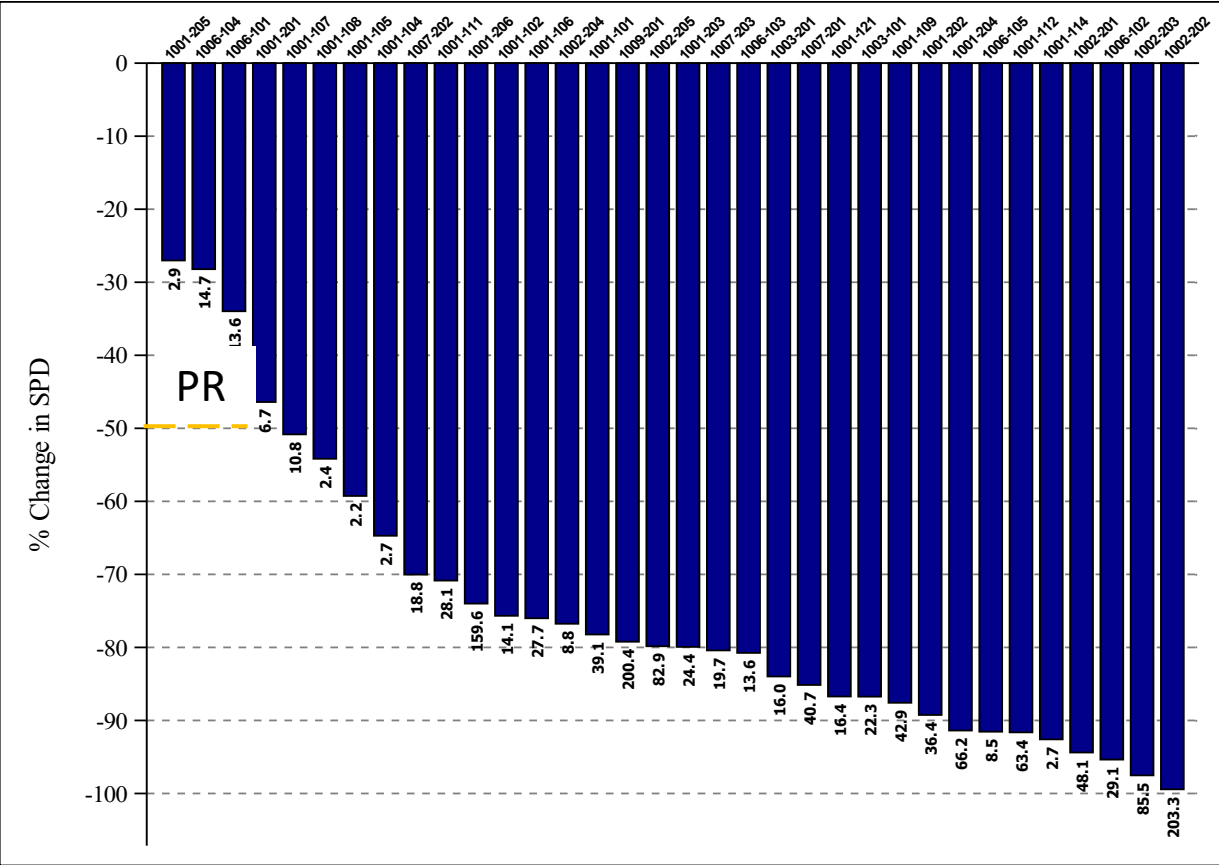


Baseline characteristics	Median lines of prior therapy	2	2
	Median follow-up	18.9 months	24-25 months
Clinical outcomes	Median PFS	Not reached. 95% CI: (16.52 months - NE)	12.8 months. 95% CI: (8.5 – 16.6 months)
	ORR	83%	66%
	CR	39%	20%

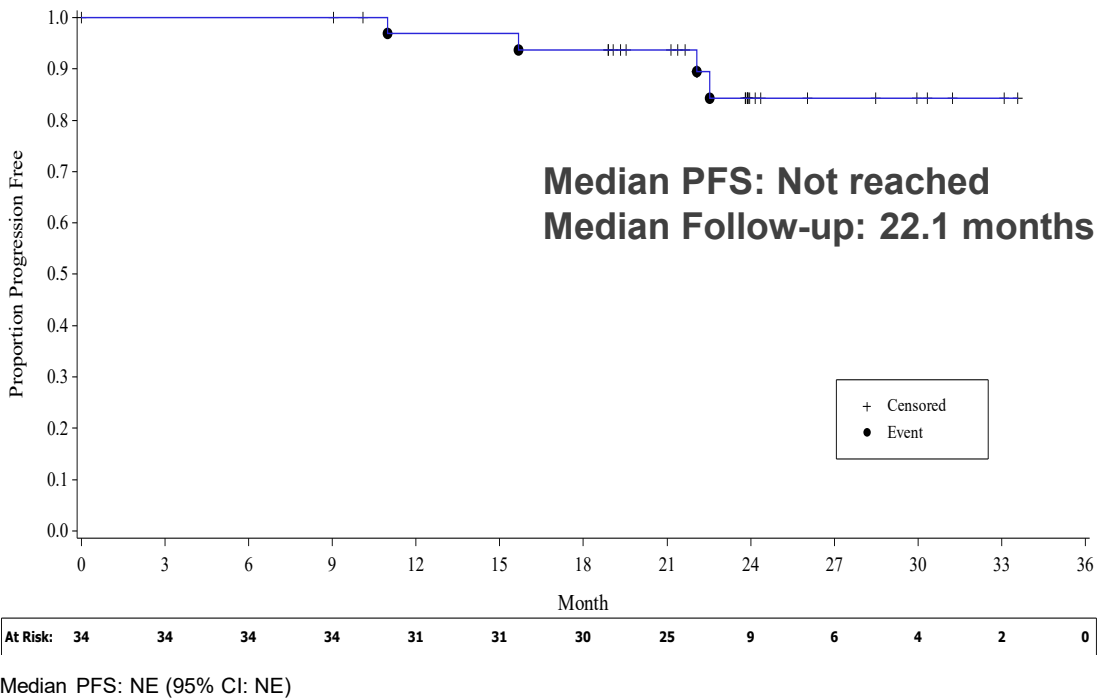
Note: Data presented are from separate studies and such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of the combination of zilovertamab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

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

Best % Tumor Reduction  
CLL Parts 1 & 2



Progression-Free Survival  
CLL Parts 1 & 2



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

### MCL:

- **Clinical activity compares favorably to published single-agent ibrutinib data<sup>(1)</sup>**
  - ORR 83% (15/18)
  - CR rate 39% (7/18)
  - CRs all durable at 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  $\geq 30\%$  (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:

- **The combination of zilovertamab plus ibrutinib is a well-tolerated 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 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 zilovertamab is combined with ibrutinib**

The combination has been well tolerated, with treatment emergent adverse events and hematologic abnormalities consistent with, or slightly lower than those reported for ibrutinib alone. For example, in patients with MCL, Grade 3-4 neutrophil decrease was documented in **11.5%** of patients with zilovertamab plus ibrutinib, compared to **29%** for ibrutinib alone from its registration study

There have been no dose-limiting toxicities and no serious adverse events attributed to zilovertamab alone

(1) 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.



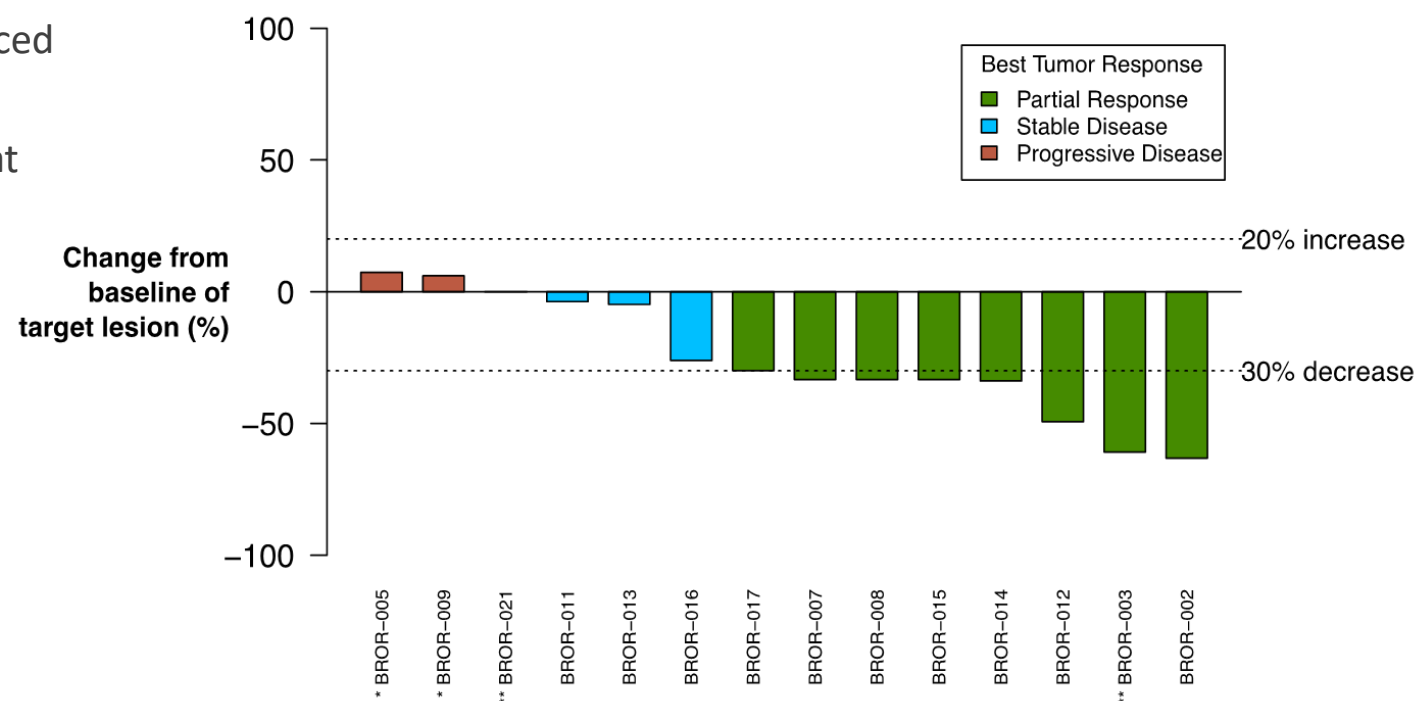
# HER2-negative Breast Cancer: Zilovertamab + Paclitaxel

Interim Data Presented at AACR: ORR 57%

- Fully enrolled investigator sponsored trial at UC San Diego (PIs: Barbara Parker & Rebecca Shatsky)
- Patients with HER2-negative, metastatic or locally-advanced unresectable breast cancer
- Zilovertamab 600 mg every 4 weeks + paclitaxel weekly at 80 mg/m<sup>2</sup> IV
- Median of 6 prior therapies for metastatic disease; 4 patients with 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 per protocol
  - One PR durable for 52 weeks, ~6 months on zilovertamab alone
  - 4 additional patients had stable disease

Shatsky 2021 AACR  
ClinicalTrials.gov Identifier: NCT02776917

## Best Tumor Response



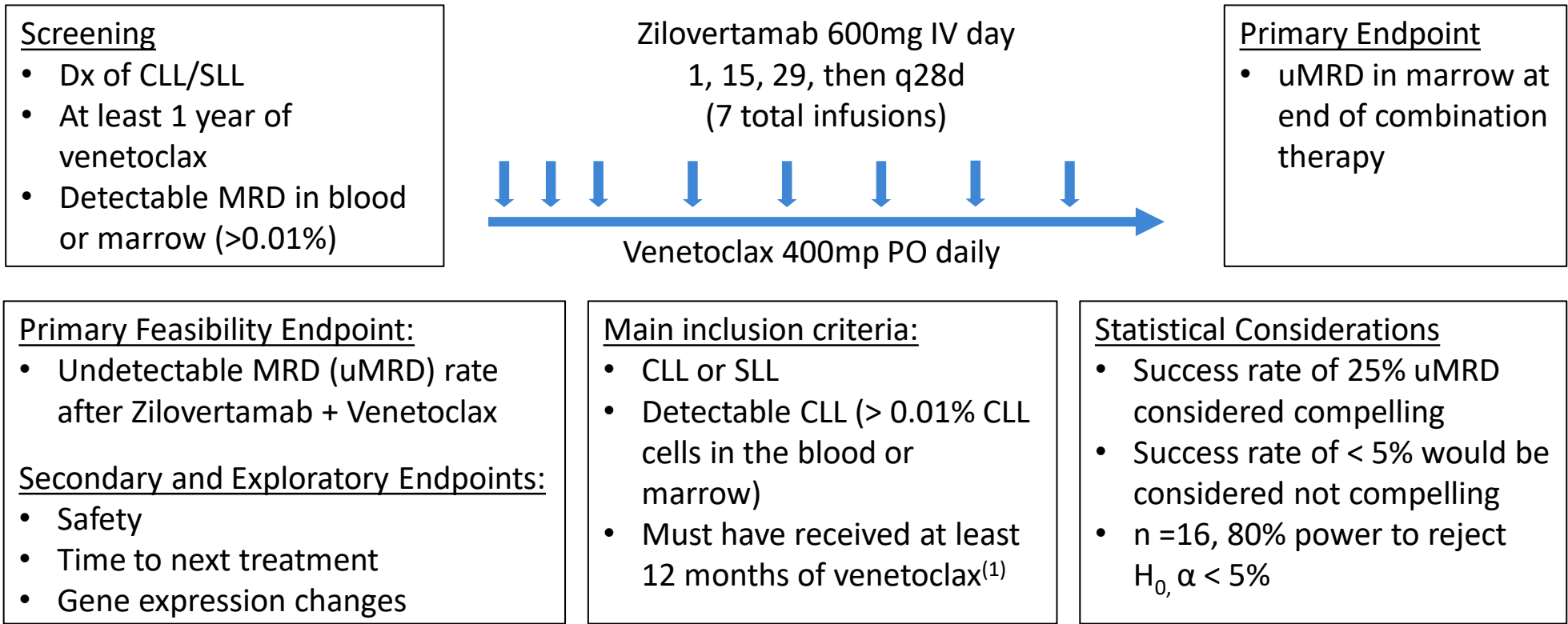
\* BROR-05 and BROR-09 had stable disease with targeted lesion response, overall response was PD due to new or worsening non-targeted lesions. \*\* BROR-03 and BROR-21 were still on treatment as of 2/26/2021. BROR-01 was not included in the graph due to progressive disease symptoms 3 weeks after treatment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

## Historical reported weekly paclitaxel ORR ~30%<sup>(1)</sup>

(1) Weekly paclitaxel ORR (21%) Miller 2007 NEJM; ORR (32-42%) Seidman 2008 JCO; ORR (32%) Kim 2017 Lancet Oncol; ORR (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 zilovertamab + paclitaxel over paclitaxel alone.

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

- Investigator-sponsored, single-center two-stage study to determine the efficacy of zilovetamab 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 zilovetamab + venetoclax, patients are assessed for MRD in the blood/marrow



(1) may be receiving venetoclax at the time of screening and study entry  
uMRD = Undetectable Minimal Residual Disease

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**ONCT-534: DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

**FINANCIAL INFO AND UPCOMING MILESTONES**

# Oncternal's Two-Stage ROR1 Cell Therapy Development Strategy

1

## ONCT-808 autologous ROR1 CAR-T cell therapy

- Quick path to clinical safety and activity
- Reduced technology risk: autologous CAR-T
- Reduced indication risk: B cell malignancies susceptible to CAR-T cell therapy
- Shanghai Pharma collaboration for clinical trials



a Miltenyi Biotec Company

2

## Next-generation allogeneic cell therapies targeting ROR1

- Incorporate cutting-edge technologies to overcome immunosuppression & CAR-T resistance
- Partnerships with Celularity and Karolinska Institutet
- Allogeneic CAR-T and CAR-NK cell therapies
- Hematologic and solid tumor indications



### Michael Wang, MD

*Endowed Professor in the Department of Lymphoma & Myeloma at MD Anderson Cancer Center*

- Director of the Mantle Cell Lymphoma Program of Excellence and Co-Director of the B-Cell Lymphoma Moon Shot Program at MD Anderson
- Lead PI in Tecartus® registrational study
- Over 200 peer-reviewed publications

### Angela Shen, MD, MBA

*Clinical and Translational Market Sector Leader  
Mass General Brigham*

- Deep clinical, regulatory, and strategic expertise in autologous and allogeneic cell therapies
- Experienced CMO in the cell therapy biotech space
- Led clinical team responsible for designing and launching Kymriah® registrational study

### Marcela Maus, MD, PhD

*Associate Professor, Medicine, Harvard Medical School  
Director of Cellular Immunotherapy, Cancer Center,  
Massachusetts General Hospital*

- Translational physician-scientist in cancer immunology
- Lab focuses on the design, generation, and use of innovative forms of immune cell engineering
- Trained in the laboratories of Katherine High, Michel Sadelain, and Carl June

### Sadik Kassim, PhD

*Chief Technology Officer at Vor Biopharma*

- Chief Scientific Officer at Mustang Bio
- Led the BLA and MAA CMC efforts for Kite's Tecartus®
- Former Head of Early Analytical Development for Novartis' Cell and Gene Therapies Unit

# Autologous ROR1 CAR-T Cell Therapy Program Overview

## Oncternal autologous CAR-T cell program progressing well:

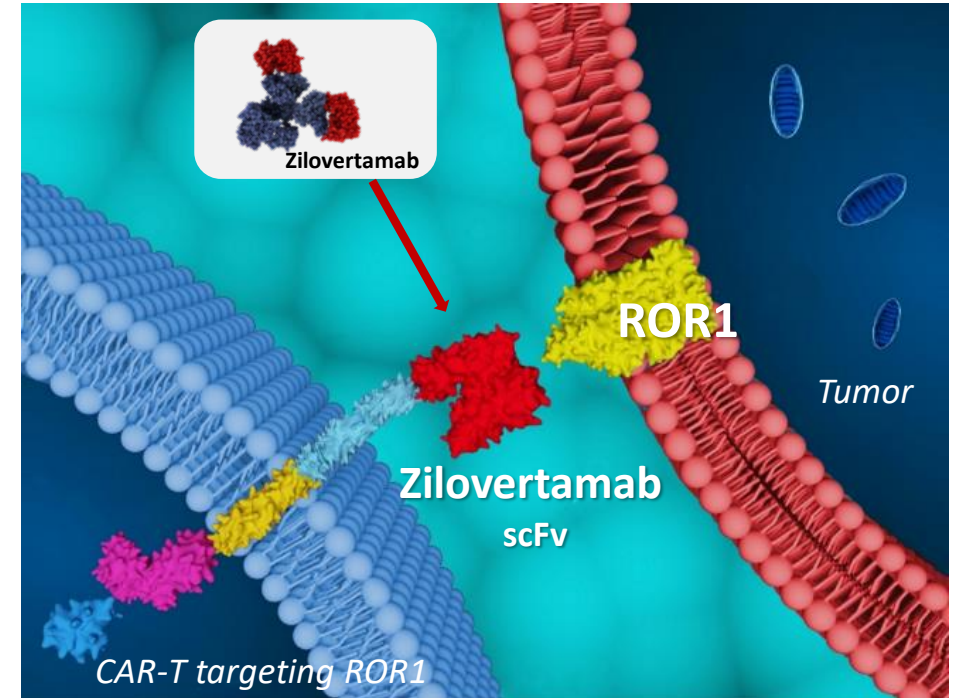
- Selected ONCT-808 as lead autologous CAR-T cell therapy product candidate

## Risk mitigation:

- Utilizing clinically-validated **ROR1-targeting moiety** derived from **zilovertamab** while retaining proven CAR signaling and co-activation domains (4-1BB/CD3zeta)
- Working with **Lentigen** for GMP lentivirus manufacturing, and **Miltenyi Biotec** for CAR T cell process development focusing on closed system automated cell processing
- **First-in-human (FIH)** study: Demonstration of **clinical safety** and **activity** in B-cell malignancies

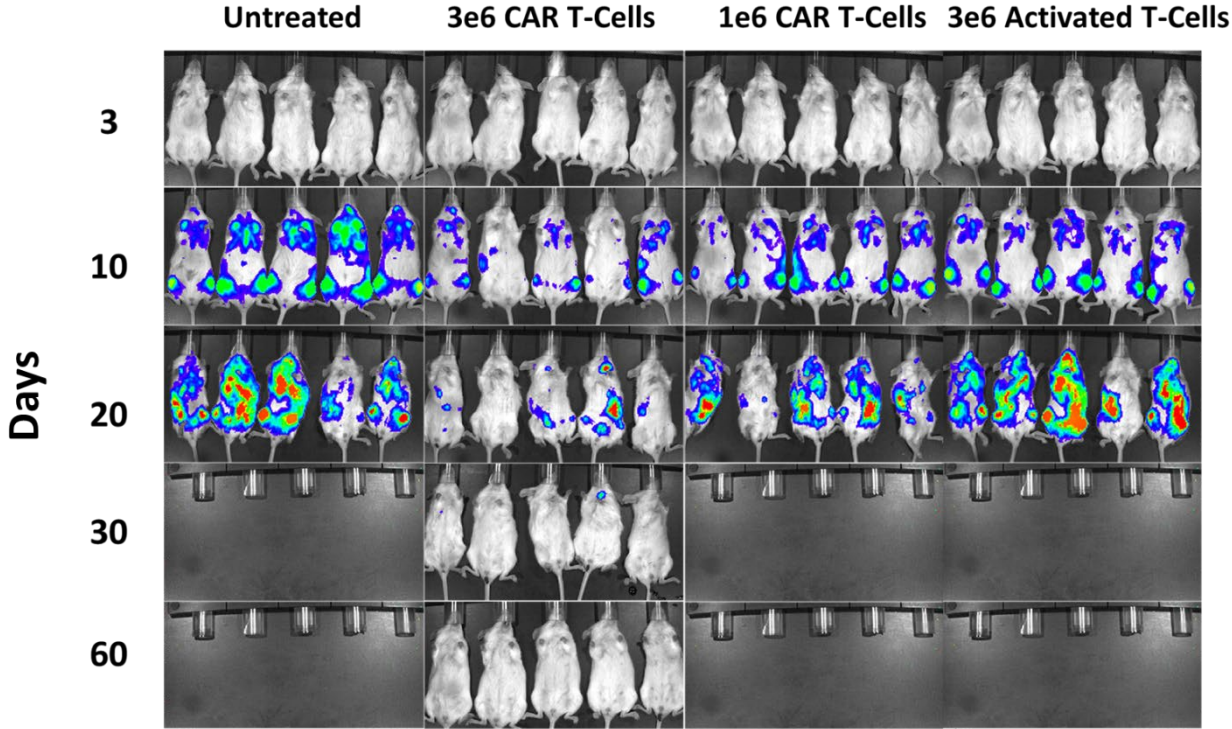
## Opportunities:

- Partnership with **Shanghai Pharma** for clinical trials in China
- Inclusion of **CD19 CAR-T cell therapy failure patients** in FIH

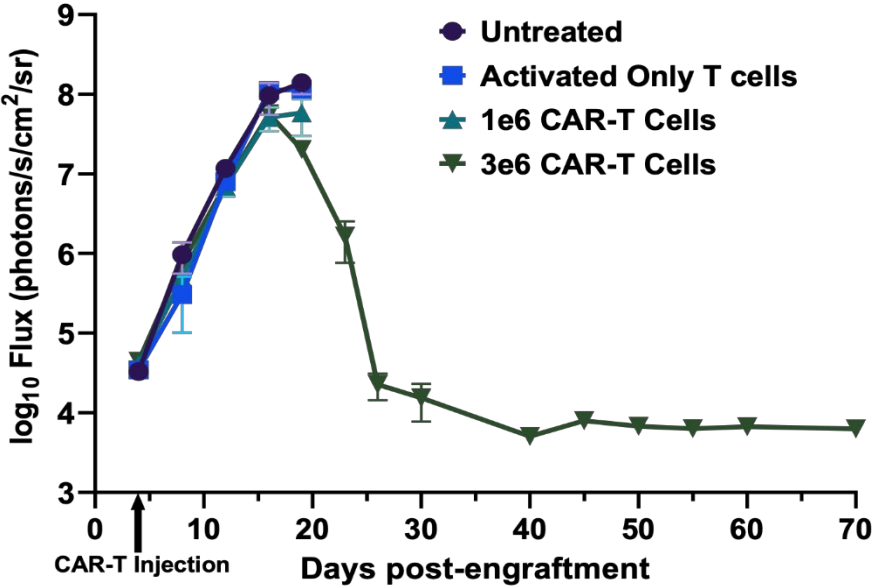




# ROR1 CAR-T Cells Showed Potent Anti-Tumor Activity in CLL Preclinical Model



**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*

## Vision

- Off-the-shelf ROR1-targeting immune cell therapy effective against hematological malignancies and solid tumors

## Mission

- Utilization of our potentially best-in-class ROR1 targeting moiety in:
  - Specific immune cell subsets or entire immune cell diversity; sourced from adult donor cells or stem cell populations
  - Genetically-fortified immune cells against tumor microenvironment (TME)-mediated immune suppression and increase trafficking
  - Dual targeting approaches to eliminate specific tumor cell populations

## Current partnerships supporting next-generation ROR1 cell therapy efforts

- **Karolinska Institutet** R&D collaboration for ROR1-targeting CAR-T cell and CAR-NK cell therapies
- Research collaboration with **Celularity, Inc.** (NASDAQ: CELU) on allogeneic ROR1-targeting cell therapies

# Collaboration with Celularity will Explore Synergies between ROR1 Targeting and Novel Placental-Derived Allogeneic Cell Therapy Platform



*First-in-class, clinically proven, ROR1-targeting monoclonal antibody and CAR construct*



*Off-the-shelf placental-derived allogeneic CAR-NK and CAR-T cell therapy platform*

- 
- Research collaboration to develop and evaluate stem cell-derived cellular therapies targeting ROR1
  - Will explore use of Oncternal's ROR1-targeting mAb and chimeric antigen receptor (CAR) constructs in combination with Celularity's natural killer (NK) and T cell therapies
  - Will leverage advantages of placental-derived cellular therapies and specificity of ROR1 targeting to address significant unmet need in a wide range of cancers

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**FINANCIAL INFO AND UPCOMING MILESTONES**

## 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
  - US prevalence ~4,000<sup>(1)</sup>
- Significant market potential in other cancers with ETS alterations
- Composition of matter patent coverage through 2037

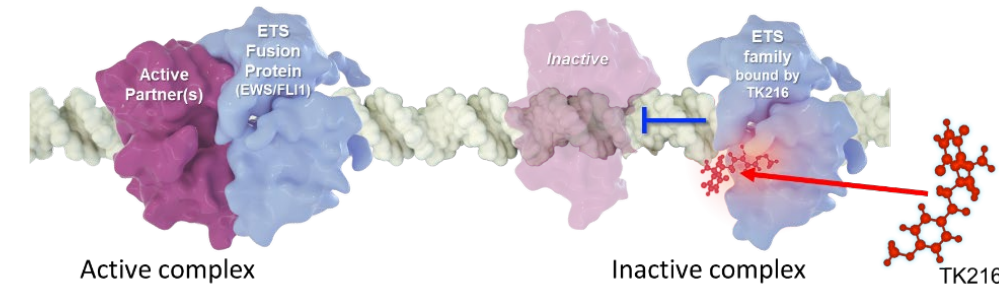
## MECHANISM OF ACTION

- Novel small molecule inhibitor of ETS family oncoproteins
- Designed to prevent/disrupt formation of transcriptionally-active protein complex

## DEVELOPMENT STATUS

- Encouraging interim clinical data for ONCT-216 in patients with relapsed or refractory Ewing sarcoma presented in an oral session at ASCO 2021 & CTOS 2021
- Additional Phase 2 expansion cohort targeting up to 21 Ewing sarcoma patients to evaluate clinical responses to single agent ONCT-216 with intensified dosing

ETS = E26 Transformation-Specific oncogene family



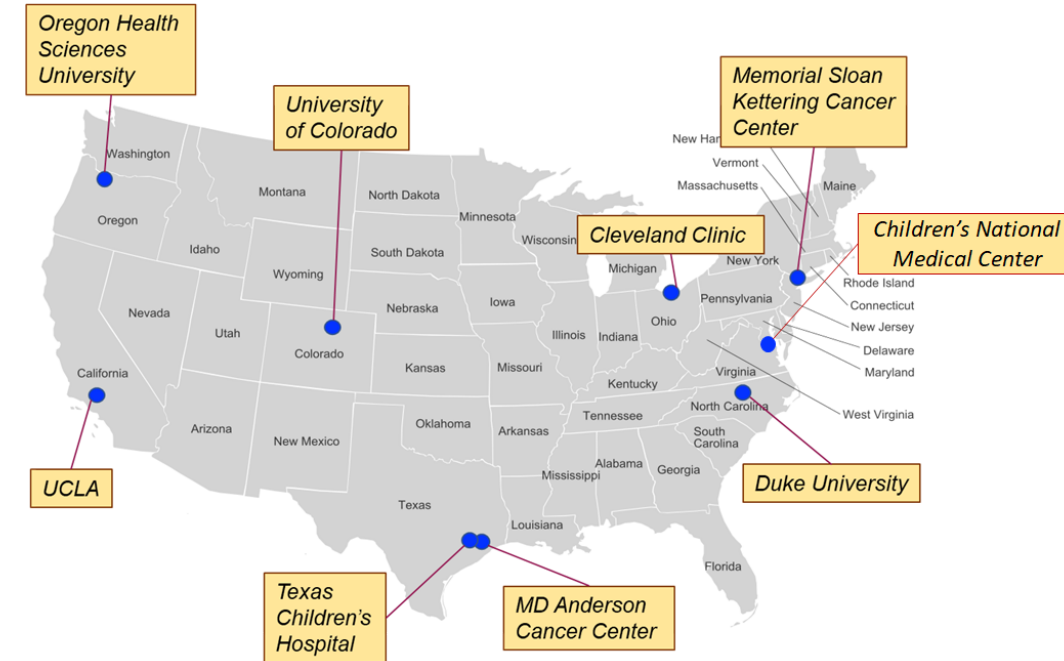
*Erkizan NatureMed 2009*

*(1) Incidence 1.3 per million, prevalence 12 per million – SEER data “ICD-O-3/WHO 2008 Ewing Tumor”, accessed January 3, 2020; NCI Ewing Sarcoma Treatment (PDQ), accessed September 11, 2019; Company analysis*

# Phase 1/2 Study of ONCT-216 in R/R Ewing Sarcoma patients

*Early Evidence of Clinical Activity, Enrolling Additional Expansion Cohort*

- 3+3 dose and schedule escalation cohorts completed
  - Total 74 patients with relapsed/refractory Ewing sarcoma treated with ONCT-216
  - Median number of prior systemic therapies: 3 (range: 1, 9)
- Safety: generally well-tolerated, with dose limiting toxicity of manageable myelosuppression and no obvious off-target toxicity
- PK: drug plasma levels at RP2D exceeded those associated with anti-cancer activity in preclinical models
- Activity: 41% disease control rate among 37 evaluable patients treated with ONCT-216 200 mg/m<sup>2</sup>/day plus vincristine (RP2D)
  - 2 durable complete responses (one surgical CR): no evidence of disease at 29 months and 20+ months on study
- Additional phase 2 expansion cohort targeting up to 21 evaluable Ewing sarcoma patients to evaluate clinical responses to single agent ONCT-216 with intensified & extended dosing



*ClinicalTrials.gov Identifier: NCT02657005*

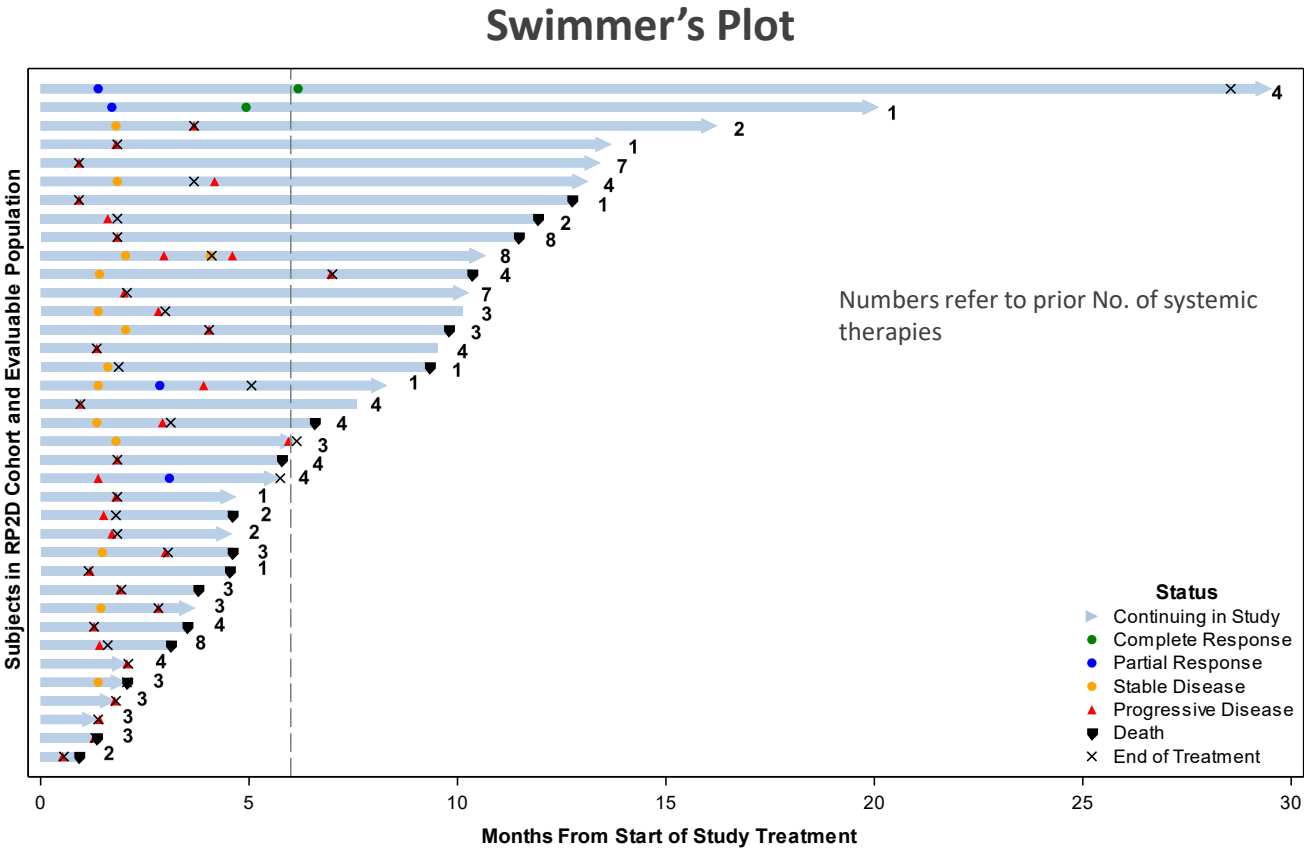


## Notable responses and disease control observed at the RP2D

### Overall Best Clinical Response

	All Subjects (N=60)	Cohort 9 & Expansion Cohort (RP2D) (N=37)
Overall Response (ORR), n (%)	3 (5.0%)	3 (8.1%)
Complete Response* (CR), n (%)	2 (3.3%)	2 (5.4%)
Partial Response** (PR), n (%)	1 (1.7%)	1 (2.7%)
Stable Disease (SD), n (%)	14 (23.3%)	12 (32.4%)
Progressive Disease (PD), n (%)	43 (71.7%)	22 (59.5%)
Disease Control Rate (DCR), n (%)	17 (28.3%)	15 (40.5%)
Duration of Response (months), median (95% CI)	14.7 (1.1, 28.6)	14.7 (1.1, 28.6)
6-month Progression-free-survival (PFS) rate (95% CI)	7.2% (2.4%, 15.8%)	12.0% (3.9%, 25.0%)

\* Two confirmed CRs with 1 completed 2-year treatment after CR, 1 ongoing with no PD at the time of data cut; \*\* Unconfirmed PR observed in target lesion at Cycle 4 then PD observed at Cycle 6 in non-target lesions



Data cut: 01OCT2021; Patients were considered evaluable for response if they completed 1-cycle of treatment and had 1-post baseline tumor assessment; continuing in study includes long-term follow-up (survival);

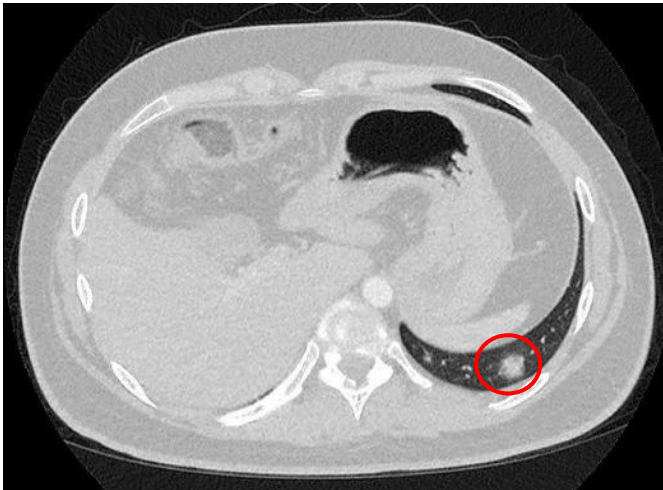
# Case Study: First Sustained Complete Response with ONCT-216 in Patient with Metastatic Relapsed/Refractory Ewing Sarcoma

## 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 ONCT-216 clinical trial
- Enrolled in Phase 1 study of ONCT-216 at MSKCC in 2019

## Treatment and outcome

- Received ONCT-216 in final dose-finding cohort (200 mg/m<sup>2</sup>/day)
- **Resolution of target lesions after two cycles of single-agent ONCT-216**
  - Treatment well tolerated, with minimal myelosuppression
  - Vincristine added starting in third cycle
- Residual non-target 7mm lung lesion excised after 6 cycles of therapy, leading to **surgical complete remission**
- **Durable complete response for 24 months on treatment, continues with no evidence of disease off all treatments for 4 months**

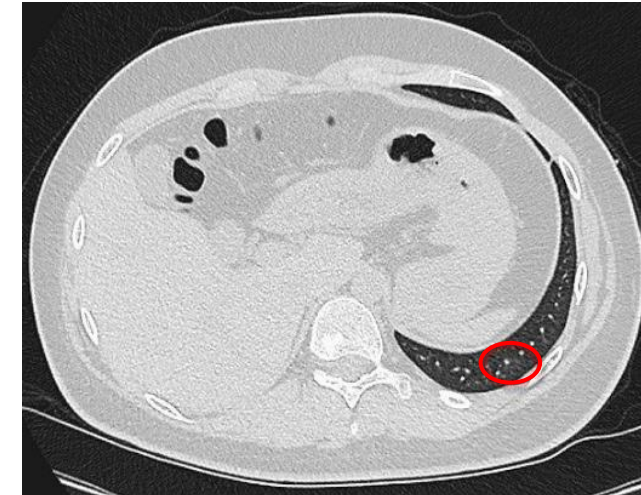


Baseline

2 cycles single-agent ONCT-216



All target lesions resolved



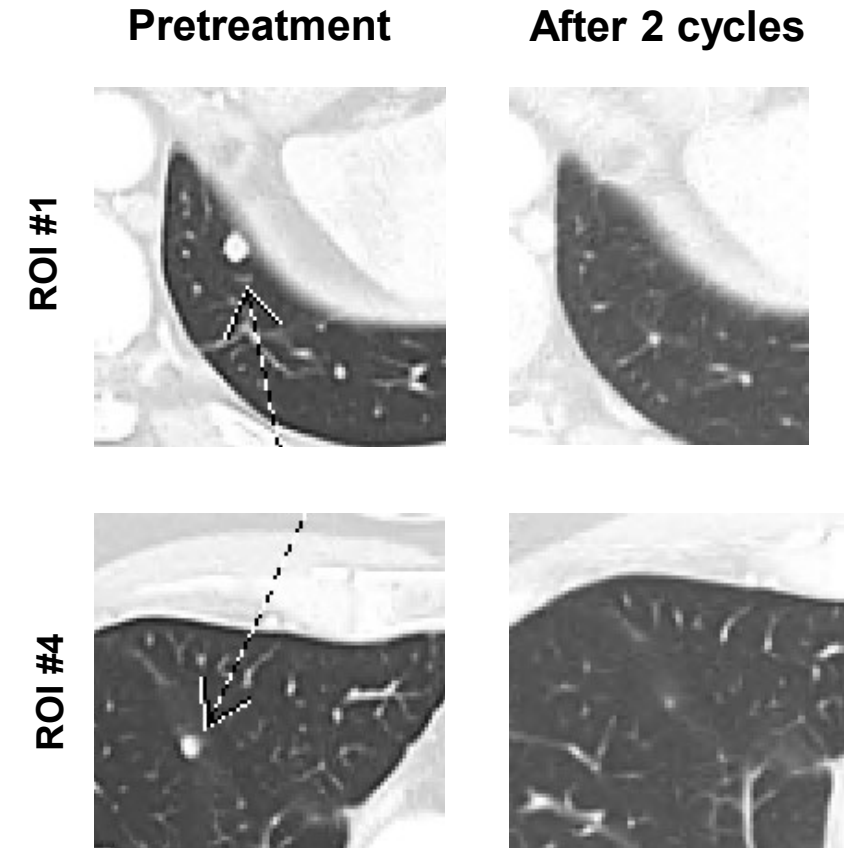
# Case Study: Second Complete Response with ONCT-216 in Patient with Metastatic Relapsed/Refractory Ewing Sarcoma

## Patient background

- 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

## Treatment and outcome

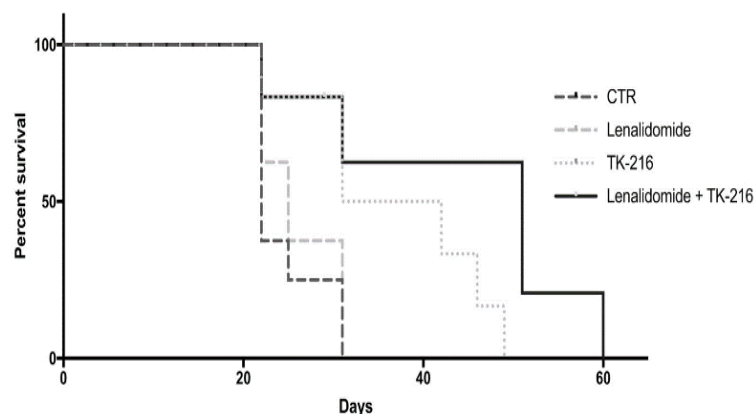
- ONCT-216: Enrolled at MD Anderson Cancer Center in January 2020
  - Treated at RP2D (ONCT-216 200 mg/m<sup>2</sup>/day for 14 days + vincristine 0.75 mg/m<sup>2</sup> day 1)
  - Myelosuppression in Cycle 1, did not recur in Cycle 2 with growth factor support and no ONCT-216 dose reduction
- **Deep 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 >20 months on study, no vincristine since month 3.7**



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

## Diffuse Large B-Cell Lymphoma

- 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 ONCT-216 and combo therapy demonstrated potent anti-tumor activity in DLBCL xenograft model

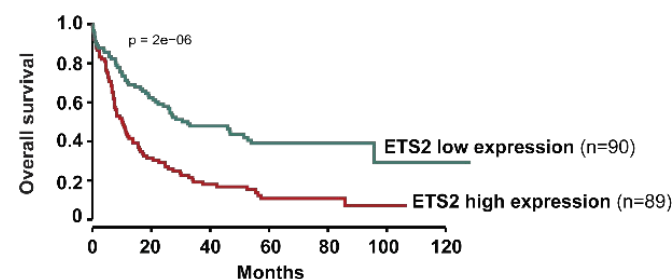


Spriano 2019 CCR

## Acute Myeloid Leukemia

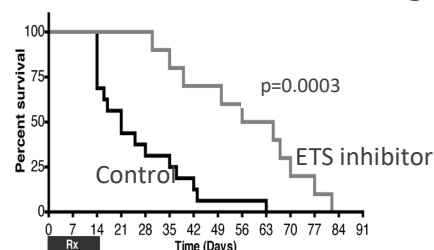
ETS family proteins overexpressed in ~30% of AML cases

- ETS2 overexpression associated w/ shorter OS



Fu 2017 JTranslMed

- ETS Sensitivity of AML cell lines to ONCT-216 was proportional to level of ETS overexpression
- ETS inhibition using ONCT-216 precursor prolonged survival in EWS-FLI1 transgenic AML model

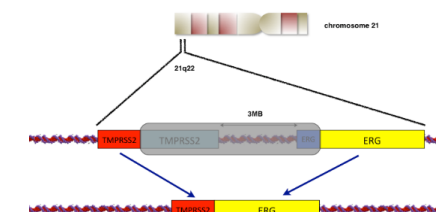


Minas 2015 Oncotarget

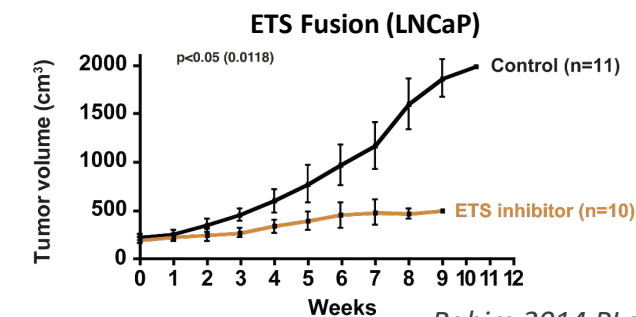
## Prostate Cancer

- 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 ONCT-216 precursor demonstrated anti-tumor activity in human prostate cancer xenograft model



Rahim 2014 PLoS One

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**ZILOVERTAMAB: MONOCLONAL ANTIBODY TARGETING ROR1**

**ROR1 TARGETED CELL THERAPY PROGRAM**

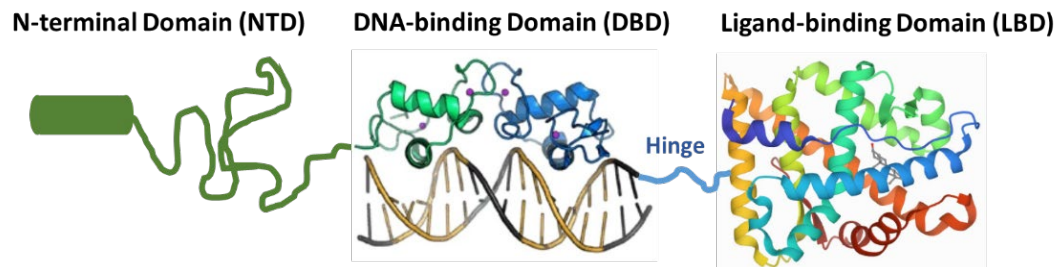
**ONCT-216: TARGETED ETS INHIBITOR**

**ONCT-534: DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

**FINANCIAL INFO AND UPCOMING MILESTONES**

## Differentiated Mechanism of Action

- ONCT-534 binds to both N-terminal Domain (NTD) and Ligand-Binding Domain (LBD) of the androgen receptor (AR) and induces AR degradation
- NTD binding potentially relevant to activity against splice-variants
- Current standard of care treatment options, such as enzalutamide or apalutamide, bind to LBD only



## Potential to address unmet needs in prostate cancer

- Potential next-generation treatment option for patients with advanced prostate cancer
  - Focus on addressing emerging unmet medical need related to resistant androgen receptor splice variant (AR-SV)-expressing tumors<sup>(1)</sup>
- Strong preclinical efficacy in vitro and in vivo
  - Activity against enzalutamide-sensitive and enzalutamide-resistant models, including AR-SV-expressing tumors
- Potential in other AR-driven disease, including luminal AR-triple negative breast cancer (LAR-TNBC) and non-oncology indications

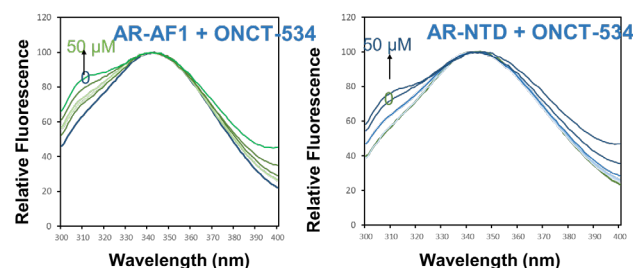
(1) Antonarakis NEJM 2014



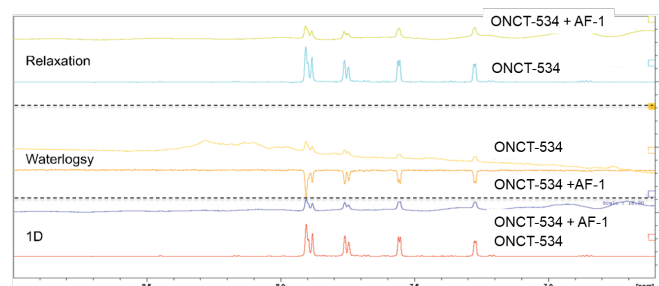
# ONCT-534 in-vivo data show potential as treatment option for splice variant-expressing prostate cancers

## Biophysical studies suggest ONCT-534 interacts with AR N-terminus (AF-1)

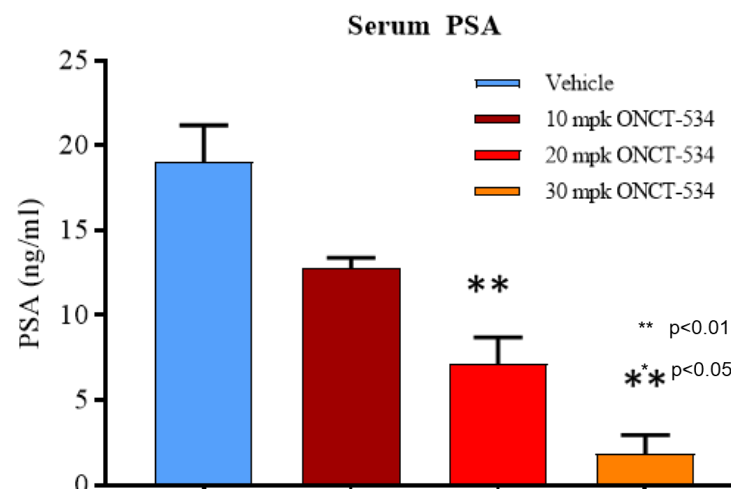
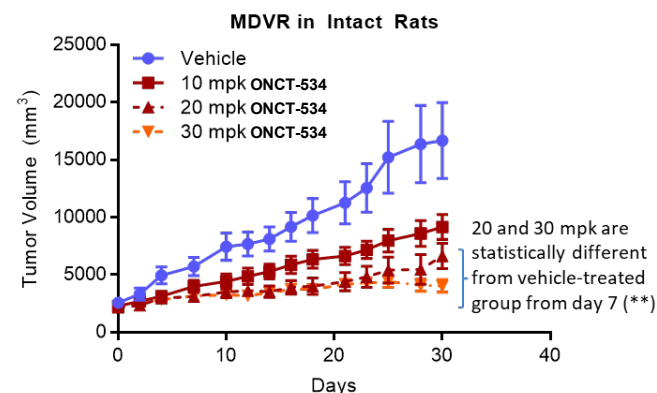
Fluorescence polarization studies with purified AR AF-1



NMR with purified AR AF-1 protein in the presence or absence of ONCT-534

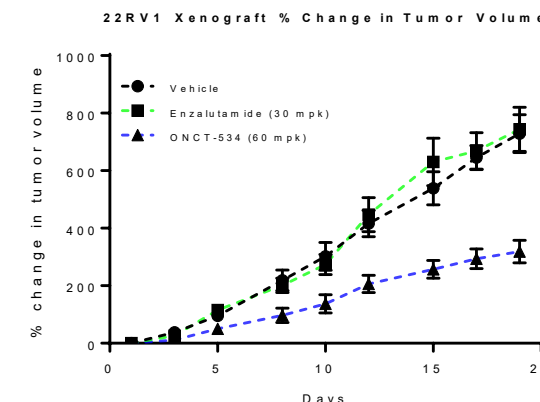


## Inhibition of enzalutamide-resistant PCa Xenograft in non-castrated animals

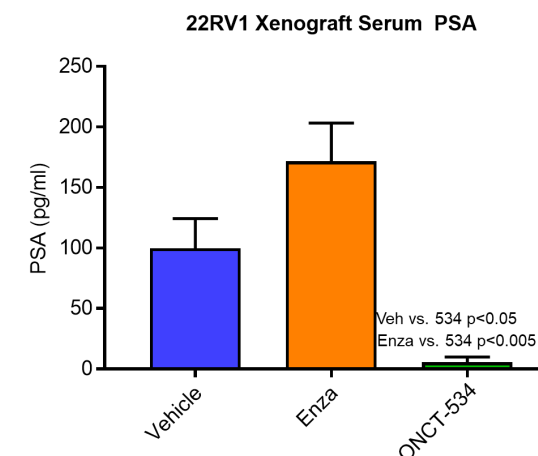


## Anti-tumor activity against AR-Variant 7 (AR-V7) xenografts in castrated animals

Inhibition of AR-V7-Positive 22RV1 CRPC Xenograft



Lowering of Serum PSA Levels in 22Rv1 Tumors



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**FINANCIAL INFO AND UPCOMING MILESTONES**

Description		Ticker: ONCT (Nasdaq)
Cash & Cash Investments @ September 30, 2021		\$97.4M
Cash Runway into 2023		
Debt		\$0M
<b>Capitalization:</b>		
Common Shares Outstanding		49.4M
Options / Warrants in the Money @ September 30, 2021 <sup>(1)</sup>		3.3M
Fully Diluted in the Money		52.7M
<b>Non-Dilutive Support</b>		
• CIRM Grant for CIRLL Study		~\$14M
• Ibrutinib CTM for CIRLL Study		Expanded Supply Agreement

(1) Excludes out-of-the-money stock options and warrants totaling ~7.0M

## Zilovertamab

- MCL & CLL clinical data update for ongoing Phase 1/2 **Dec 2021 (ASH)**
- HER2-negative breast cancer clinical data update for ongoing Phase 1b (IST) **Fully Enrolled**
- FDA interactions to align on registration pathways **Ongoing**

## ONCT-808 ROR1 CAR-T cell therapy

- B-Cell malignancies: IND submission planned for **1H 2022**

## ONCT-216

- Ewing sarcoma Phase 1/2 expansion cohort data update **Nov 2021 (CTOS)**

## ONCT-534

- Prostate Cancer IND-enabling pre-clinical development **Ongoing**

## R&D Day to review development priorities

**Jan 25, 2022**

## **ZILOVERTAMAB (FORMERLY CIRMTUZUMAB): POTENTIALLY FIRST-IN-CLASS MONOCLONAL ANTIBODY TARGETING ROR1**

- Interim Phase 1/2 results for zilovetamab + ibrutinib in MCL compare favorably to historical single-agent ibrutinib data
- Ongoing FDA interactions regarding potential registration trial in patients with MCL

## **ONCT-808: AUTOLOGOUS CAR-T CELL THERAPY TARGETING ROR1**

- IND-enabling activities supported by Lentigen (lentivirus manufacturing) and Miltenyi Biotec (process development)
- Research collaborations for next-gen allogeneic CAR-T and CAR-NK cell therapies with Karolinska Institutet & Celularity

## **ONCT-216 (FORMERLY 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

## **ONCT-534 (FORMERLY GTX-534): DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

- Pre-clinical data in prostate cancer models suggest activity against tumors expressing androgen receptor splice variants

## **MULTIPLE DATA CATALYSTS**

- Clinical data updates in MCL, CLL, breast cancer and Ewing sarcoma
- Regulatory agreement on zilovetamab registration pathways
- ONCT-808 ROR1 CAR-T cell therapy IND submission planned in 1H 2022