



TARGETING CANCER

New Science. New Cancer Therapies. New Hope.

Company Overview – April 2022

#### 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 expected initiation of, and elements constituting, the ZILO-301 and ZILO-302 studies, the potential that the ZILO-301 study can serve as a registrational study, 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, Oncternal's estimated cash and cash equivalents as of March 31, 2022, 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-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.

# **Corporate Highlights**



#### **ZILOVERTAMAB: POTENTIALLY FIRST-IN-CLASS MONOCLONAL ANTIBODY TARGETING ROR1**

- Safety and efficacy results for zilovertamab + ibrutinib in patients with MCL/CLL compare favorably to historical single-agent ibrutinib
- Agreement with U.S. FDA on Phase 3 global registrational study design for the treatment of patients with R/R 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-534: DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

 Activity against prostate cancer preclinical models with androgen receptor mutations including overexpression and splice variants such as AR-V7

#### **MULTIPLE DATA CATALYSTS**

- Expected initiation of zilovertamab + ibrutinib global registrational Phase 3 Study ZILO-301 in 3Q 2022
- Clinical data updates in MCL and CLL
- ONCT-808 ROR1 CAR-T cell therapy IND submission planned in mid-2022

# Clinical Stage Biotech Focused on Hematological Malignancies and Prostate Cancer with Multiple Modalities and Deep ROR1 Expertise



### **Hematological Malignancies**

### Zilovertamab – ROR1 monoclonal antibody

- Demonstrated clinical benefit of combination with ibrutinib compared to historical ibrutinib monotherapy
- Expect MCL registrational study initiation in 3Q 2022

## **ONCT-808 – ROR1 CAR-T Cell Therapy**

Expect IND submission in mid-2022

#### **Prostate Cancer**

### **ONCT-534 – Dual Action AR Inhibitor (DAARI)**

- First-in-class MOA interacting with both Nterminal Domain and Ligand-Binding Domain of the androgen receptor inducing AR degradation
- Active preclinically against AR amplification, splice variant and LBD mutation models

### Zilovertamab – ROR1 monoclonal antibody

IND open for advanced prostate cancer

## **Experienced Team**





James Breitmeyer, MD, PhD CEO, Founder, Director





**Richard Vincent CFO** 





Salim Yazji, MD CMO



Gunnar Kaufmann, PhD CSO



Raj Krishnan, PhD CTO

**GILEAD** 



**Chase Leavitt** General Counsel

Tang Capital

LINEAGE
Management



Pablo Urbaneja SVP, Corporate Development

**Coherus** 



Steve Hamburger, PhD

SVP, Regulatory Affairs &













Daniel Kisner, MD Rosemary Mazanet, MD, PhD



**AMGEN** 

Director



DYNAVAX

MERCK



Director



Xin Nakanishi, PhD Charles Theuer, MD, PhD Robert Wills, PhD

Director



Director

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











Jinzhu Chen, PhD

Director



Director







**Bill LaRue** 

Director



























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



Modality	Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3
	Zilovertamab	Mantle Cell Lymphoma (MCL)				
ROR1 mAb		Chronic Lymphocytic Leukemia (CLL)				
		Prostate Cancer				
ROR1	ONCT-808 (Autologous CAR-T)	Hematological Malignancies		•		
Cell Therapy	Allogeneic	Hematological Malignancies and Solid Tumors				
Dual-Action AR Inhibitor	ONCT-534	Prostate Cancer				

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

**ROR1 TARGETED CELL THERAPY PROGRAM** 

**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%

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 Targeting ROR1**



## Zilovertamab ROR1 mAb



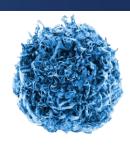
#### Background

- 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 MK-2140 ADC
  - VelosBio spun out in 2018, acquired by Merck for \$2.75B

#### **Development status**

- MCL: Agreement with U.S. FDA on Phase 3 study design for ibrutinib combo in patients with R/R MCL
- CLL: Phase 2 with ibrutinib (data: ASH 2021)
- FDA Orphan Drug Designations for MCL and CLL
- mCRPC: P1b IST with docetaxel IND in effect

# ROR1 CELL THERAPY PROGRAM



#### **Background**

- ROR1 expression on many tumor types
- Potential safety and efficacy advantages
- MK-2140 ADC data at ASH 2021: no apparent offtumor ROR1 organ toxicities

#### **Development status**

- ONCT-808 utilizing zilovertamab scFv selected as the lead autologous CAR-T product candidate
- Collaborations with Celularity, Karolinska Institutet and Shanghai Pharma (China)
- IND enabling work ongoing including WuXi, Lentigen and Miltenyi Biotec
- Productive pre-IND meeting Jan '22, IND submission expected in mid-2022

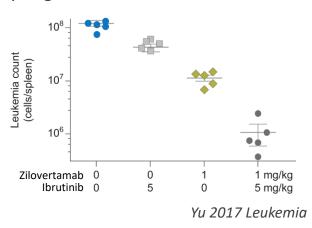
### **Zilovertamab Extensive Preclinical Research**

Potential as combination therapy, multiple tumor indications and safety advantage

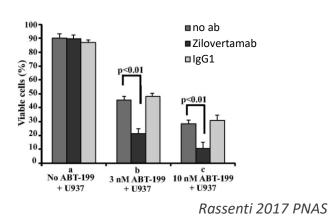


#### **Synergistic with Targeted Agents**

Synergistic with ibrutinib in CLL + MCL

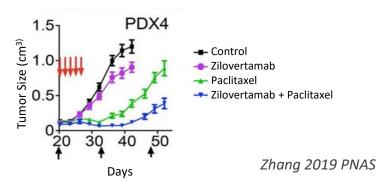


Synergistic with venetoclax (ABT-199)

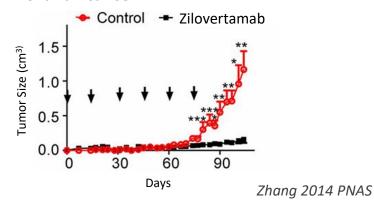


#### **Active in Solid Tumor Models**

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

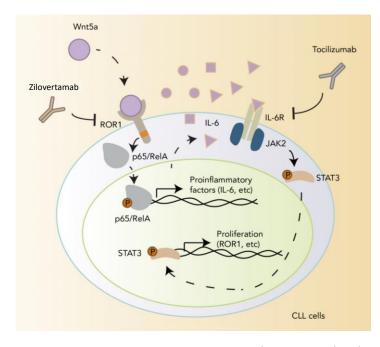


 Anti-tumor activity in PDX models of ovarian cancer



#### **Inhibits Inflammatory Pathway**

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

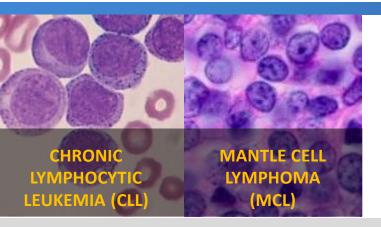


Chen 2019 Blood

CHEH ZOIS BIOOC

# 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 ASH 2021
- Data support Phase 3 registrational study design

#### **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

# MCL Phase 2 enrolling CLL enrolled

#### PART 3 (in CLL)

#### RANDOMIZED EFFICACY

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

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

Enrolled

ClinicalTrials.gov Identifier: NCT03088878

**CIRLL = C**irmtuzumab and Ibrutinib targeting **R**OR1 for **L**eukemia and **L**ymphoma **CIRM = C**alifornia **I**nstitute for **R**egenerative **M**edicine

## **CIRLL Trial Summary**

#### Zilovertamab + Ibrutinib Data Update at ASH 2021



#### MCL:

- Clinical activity compares favorably to published singleagent ibrutinib data<sup>(1)</sup>
  - ORR 81% (21/26)
  - CR rate 35% (9/26)
  - CRs durable for up to 32 months
  - Median PFS of 35.9 months and OS not reached, regardless of prior # of therapies, after a median follow-up of 14.4 months
- Encouraging clinical activity in high-risk sub-populations
  - Prior SCT or CAR-T (n=7): 100% ORR (5 CR, 2 PR)
  - Ki-67 levels ≥30% (n=13): 85% ORR (4 CR, 7 PR)
  - > 1 prior systemic therapy (n=11): 82% ORR (5 CR, 4 PR)
  - Prior ibrutinib (n=5): 80% ORR (2 CR, 2 PR)

#### CLL:

- The combination of zilovertamab plus ibrutinib is a welltolerated and active regimen in CLL
  - Updated Part 1 & 2 results:
    - ORR 91% (31/34)
    - CR rate 6% (2/34)
    - Clinical Benefit 100% (34/34)
    - Median PFS not reached after median follow-up of 29 months
  - Randomized cohort (Part 3) results
    - Data continue to mature with time
    - ORR 93.3% (14/15 combo) vs 100% (7/7 mono)
    - Median PFS not reached for either arm after median follow up of ~18 months

#### 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 9.7% of patients with zilovertamab plus ibrutinib, compared to 29% for ibrutinib alone from its registration study

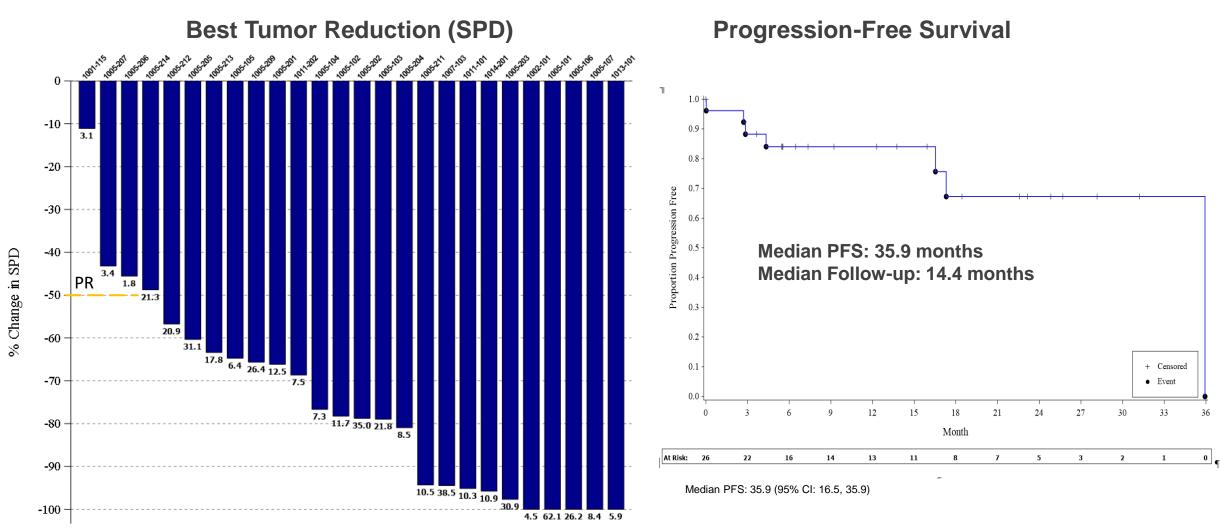
There have been no dose-limiting toxicities and no serious adverse events attributed to zilovertamab alone

# R/R MCL: Tumor Reduction and Progression-Free Survival

Zilovertamab + Ibrutinib Data Update at ASH 2021



### 81% ORR and median PFS of 35.9 months

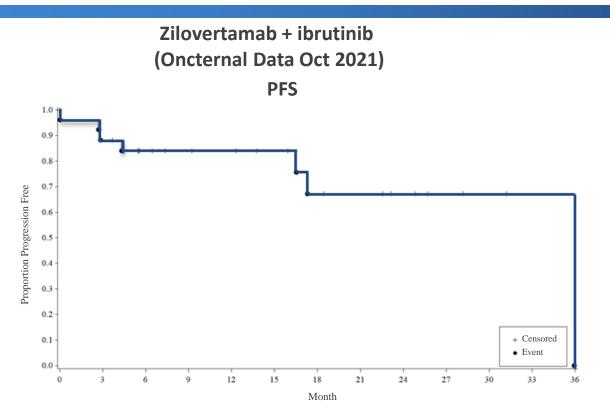


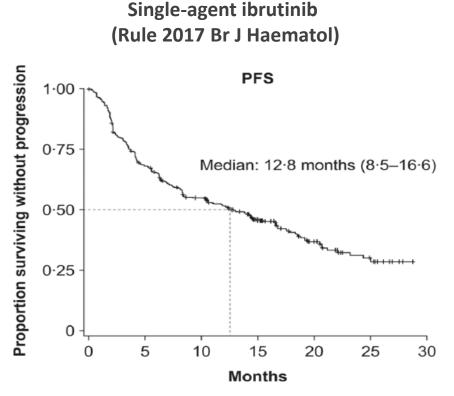
Data: 01OCT2021; Evaluable MCL Part 1 & 2 patients (n=26); Patients were considered evaluable for response if they had 1-dose of zilovertamab and had 1-post baseline tumor assessment; SPD= sum of product of diameters; Number under bars represent baseline SPD; NE= not estimable

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

Zilovertamab + Ibrutinib Data Update at ASH 2021







Baseline characteristics	Median follow-up 14.4 months		24-25 months	
	Median PFS	35.9 months 95% CI: (16.5 – 35.9 months)	12.8 months. 95% CI: ( <b>8.5 – 16.6 months</b> )	
Clinical outcomes	ORR	80.8%	66%	
	CR	34.6%	20%	

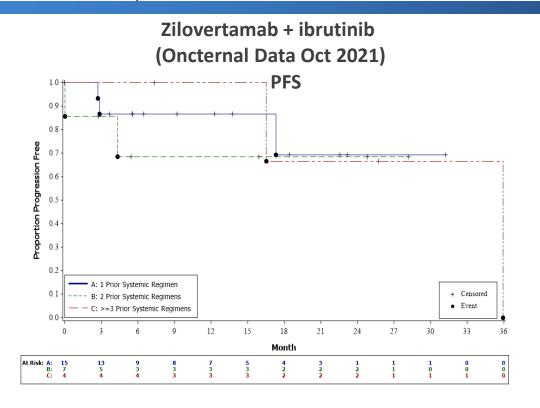
Note: Data presented are from separate studies and such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of the combination of zilovertamab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

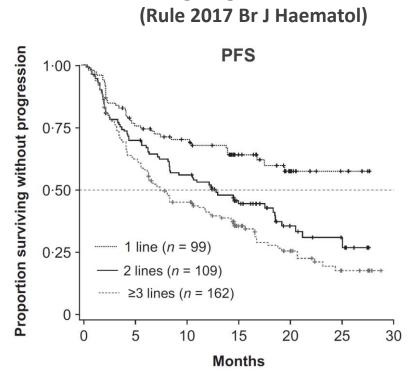
# R/R MCL: Encouraging PFS Observed Based on Prior Line of Therapy Compared to Historical Ibrutinib Alone



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Zilovertamab + Ibrutinib Data Update at ASH 2021





Single-agent ibrutinib

PFS by
Subtypes –
Prior
Systemic
Therapy
(months)

Prior sys. therapy	Zilovertamab + Ibrutinib PFS , median (95% CI)	Ibrutinib PFS median
1	NR (17.3, NE)	NR
2	NR (0.03, NE)	~12
≥ 3	35.9 (16.5, 35.9)	~8

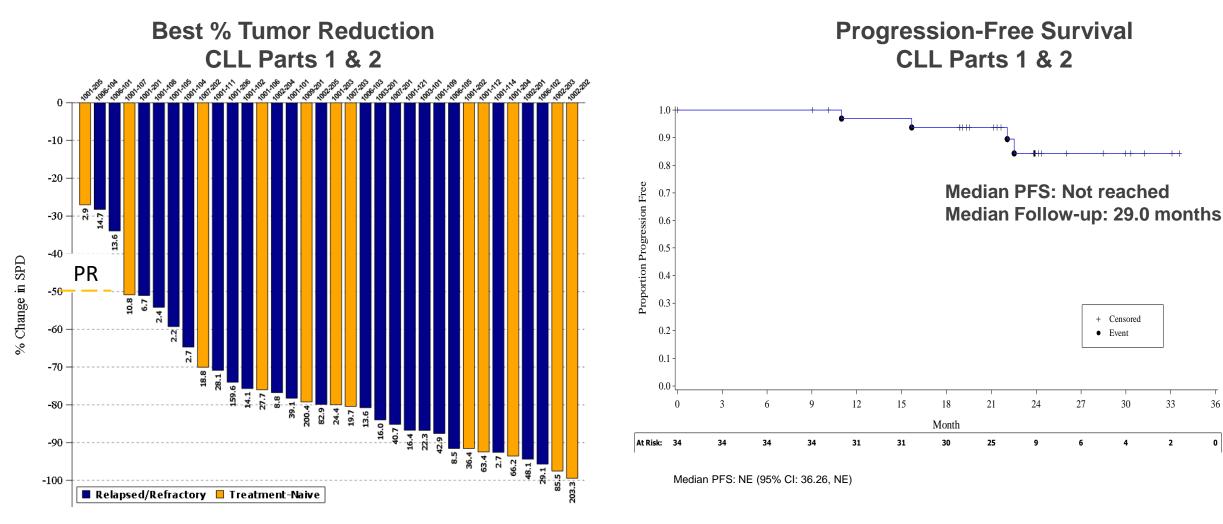
Note: Data presented are from separate studies and such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of the combination of zilovertamab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

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

Zilovertamab + Ibrutinib Data Update at ASH 2021



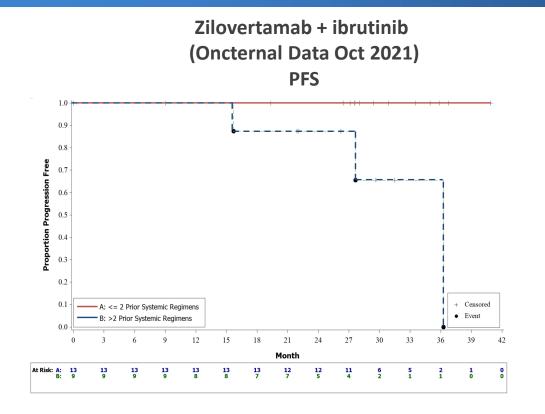
### 91% ORR and median PFS was not reached in CLL

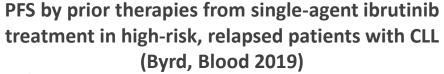


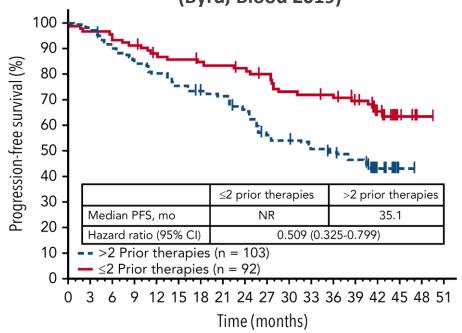
Data: 01OCT2021; Evaluable CLL Part 1 & 2 patients (n=34); Patients were considered evaluable for response if they had 1-dose of zilovertamab and had 1-post baseline tumor assessment; SPD= sum of product of diameters; Number under bars represent baseline SPD; NE= not estimable

# CLL: Encouraging Landmark PFS Based on Number of Prior Lines of Therapy ONCTERNAL

Zilovertamab + Ibrutinib Data Update at ASH 2021







PFS by	Prior sys. therapy	Landmark PFS 24 months	Landmark PFS 36 months	Landmark PFS 24 months	Landmark PFS 36 months
Subtypes - Prior Systemic	1 or 2	~100%	~100%	~85%	~75%
Therapy	> 2	~85%	~65%	~65%	~50%

Data: 01OCT2021; PFS is defined as the time from the first dose to the time of objective disease progression or death from any cause, whichever occurs first; NR- not reached. NE – not evaluable



# Successful End-of-Phase 2 FDA meeting (December 2021)

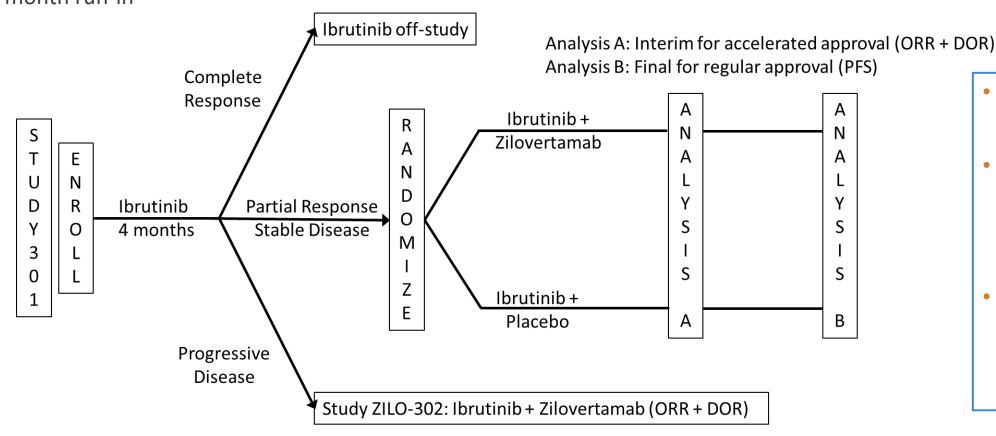
- Reached consensus on design and major details of Phase 3 Study ZILO-301, to treat patients with R/R MCL with zilovertamab plus ibrutinib
- Positive feedback on the proposed key clinical and regulatory requirements of our development program for zilovertamab in MCL
- Agency previously provided positive feedback on the sufficiency of the preclinical and pharmacology studies of zilovertamab needed to support a BLA submission

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# Zilovertamab Registrational Study Plan



**ZILO-301:** Randomized, Double-blind, Placebo-controlled, Multi-center Phase 3 Study of Zilovertamab (A ROR1 Antibody) Plus Ibrutinib Versus Ibrutinib Plus Placebo in Patients with Relapsed or Refractory Mantle Cell Lymphoma **ZILO-302:** Open-label companion study of zilovertamab plus ibrutinib for rescue of patients refractory to ibrutinib during 4-month run-in



- Plan to randomize250 patients
- Interim data as early as 2 years from first-patient-in (85% power)
- Final data as early as 3 years from first-patient-in (>90% power)

Global registrational study expected to be initiated in 3Q 2022

# **Zilovertamab Opportunities Beyond MCL**

# Prostate Cancer (PC)

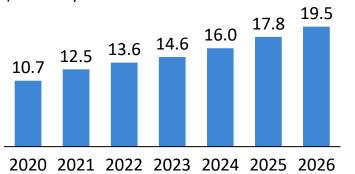


#### **Market Opportunity**

#### **High Unmet Medical Need**

- Second most frequently diagnosed cancer among men in the U.S. behind skin cancer
- 5-year survival of 30% in the metastatic setting
- >34,000 deaths per year in the US

#### **Prostate Cancer Global Sales Projections** \$ billion; Evaluate Pharma



#### **Clinical/Scientific Rationale**

- ROR1 is expressed by ~90% of prostate cancers
- ROR1 expression has also been demonstrated on neuro-endocrine prostate cancer cells
- Wnt5a signaling pathway is activated in patients with advanced PC progressing while on AR inhibitor treatment
- Expression of Wnt5a in patients with mCRPC has been associated with poor OS

#### **Clinical Strategy**

**Ongoing Phase 1b Randomized Study** in Metastatic Castration-Resistant **Prostate Cancer (UCSD IST)** 

#### Patient Population:

- Metastatic CRPC
- Prior abiraterone and/or next generation anti-androgen

#### Design:

- 3+3 dose escalation design with expansion (n=32)
- Docetaxel + Zilo (every 3 weeks x 6)

#### **Primary End Points:**

RP2D

#### Secondary End Point:

Clinical benefit rate



ClinicalTrials.gov Identifier: NCT05156905

# Zilovertamab Opportunities Beyond MCL

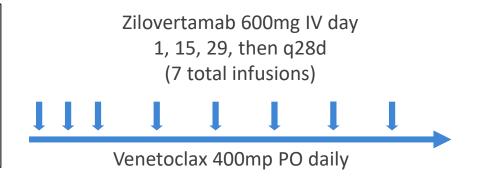
# Consolidation for CLL Patients on Venetoclax



- Investigator-sponsored, single-center two-stage study to determine the efficacy of zilovertamab 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 zilovertamab + 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%)



#### **Primary Endpoint**

 uMRD in marrow at end of combination therapy

#### **Primary Feasibility Endpoint:**

 Undetectable MRD (uMRD) rate after Zilovertamab + Venetoclax

#### Secondary and Exploratory Endpoints:

- Safety
- Time to next treatment
- Gene expression changes

#### Main inclusion criteria:

- CII or SII
- Detectable CLL (> 0.01% CLL cells in the blood or marrow)
- Must have received at least 12 months of venetoclax<sup>(1)</sup>

#### **Statistical Considerations**

- Success rate of 25% uMRD considered compelling
- Success rate of < 5% would be considered not compelling
- n =16, 80% power to reject  $H_{0.} \alpha < 5\%$



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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 demonstration of safety and efficacy
- Reduced technology risk: autologous CAR-T cells
- Reduced indication risk: B-cell malignancies, including failures to prior CD19 CAR-T cell therapy
- US IND on track for submission in mid-2022



(2)

Next-generation allogeneic cell therapies targeting ROR1

- Incorporate 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





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# **Cell Therapy Scientific Advisory Board**

# Supporting ONCT-808 development and next-gen ROR1 Cell Therapies



#### 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 Cancer Center
- Lead PI in Tecartus® registrational study
- Over 200 peer-reviewed publications

#### 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

#### 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

#### Sadik Kassim, PhD

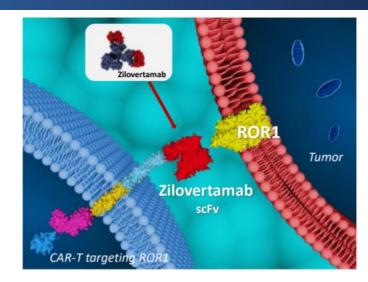
CTO (Genomic Medicines) · Danaher Corporation

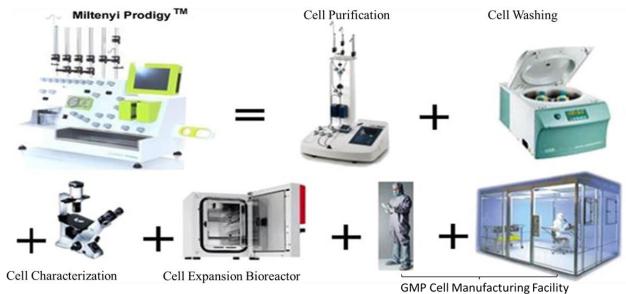
- Chief Technology Officer at Vor Biopharma
- Chief Scientific Officer at Mustang Bio
- Led the BLA and MAA CMC efforts for Kite's Tecartus®
- Former Head of Early Analytical Development for Novartis' Cell and Gene Therapies Unit

# **ONCT-808 CMC and Manufacturing Progress**



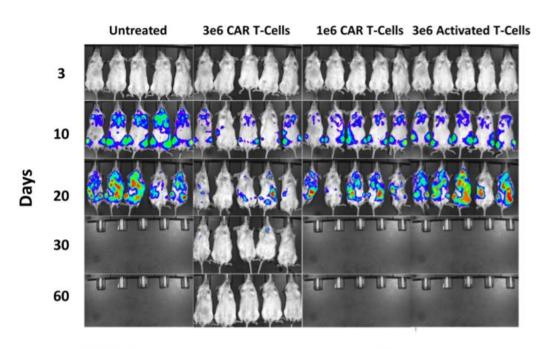
- 1. Lead ROR1 CAR construct optimized and selected with demonstrated high potency against ROR1+ cancer cell lines
- 2. Lentivirus production process confirmed with robust titers of greater than 1 E9 IFU/mL achieved
- 3. Oncternal ROR1 CAR-T cell product process optimized and confirmed
  - Leveraging a flexible, closed fully-automated platform
  - One week production process post-activation
  - Greater than 2 billion CAR+ T cells produced with over 60% CAR+ expression
  - Majority of CAR T cells with juvenile phenotypes (CD4 and CD8 stem central memory T cells)





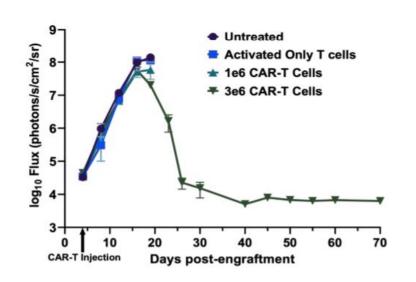
# **ONCT-808** Preclinical Update – Strong Anti-tumor Activity





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.

- Strong anti-tumor activity of ROR1 CAR-T cells demonstrated in CLL xenograft mouse model
- Additional IND-supporting in vivo studies are ongoing

# **Oncternal Next-generation ROR1 Cell Therapy Effort Overview**



#### Vision

Off-the-shelf ROR1-targeting immune cell therapy for both liquid and solid malignancies

#### Mission

- Utilization of our potentially best-in-class ROR1 targeting moiety with:
  - Specific immune cell subsets or entire immune cell populations
  - Adult donor cells or stem cells
  - Fortified against tumor microenvironment
  - Dual targeting approaches to eliminate specific tumor cell populations

# Current partnerships supporting next-generation ROR1 cell therapy efforts

- Karolinska Institutet R&D collaboration for CAR-T cell and CAR-NK cell therapies
- Celularity research collaboration with on allogeneic 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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**ZILOVERTAMAB: MONOCLONAL ANTIBODY TARGETING ROR1** 

**ROR1 TARGETED CELL THERAPY PROGRAM** 

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

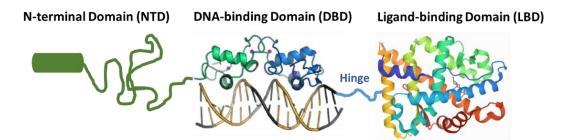
FINANCIAL INFO AND UPCOMING MILESTONES

# **ONCT-534: Dual-Action Androgen Receptor Inhibitor (DAARI)**



#### **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-SVexpressing tumors
- Potential in other AR-driven disease, including luminal AR-triple negative breast cancer (LAR-TNBC) and non-oncology indications

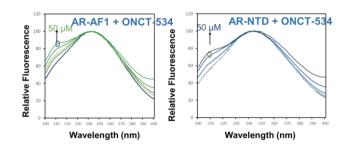
(1) Antonarakis NEJM 2014

# ONCT-534 In-Vivo Data Show Potential as Treatment Option for Splice Variant-Expressing Prostate Cancers

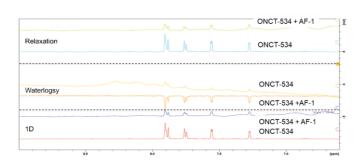


# Biophysical studies suggest ONCT-534 interacts with AR N-terminus (AF-1)

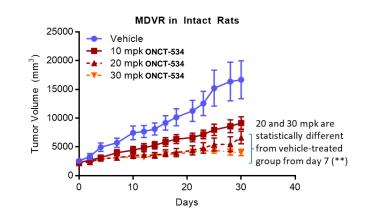
Fluorescence polarization studies with purified AR AF-1

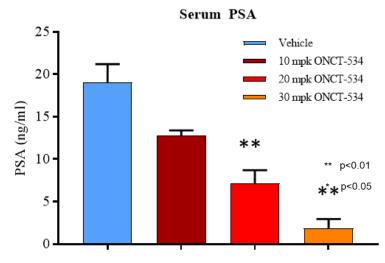


NMR with purified AR AF-1 protein in the presence or absence of ONCT-534



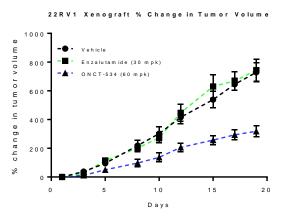
Inhibition of enzalutamide-resistant PCa xenograft in <u>non-castrated</u> animals



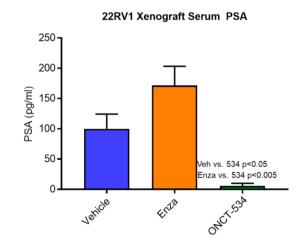


# Activity against AR-Splice Variant 7 (AR-V7) xenografts in castrated animals

Inhibition of AR-V7-positive 22RV1 CRPC xenograft



Lowering of serum PSA levels in 22Rv1 tumors



Source: Narayanan, Virtual Poster Presentation at 2021 AACR-NCI-EORTC Virtual International Conference on Molecular Targets ONCT Corporate Presentation April 2022

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FINANCIAL INFO AND UPCOMING MILESTONES

# **Financial Information: ONCT (Nasdaq)**



Cash & Cash Investments @ March 31, 2022 (Estimated) Cash Runway well into 3Q 2023	\$82.2M
Debt	\$0M
Capitalization:	
Common Shares Outstanding	49.4M
Options / Warrants in the Money @ December 31, 2021 <sup>(1)</sup>	0.4M
Fully Diluted in the Money	49.8M
Non-Dilutive Support	
<ul> <li>CIRM Grant for CIRLL Study thru March 2022</li> </ul>	~\$14.4M
<ul> <li>Ibrutinib CTM for CIRLL Study</li> </ul>	Supply Agreement

# **Anticipated Pipeline Milestones**



### **Zilovertamab**

•	MCL global registrational Phase 3 Study ZILO-301 initiation	3Q 2022
•	MCL & CLL clinical data update for ongoing Phase 2	2Q 2022
•	Prostate cancer (mCRPC) IST Phase 1b enrollment	mid-2022

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

B-Cell malignancies IND submission
 mid-2022

#### **ONCT-534**

Prostate cancer GLP toxicology studies and GMP manufacturing initiation
 2Q 2022

# **Corporate Highlights**



#### **ZILOVERTAMAB: POTENTIALLY FIRST-IN-CLASS MONOCLONAL ANTIBODY TARGETING ROR1**

- Safety and efficacy results for zilovertamab + ibrutinib in patients with MCL/CLL compare favorably to historical singleagent ibrutinib
- Agreement with U.S. FDA on Phase 3 global registrational study design for the treatment of patients with R/R 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-534: DUAL-ACTION ANDROGEN RECEPTOR INHIBITOR (DAARI)**

 Activity against prostate cancer preclinical models with androgen receptor mutations including overexpression and splice variants such as AR-V7

#### **MULTIPLE DATA CATALYSTS**

- Expected initiation of zilovertamab + ibrutinib global registrational Phase 3 Study ZILO-301 in 3Q 2022
- Clinical data updates in MCL and CLL
- ONCT-808 ROR1 CAR-T cell therapy IND submission planned in mid-2022