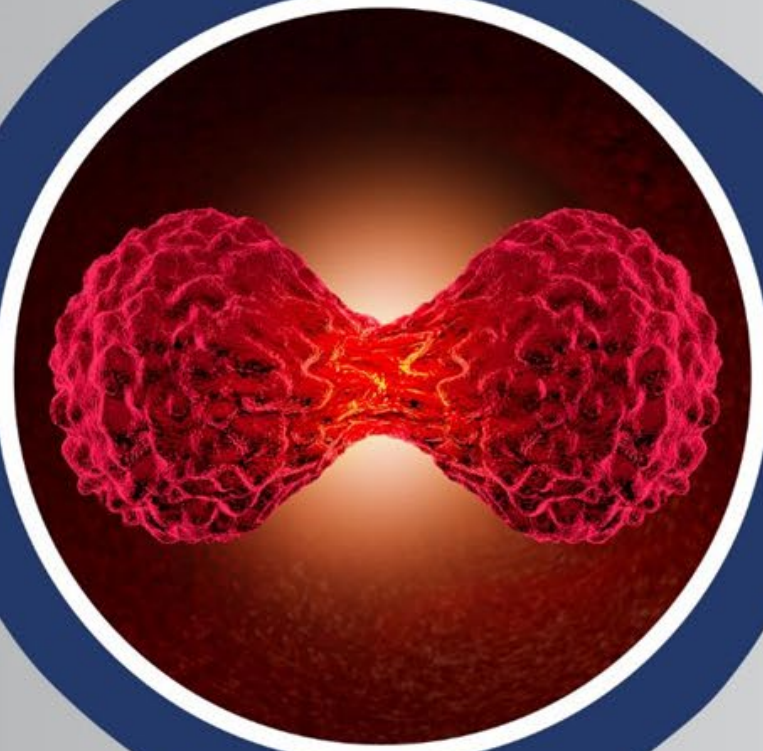

ONCTERNAL therapeutics™

TARGETING CANCER

New Science. New Cancer Therapies. New Hope.

Company Overview – December 2020

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 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.

Corporate Highlights

ONCTERNAL therapeutics™

THREE NOVEL ONCOLOGY PRODUCT CANDIDATES IN DEVELOPMENT

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: PRECLINICAL DEVELOPMENT WITH CIRM AND SHANGHAI PHARMA

- Potential to improve on CAR-T efficacy and safety

TK216: TARGETED ETS INHIBITOR

- Two durable complete responses in patients with metastatic relapsed/refractory Ewing sarcoma in ongoing Phase 1/2
- Additional opportunities in other cancers with ETS alterations

MULTIPLE DATA CATALYSTS EXPECTED IN NEXT 12 MONTHS

- Clinical data updates expected in MCL, CLL, breast cancer and Ewing sarcoma
- ROR1 CAR-T expected to reach clinic in 2H 2021 in China

EXPERIENCED MANAGEMENT AND BOARD OF DIRECTORS

Experienced Team

ONCTERNAL therapeutics™

James Breitmeyer, MD, PhD
CEO, Founder, Director

Richard Vincent
CFO

Igor Bilinsky, PhD
CBO

Frank Hsu, MD
CMO

Gunnar Kaufmann, PhD
CSO

Raj Krishnan PhD
SVP, Manufacturing

David Hale
Co-founder, Board Chairman

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

Daniel Kisner, MD
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

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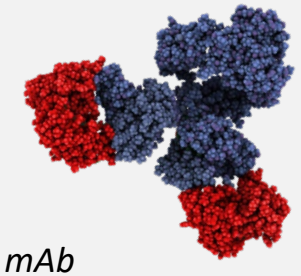
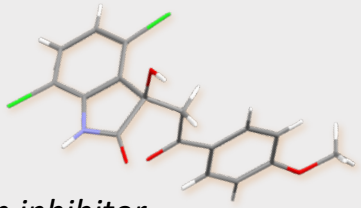
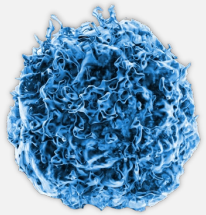
Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Modality
Cirmtuzumab	Mantle Cell Lymphoma (MCL)					 *ROR1 mAb*
	Chronic Lymphocytic Leukemia (CLL)					
	Breast Cancer					
TK216	Ewing Sarcoma					 *ETS oncoprotein inhibitor*
	Acute Myeloid Leukemia (AML)					
	Prostate Cancer					
ROR1 CAR-T	Heme Cancers					 *ROR1 CAR-T cell therapy*
	Solid Tumors					

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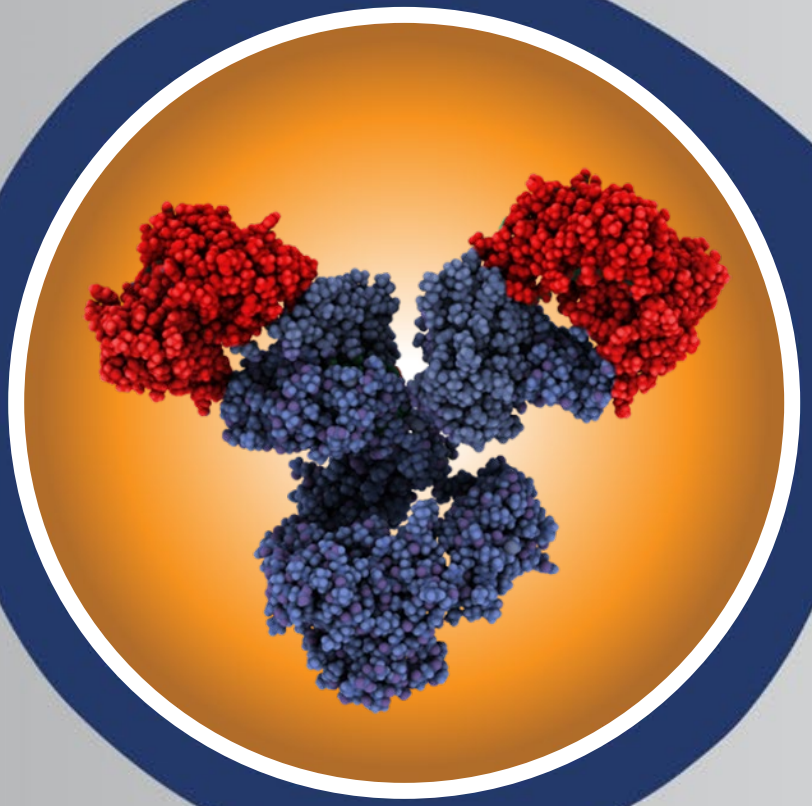

CIRMTUZUMAB

ROR1 monoclonal antibody

Cirmtuzumab: Potentially First-in-class ROR1 Monoclonal Antibody

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OPPORTUNITY

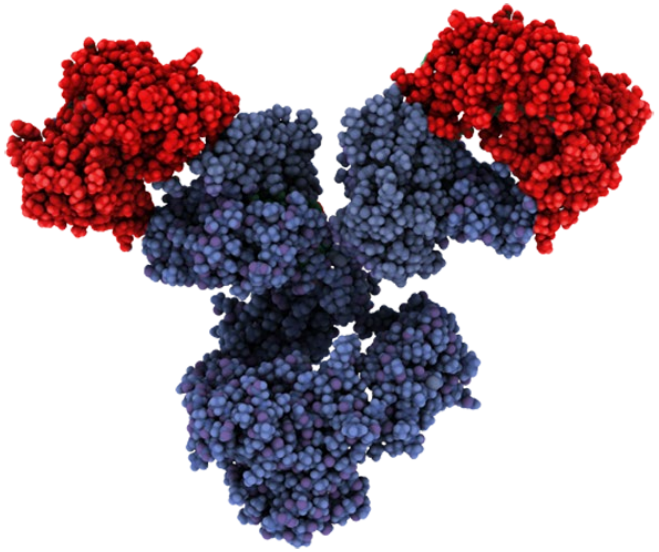
- Potential in multiple hematologic and solid cancers
- Supported by ~$14M non-dilutive CIRM grant
- Patent coverage through 2033

MECHANISM OF ACTION

- High-affinity humanized ROR1 monoclonal antibody
- Inhibits Wnt5a stimulated ROR1 signaling
  - Decreased proliferation, invasion, metastasis, stemness
- Preclinical synergy observed with ibrutinib or paclitaxel

DEVELOPMENT STATUS

- Well-tolerated and active in completed CLL Phase 1
- Phase 2 enrolling in MCL in combination with ibrutinib
- Randomized Phase 2 enrolled in CLL in combination with ibrutinib
- Phase 1b enrolling in HER2-negative breast cancer
- Orphan Drug Designations for MCL and CLL granted by FDA



ROR1 = **R**eceptor tyrosine kinase-like **O**rphan **R**eceptor **1**
CIRM = **C**alifornia **I**nstitute for **R**egenerative **M**edicine

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

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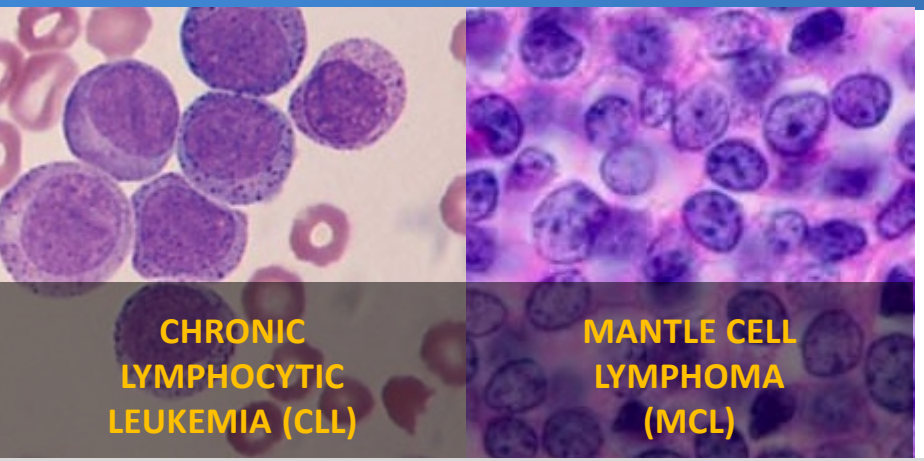

CIRLL Study:

- **C**irmtuzumab and **I**brutinib targeting **R**OR1 for **L**eukemia and **L**ymphoma
- MCL enrollment recently expanded
- Dialogue with FDA regarding potential accelerated approval study design in MCL

STUDY DESIGN

PART 1 (in CLL & MCL)	PART 2 (in CLL & MCL)	PART 3 (in CLL)
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)	**DOSE-EXPANSION COHORT** • Confirm Recommended Dosing Regimen (RDR) of cirmtuzumab (600 mg) + ibrutinib at approved dose (420 mg CLL, 560 mg MCL)	**RANDOMIZED EFFICACY** • Cirmtuzumab + ibrutinib vs ibrutinib • Primary endpoint: Complete Response rate
Enrolled	***MCL Phase 2 enrolling*** *CLL enrolled*	*Enrolled*

CIRLL Trial Cirmtuzumab + Ibrutinib: Patient Characteristics

Data Update at ASH 2020

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Baseline Characteristics			MCL	CLL/SLL
			Evaluable Patients: n=15	Evaluable Patients[1]: n= 56
Age (years)	Median (Range)		64 (49 - 73)	67 (37 - 86)
Gender:	Male / Female	n (%)	13 (87%) / 2 (13%)	37 (66%) / 19 (34%)
MIPI Score[2]:	Intermediate or High	n (%)	14 (93%)	NA
Ki-67%[3]:	Median (range) ≥30% expression	(%) n (%)	35% (10 - 95%) 9 (64%)	NA
Prior Systemic Regimens			**Evaluable R/R pts: n= 15**	**Evaluable R/R Pts: n= 32**
Number:	Median (Range)		2 (1 - 5)	1.5 (1 - 9)
>1 Prior Regimens:		n (%)	11 (73%)	16 (50%)
Ibrutinib:		n	4	0
Stem Cell Transplant:		n	5 Auto-SCT, 1 Allo-SCT	1 Auto-SCT
CAR-T:		n	1	0

(1) CLL: 57% relapsed/refractory, 43% treatment naïve
(2) MIPI-b scores were determined in 14 pts with Ki-67 data, 1 pt had no Ki-67 and used standard MIPI
(3) Ki-67 data available on 14/15 pts

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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%

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	Evaluable* Pts N=	Best ORR** (CR & PR)	Clinical Benefit (CR, PR, SD)	CR	PR	SD	PD
MCL Part 1	12	10/12 (83.3%)	12 (100%)	7 (58.3%)	3 (25%)	2 (16.7%)	0
Part 2	3	3/3 (100%)	3 (100%)	0	3 (100%)	0	0
CLL Parts 1&2	34	31 (91.2%)	34 (100%)	1 (3%)	30 (88%) 26 PR; 4 PR-L	3 (8.8%)	0
Part 3	15 Cirm + Ibrutinib	14 (93.3%)	15 (100%)	0	14 (93.3%) 12 PR; 2 PR-L	1 (6.7%)	0
	7 ibrutinib	7 (100%)	7 (100%)	0	7 PR (100%)	0	0

*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.

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MCL Patient Characteristics and Swimmer Plot

Data Update at ASH 2020

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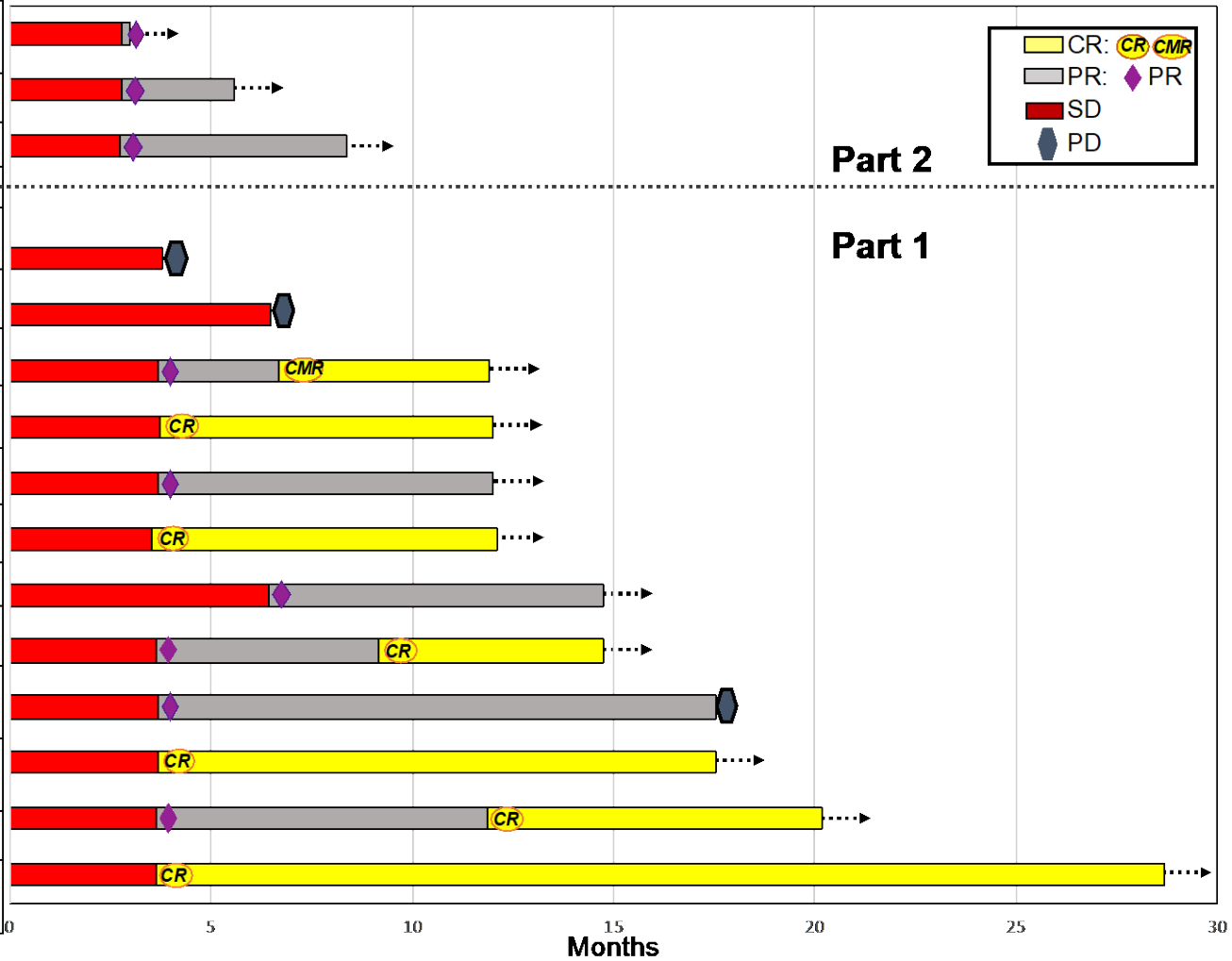
Resp to Cirm	# Prior Tx	Prior Treatment Regimens	MCL Variant / Ki67	MIPIb Score at SCR	Bulky >5cm LD	Cirm Dose	Change Tumor Size
PR	2	R-CHOP/ Lenalidomide; Rituximab/High dose Cytarabine/Lenalidomide	Ki67 20%	Int. 6.2	Yes	600 mg	-97%
PR	1	R-HyperCVAD and R-Methotrexate/Cytarabine	Blastoid Ki67 95%	High 8.1	Yes	600 mg	-64%
PR	1	Rituximab	Ki67 50%	High 6.6		600 mg	-66%
SD*	2	RCHOP/ITMTX, R-hyperCVAD	Pleo. Ki67 90%	High 7.1	(4.8cm)	8 mg/kg	-79%
SD	2	RCHOP, R-DHAP	Ki67 10%	High 6.7		16 mg/kg	-11%
CMR	2	RCHOP; R-BEAM/Auto-SCT	Ki67 10%	High 6.8		2 mg/kg	-100%
CR	2	R/Ibrutinib (10mths); R-HyperCVAD	Pleo. Ki67 70%	High 7	Yes	8 mg/kg	-97%
PR	2	R/Ibrutinib (10mths); R-HyperCVAD	Ki67 40%	High 6.6		4 mg/kg	-54%
CR	2	R/Ibrutinib (7mths); R-HyperCVAD	Nodular Ki67 30%	Int. 5.8		16 mg/kg	-100%
PR	1	R/Ibrutinib	NA	Int. 5.7 No KI-67	Yes	8 mg/kg	-91%
CR	4	R/hyperCVAD, RCHOP, RICE, BEAM/Auto-SCT	Ki67 ~30%	Int. 5.8		16 mg/kg	-95%
PR	3	Benda/R, R/AraC/Cisplt/Dex, BEAM/ Auto-SCT	Ki67 60%	High 7.8		4 mg/kg	-78%
CR	4	RCHOP/HDMTX/R, R/velcade/ITMTX, Auto-SCT, CAR-T	Nodular Ki67 ~15%	Low 5.5		4 mg/kg	-100%
CR	1	RCHOP (Plus RT to orbits)	Blastoid Ki67 75%	High 7.6		2 mg/kg	-77%
CR	5	RCHOP, BEAMR/ Auto-SCT, Benda/R/Allo-SCT, ICE-R, R	Diffuse Ki67 20%	High 7	Yes	2 mg/kg	-100%



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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.

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

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

Data Update at ASH 2020

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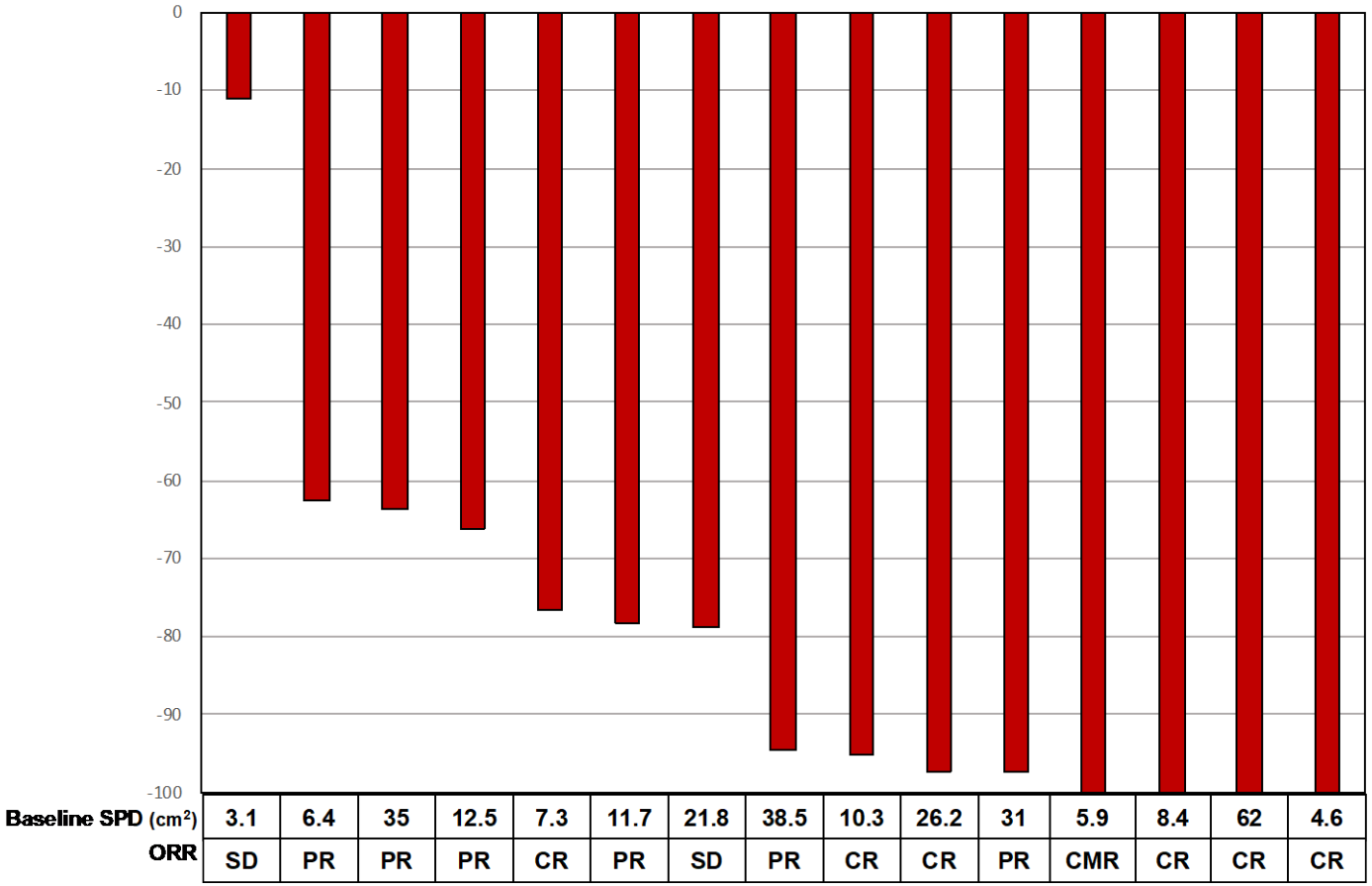
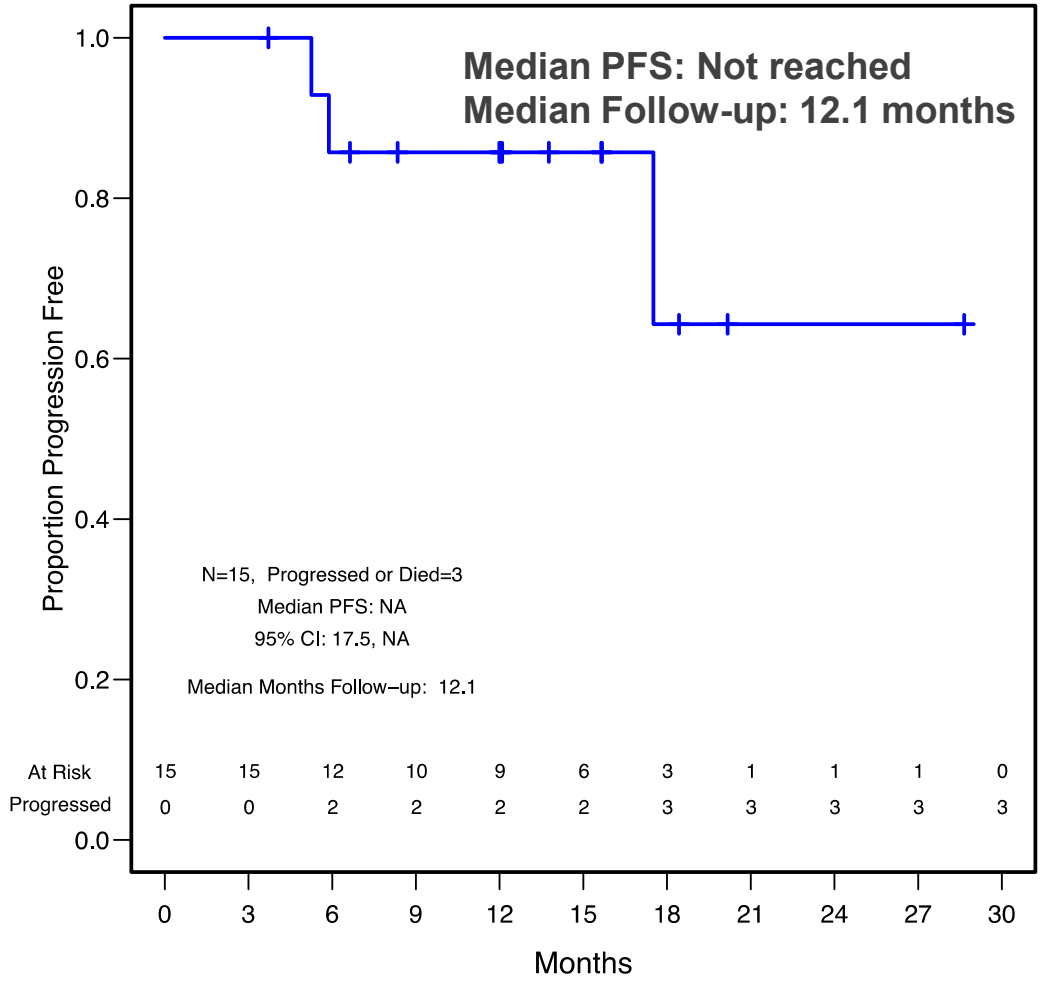
Best Tumor Reduction (SPD cm²)



Progression-Free Survival



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).

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

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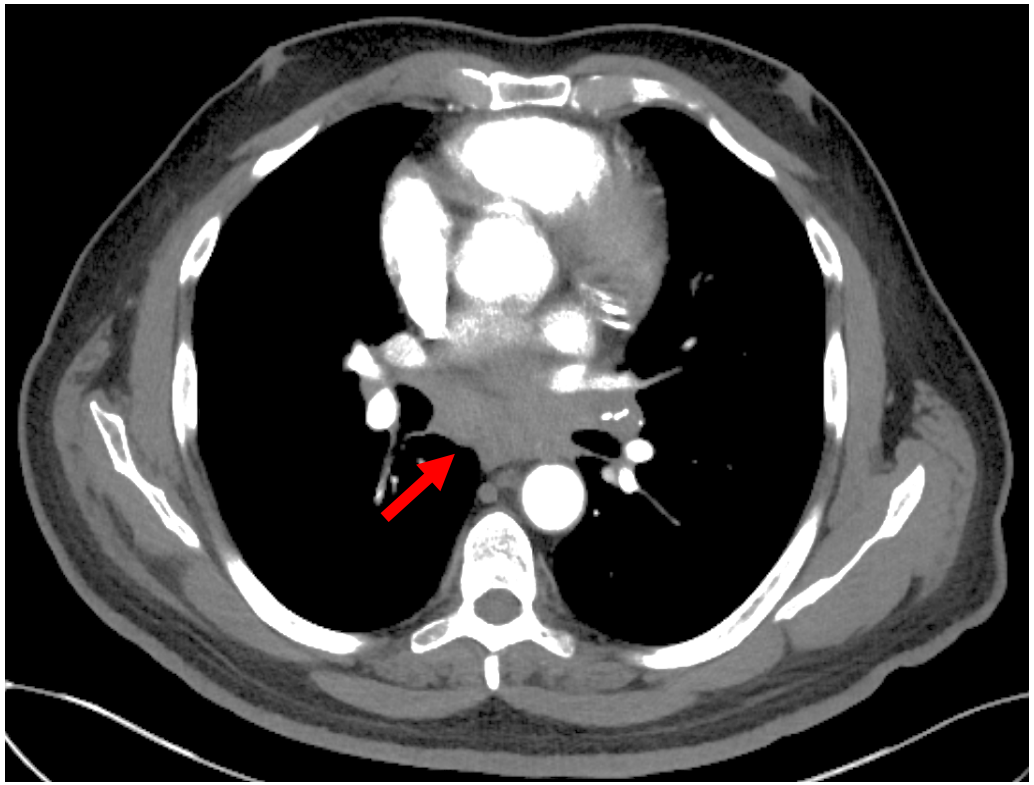
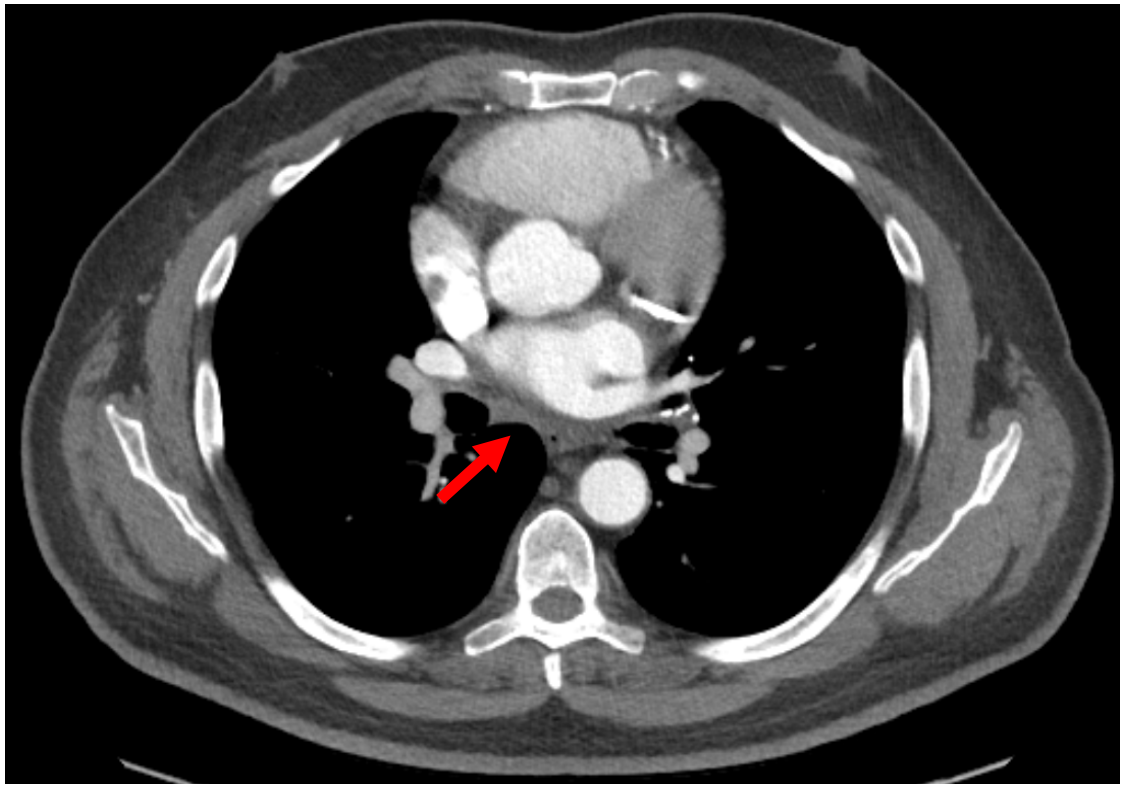
- 65-year-old male initially diagnosed in 2016 with MCL stage IV including involvement of bilateral orbits
- Initial treatment: radiation therapy and R-CHOP
- Recurred and enrolled onto Part 1 Cirmtuzumab/Ibrutinib study in 2019 at the 2mg/kg dose level
- High risk factors: Blastoid subtype; Ki-67: 75%;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

Pretreatment



<4 months Post Cirmtuzumab/Ibrutinib



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Cirmtuzumab + Ibrutinib Interim Clinical Results in MCL Compare Favorably to Historical Single-Agent Ibrutinib Data

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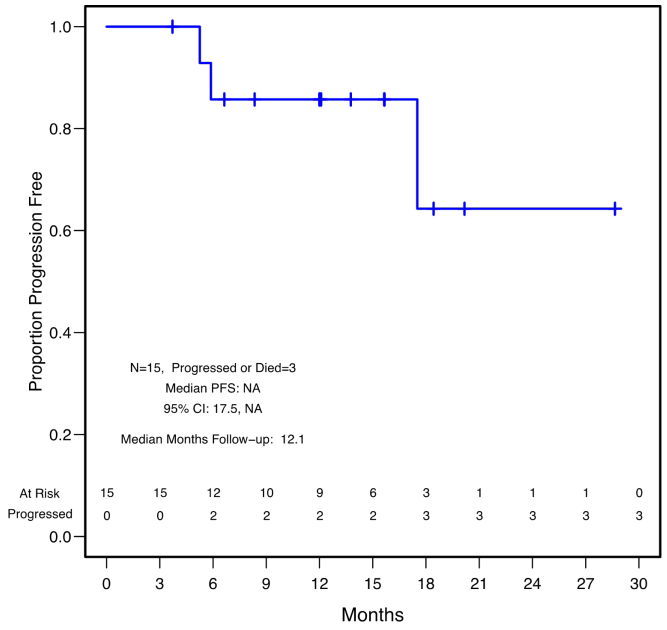
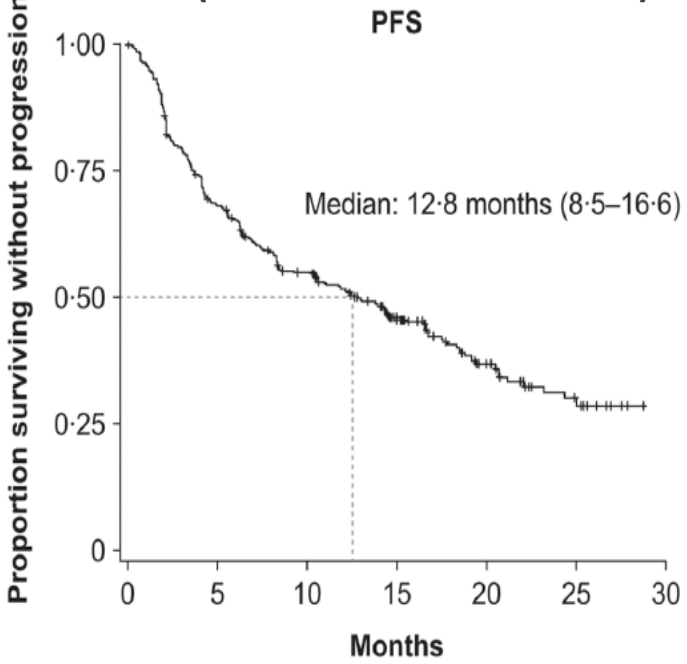
Progression-free survival

Cirmtuzumab + ibrutinib (Lee 2020 ASH)



Single-agent ibrutinib (Rule 2017 Br J Haematol)



Baseline characteristics	**Median lines of prior therapy**	2 (73.3% with >1 prior lines)	2 (73.2% with >1 prior lines)
	Median follow-up	12.1 months	24-25 months
Clinical outcomes	**Median PFS**	Not reached. 95% CI: (17.5 months - NA)	12.8 months. 95% CI: (8.5 – 16.6 months)
	ORR	87%	66%
	CR	47%	20%

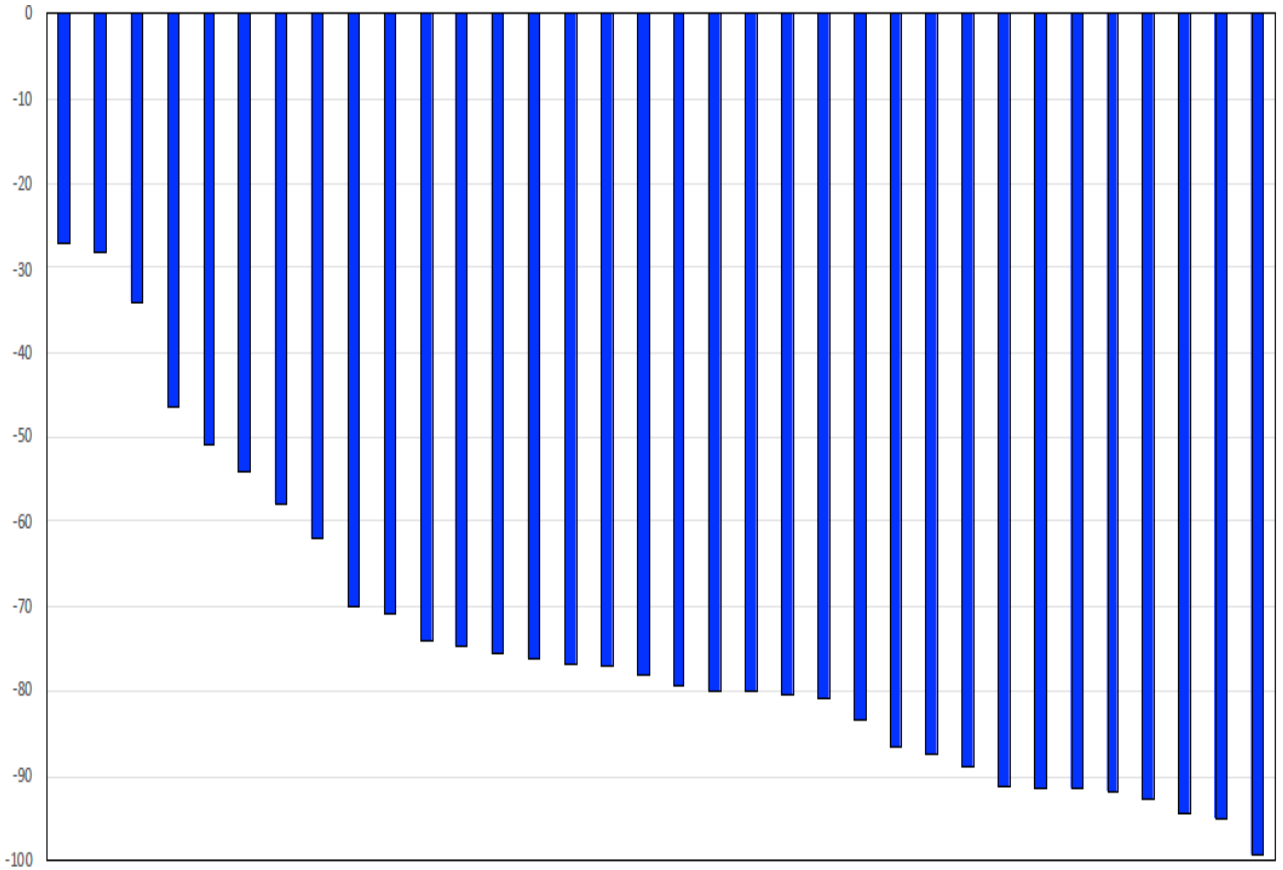
Note: Data presented are from separate studies and such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of the combination of cirmtuzumab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

CLL: Tumor Reduction and Progression-Free Survival

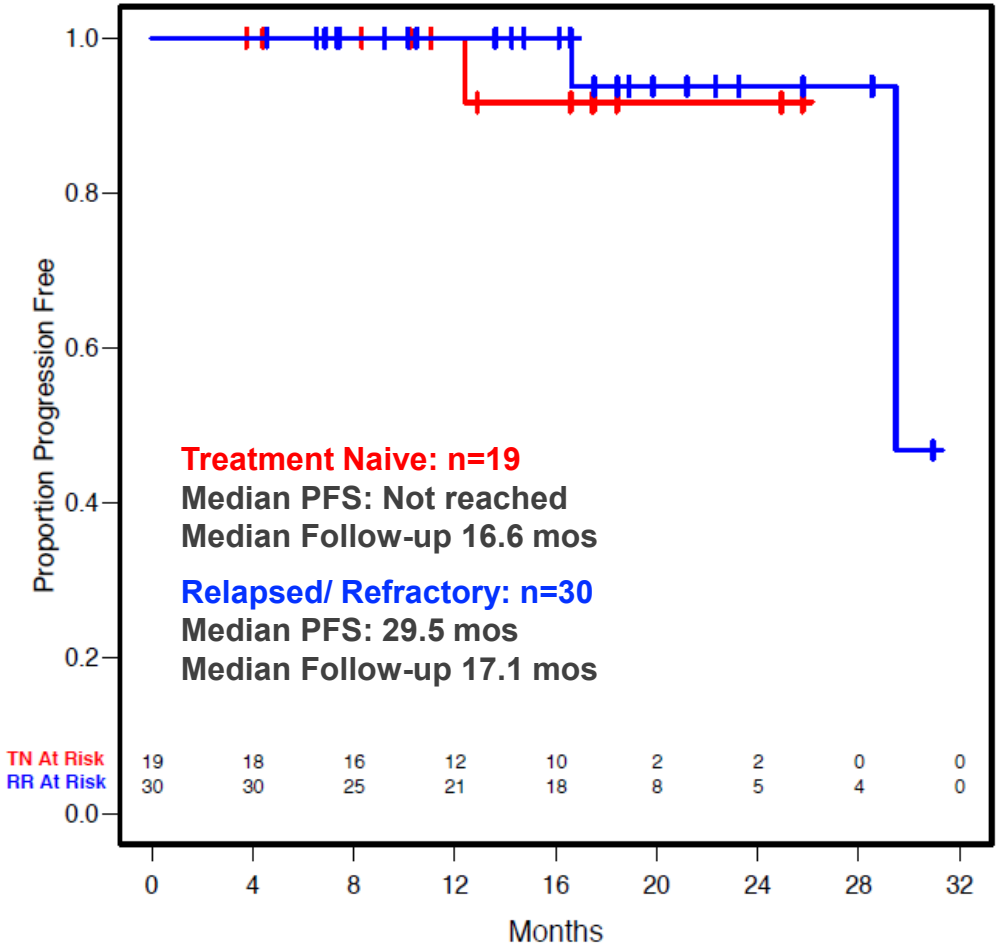
Data Update at ASH 2020

ONCTERNAL therapeutics™

CLL Parts 1 & 2: Best % Tumor Reduction (SPD cm²)



Progression-Free Survival



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CIRLL Trial Cirmtuzumab + Ibrutinib: Summary

Data Update at ASH 2020

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MCL:

- The combination of cirmtuzumab plus ibrutinib is a well-tolerated and active regimen
  The time to response, depth, and durability of responses are compelling for further development
- High response rate*: ORR 87% (13/15), clinical benefit 100% (7 CR/CMR, 6 PR, 2 SD)
  Complete responses durable for 5 - 25+ months, with no progressions reported after CR
- Encouraging PFS: median not reached at median follow-up now >12 months
- Encouraging efficacy (objective responses) in high-risk sub-populations:
  - Prior SCT or CAR-T (5/15): 4 CR, 1 PR
  - Ki-67 levels ≥30% (9/14): 4 CR, 4 PR
  - Intermediate/high MIPI (14/15): 6 CR, 6 PR
  - Prior ibrutinib (4/15): 100% responded, 2 CR, 2 PR

CLL/SLL:

- The combination of cirmtuzumab plus ibrutinib is a well-tolerated and active regimen in CLL.
  Parts 1, 2, & 3: ORR 91.8% (45/49) and Clinical Benefit 100% (49/49)
- One patient achieved a CR that was durable for >17 months off all therapy
- Median PFS: not reached for treatment-naïve CLL after median follow-up of 16.6 months
- Median PFS: 29.5 months for patients with r/r CLL after median follow-up of 17.1 months

- Adverse events 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

*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.

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Unmet Medical Need: Mantle Cell Lymphoma and Chronic Lymphocytic Leukemia

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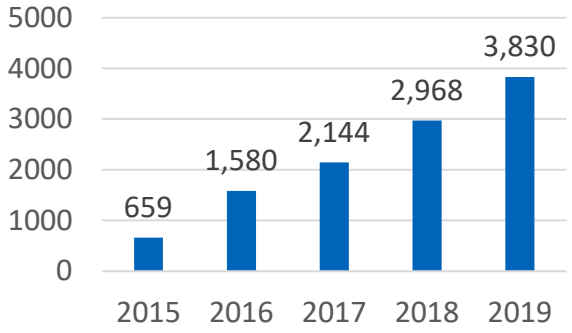
Unmet Medical Need

- While ibrutinib alone is active in MCL and CLL, patients are not cured and must continue treatment until intolerance or resistance develops:
  - MCL ibrutinib CR rate ~25%[1]
  - CLL ibrutinib CR rate < 10%[2]
- US incidence[3]
  - MCL ~4,200 p.a.
  - CLL ~20,000 p.a.
- Average age at diagnosis
  - MCL: mid-60s[3]
  - CLL: 71[4]

Cirmtuzumab + BTKi Target Product Profile

- Potential differentiation in MCL and CLL: achieve deeper and more durable responses than BTKi alone, with better tolerability or minimal added toxicity
- Become standard-of-care combination therapy for patients with MCL and CLL, particularly for patients who are older and/or have significant co-morbidities
  - Certain other combination therapies are associated with significant toxicities

Ibrutinib U.S. Sales ($M)[5]



(1) Wang 2015 Blood, Rule 2019 Haematologica
(2) O'Brien 2018 Blood; CR rate at 12 months of therapy
(3) seer.cancer.gov, Dec. 2019; Leukemia and Lymphoma Society
(4) cancer.net, Dec. 2019
(5) AbbVie Form 10-K Feb. 2020

BTKi = Bruton tyrosine kinase inhibitor

Strong Rationale for Treating TN Breast Cancer with Cirmtuzumab

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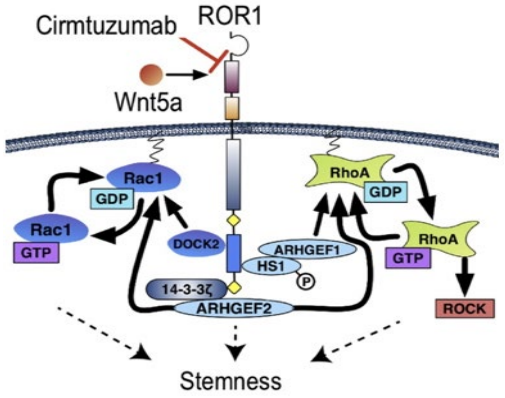
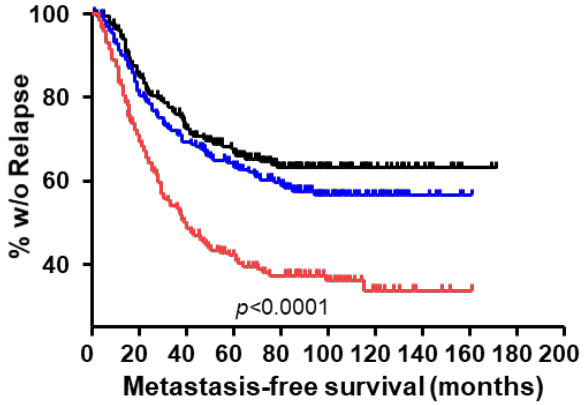
ROR1 Expressed on Multiple Solid and Liquid Tumors

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%

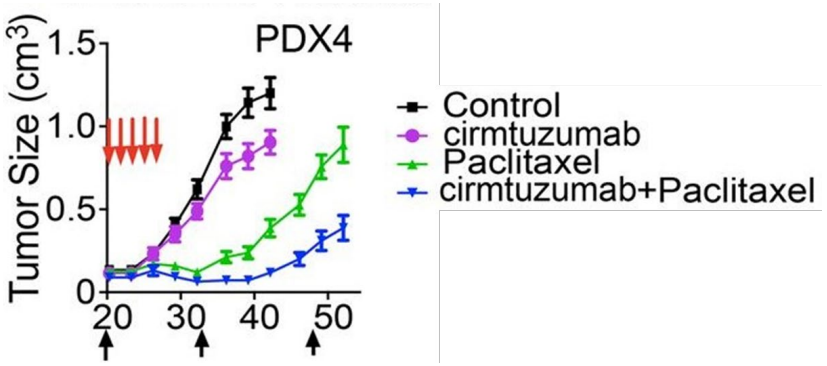
Zhang 2012 AJP



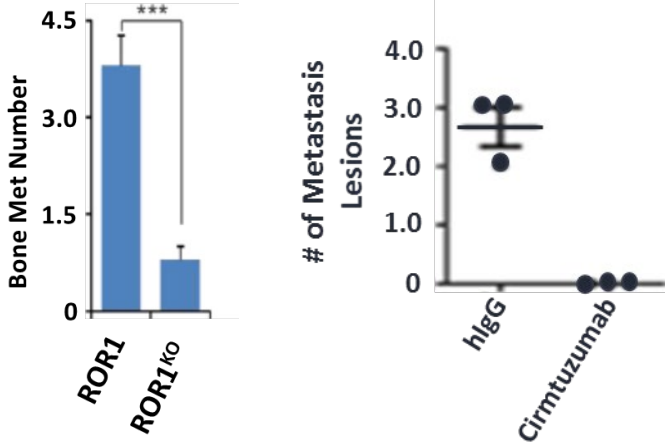
Wnt5a activation of tumor ROR1 is associated with a primitive, stem-like phenotype
Choi 2018 Cell Stem Cell



High ROR1 expression in the breast cancer primary tumor is associated with a poor long-term prognosis
Cui 2013 CaRes



Cirmtuzumab and paclitaxel are at least additive against TNBC PDX growth, and eliminate tumor forming cells
Zhang 2019 PNAS



ROR1 knockout (L) or Cirmtuzumab (R) inhibit breast cancer xenograft metastases
Li 2017 Nature Cell Bio, Zhang 2019 PNAS

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

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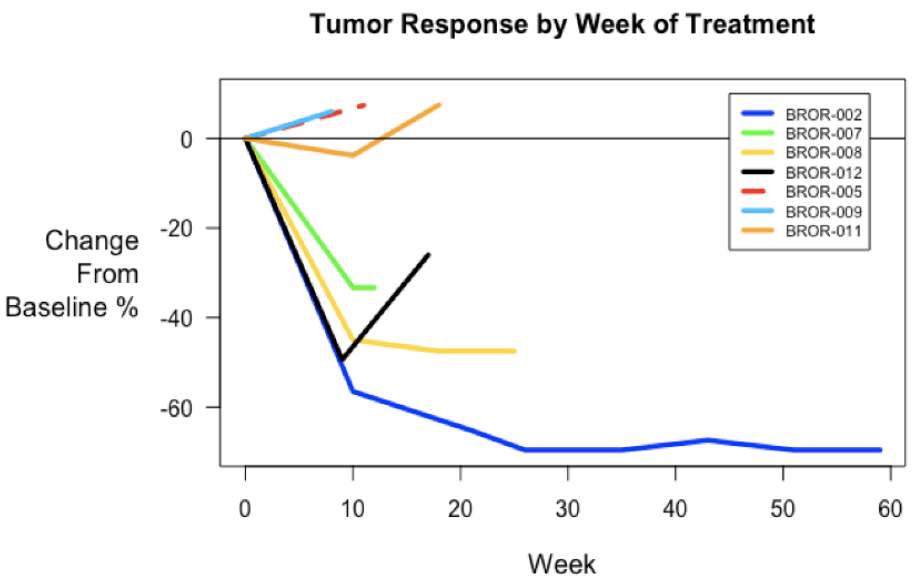
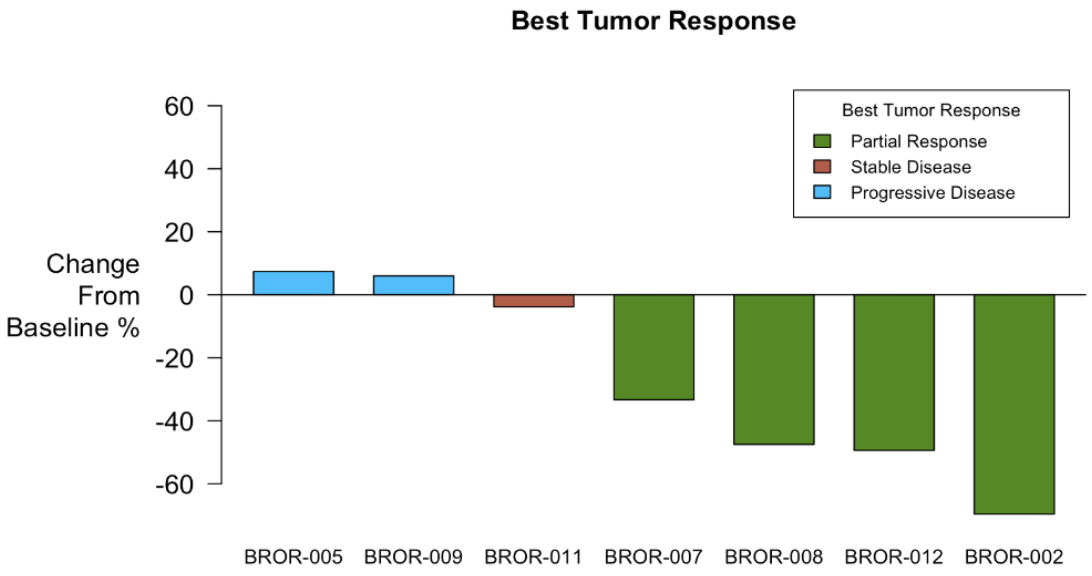
% Tumor Volume Reduction by Week of Therapy



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



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.

Shatsky 2019 SABCS
(data cutoff November 27, 2019)

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/m^2 paclitaxel weekly
- No DLTs or discontinuations
- Adverse events consistent with paclitaxel profile
- PK consistent with half-life of 30 days

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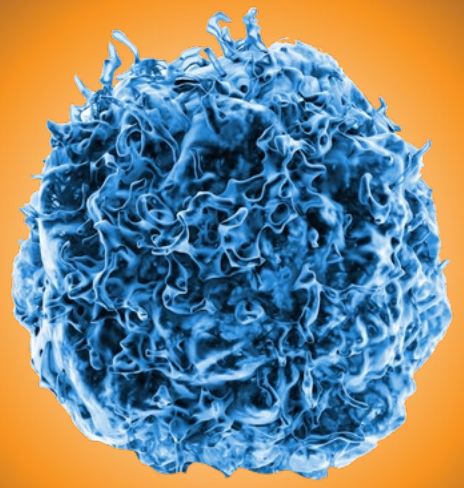

CAR-T Program

Targeting ROR1

CAR-T Targeting ROR1 Designed to Avoid Two Common CAR-T Challenges

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Unmet Need: Emerging CAR-T Issues		Advantages to Targeting ROR1
Treatment failures • Increasing number of patient relapses following CAR-T therapy, frequently due to mutations or loss of the target antigen tumor (e.g. CD19), evading CAR-T efficacy	→	**Potential for fewer antigen negative relapses** • ROR1 expression associated with aggressive tumor phenotype • ROR1 mutation or antigen loss might render cancer cells less aggressive and susceptible to chemotherapy
Safety concerns • Persistent CAR-T safety issues including deaths potentially related to activation by normal cells expressing the target antigen	→	**Potential safety advantages** • Cirmtuzumab did not bind to normal human tissues in GLP tissue cross-reactivity studies • No serious adverse events related to cirmtuzumab-only reported in clinical studies

ROR1 CAR-T Cells Showed Potent Anti-tumor Activity in CLL model

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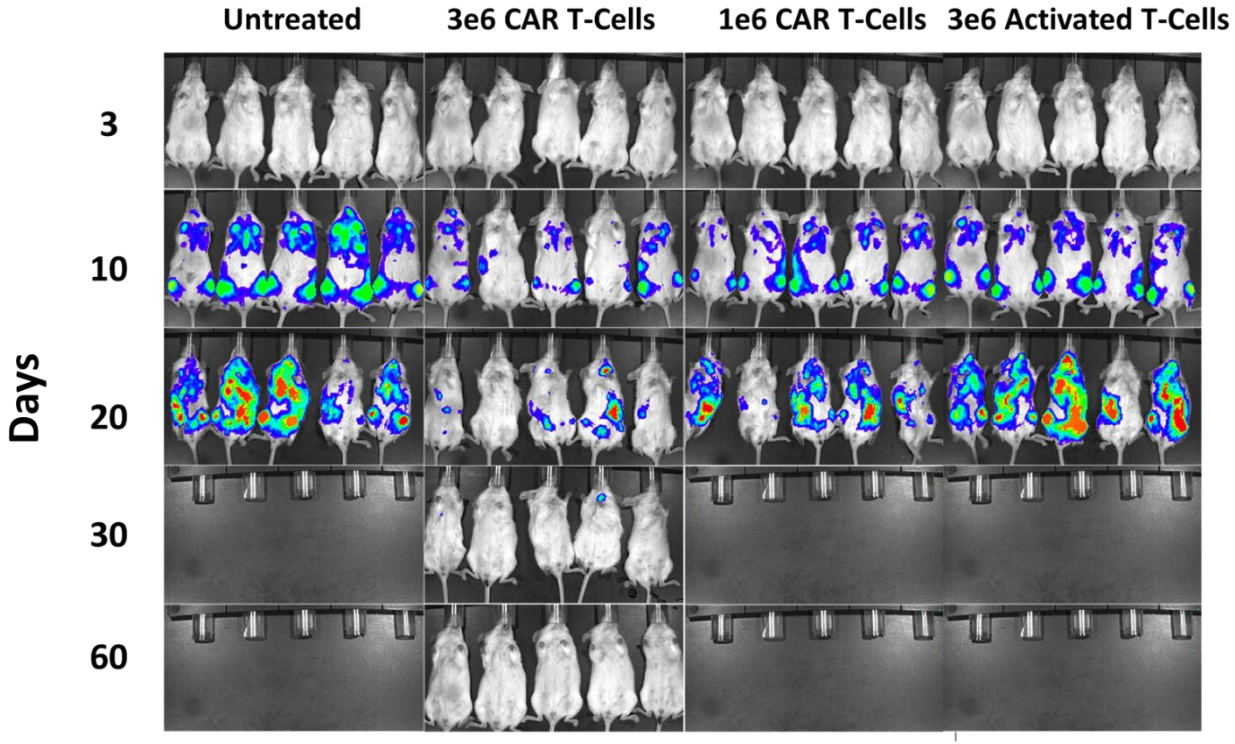
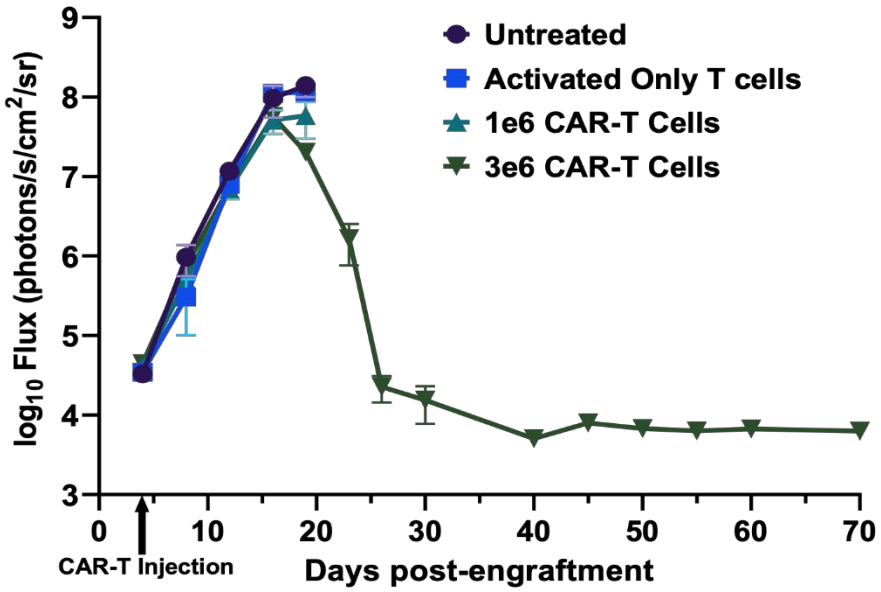


Bioluminescence imaging of mice inoculated with MEC1-ROR1 cells and with ROR1 CAR T-cells. Animals treated with CAR-T cells had reduced disease burden compared to controls.



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

ROR1 CAR-T: Program Overview

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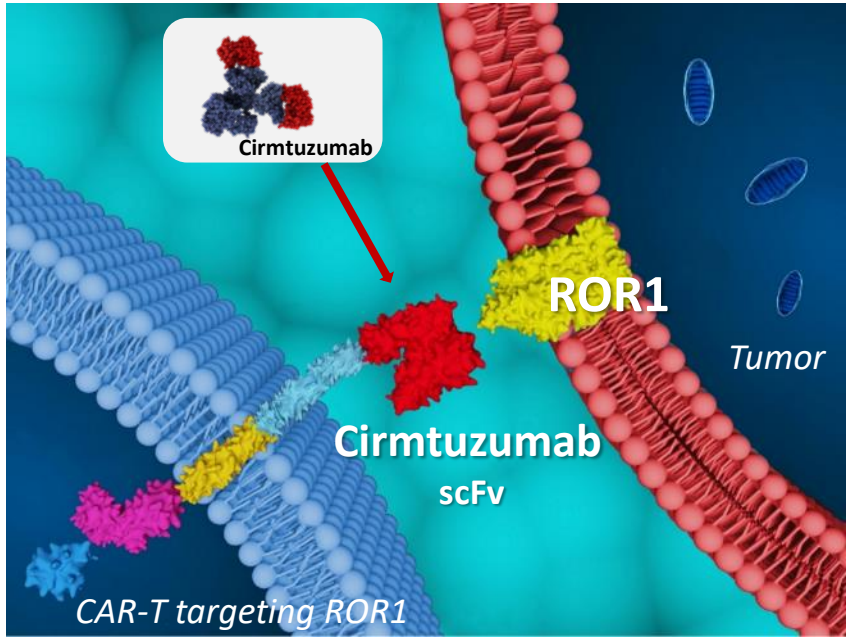
DEVELOPMENT STATUS

- Preclinical data in hematologic and solid tumor models
- Utilizing cirmtuzumab scFv as targeting component
- Ongoing process optimization and scale-up
- UCSD collaboration with non-dilutive financing from California Institute for Regenerative Medicine (CIRM)
- Shanghai Pharma collaboration, which covers certain manufacturing and clinical development costs

OPPORTUNITY

- Selective targeting strategy applicable to multiple tumors with ROR1 expression
- Target initial human proof-of-concept in hematological cancers, then expansion into solid tumors



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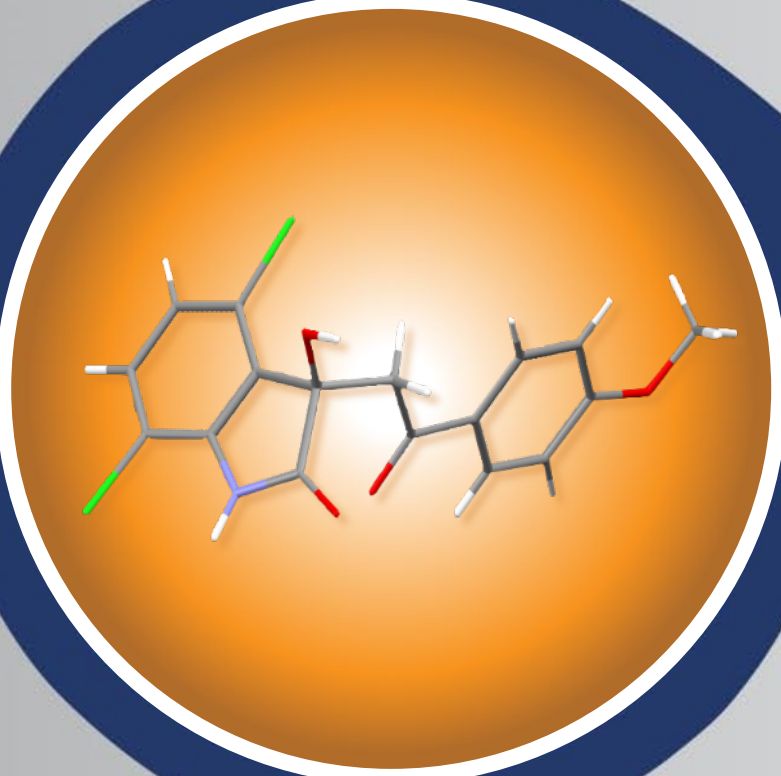

TK216

Targeted ETS Oncoprotein Inhibitor

TK216: First-in-Class Targeted ETS Oncoprotein Inhibitor

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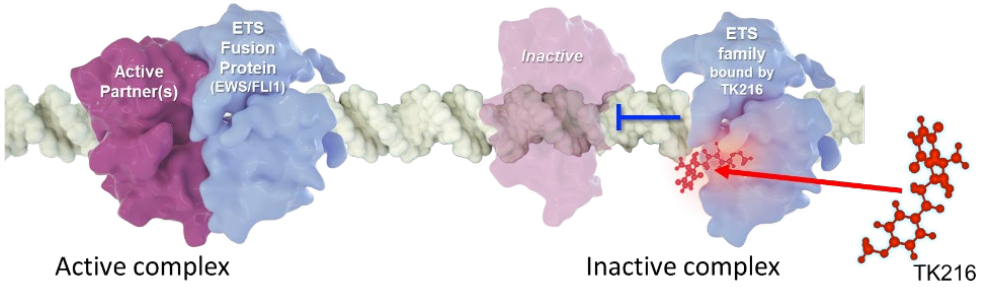
OPPORTUNITY

- Fast-to-market strategy in Ewing sarcoma
  - Potentially Pediatric Voucher eligible
- Significant market potential in other cancers with ETS alterations
  - AML, prostate cancer, DLBCL
- 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

ETS = **E**26 **T**ransformation-**S**pecific oncogene family

DEVELOPMENT STATUS

- Enrolling expansion cohort for relapsed/refractory Ewing sarcoma
- Rare Pediatric Disease Designation, Orphan Drug Designation and Fast Track Status granted by FDA

Erkizan NatureMed 2009

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

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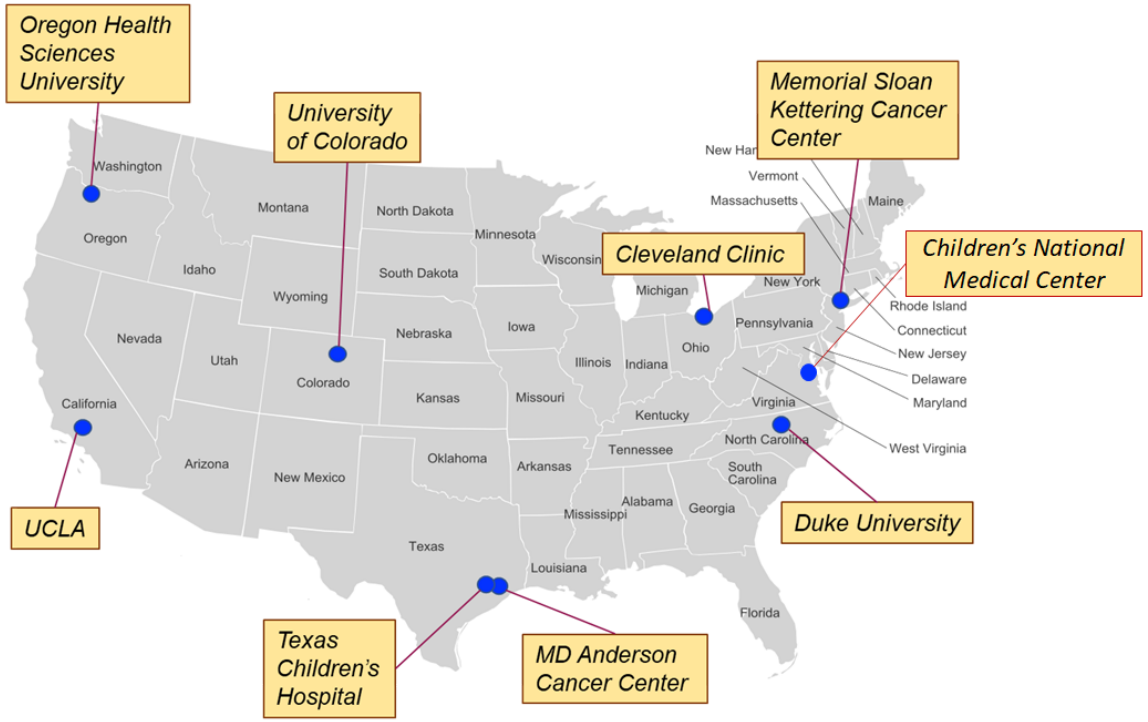
- 3+3 dose and schedule escalation cohorts completed
  - 32 evaluable patients with relapsed/refractory Ewing sarcoma
  - Average of 4 prior therapies
  - Recommended Phase 2 dose (RP2D) established: TK216 200 mg/m^2/day for 14 days + vincristine 0.75 mg/m^2 day 1
- Safety: generally well-tolerated, 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 at RP2D: 2 complete responses (one surgical CR), 8 SD[1]
  - 23 evaluable patients
- Enrollment in expansion cohort is ongoing



(1) Ludwig 2020 CTOS, efficacy data cutoff 10/16/2020

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

Interim Data Presented at CTOS 2020

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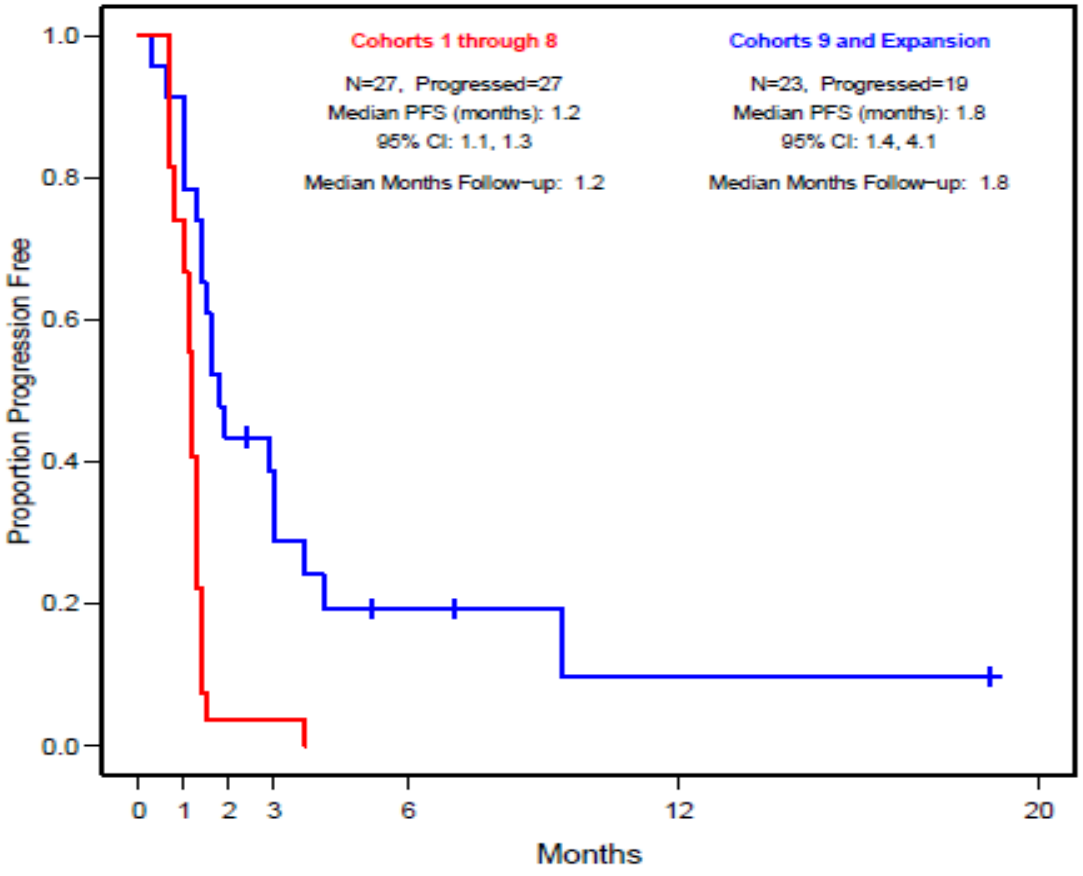
Overall Best Clinical Response

	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



(1) Ludwig 2020 CTOS, efficacy data cutoff 10/16/2020

TK216 Elimination Pharmacokinetics

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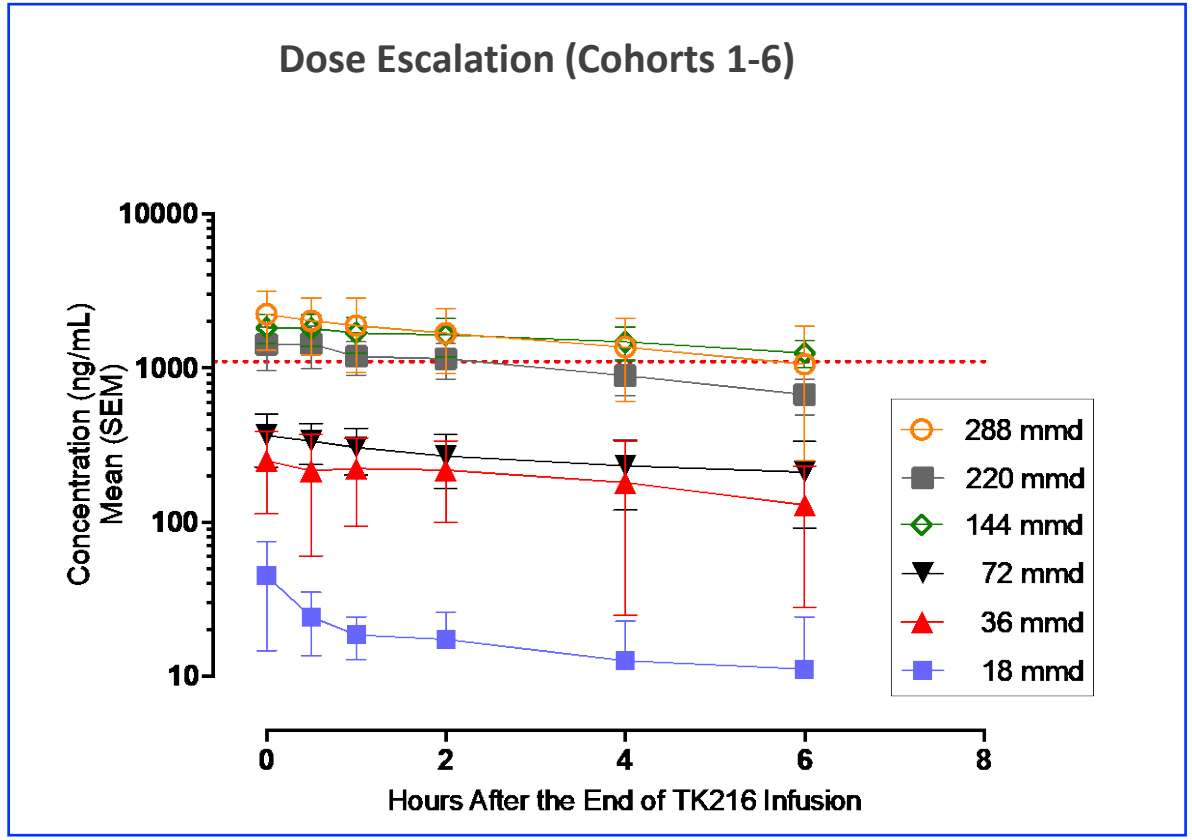

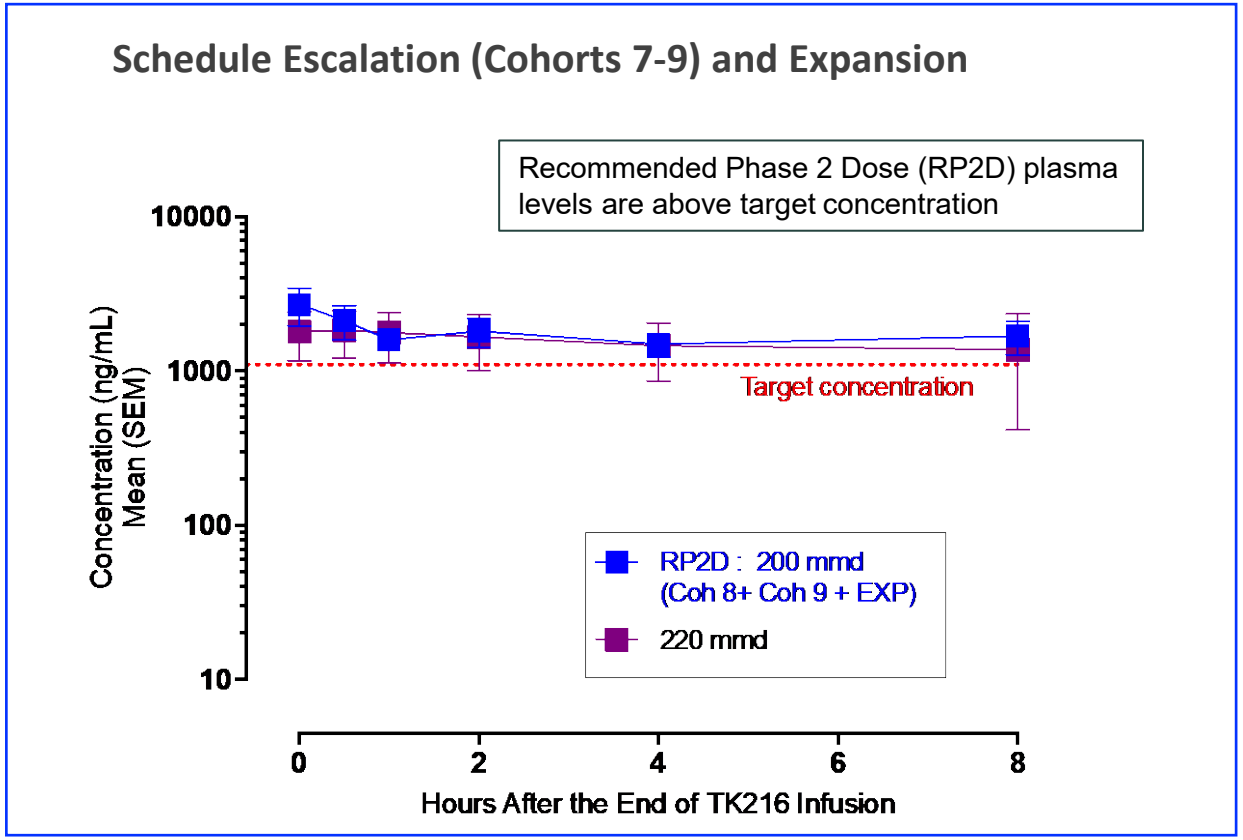

- Time = 0 values reflect steady state at the end of the TK216 infusion
- Half-life is relatively long (8-12 h) with dose proportional increase in concentrations
- Preclinical data suggest that TK216 levels in the 75 to 188 ng/mL range were effective at tumor killing in vitro, and plasma levels in the 265 to ~1500 ng/mL were associated with efficacy in animal tumor model

(1) Ludwig 2020 CTOS, efficacy data cutoff 10/16/2020

First Sustained Complete Response with TK216 in Patient with Metastatic Relapsed/Refractory Ewing Sarcoma

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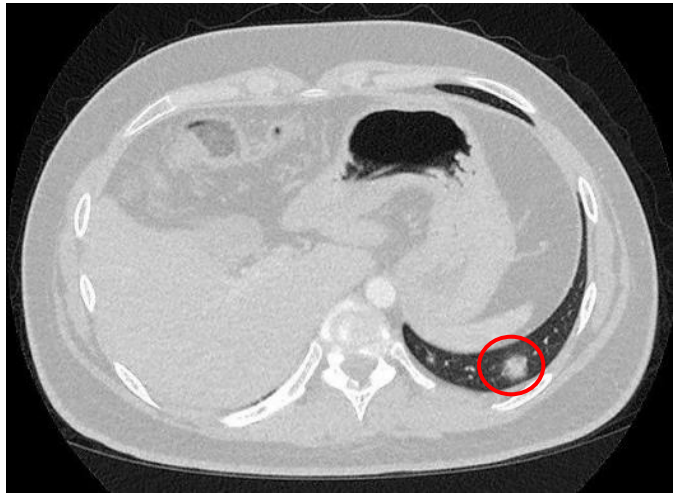
Patient background

- 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

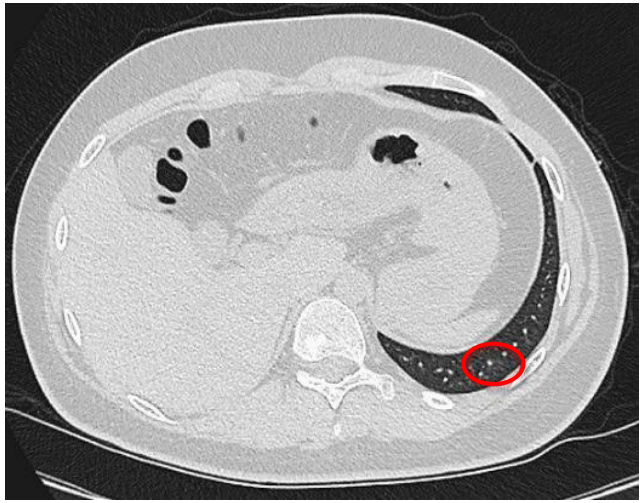
- Received TK216 in final dose-finding cohort (200 mg/m^2/day)
- **Resolution of target lesion after two cycles of single-agent TK216**
  - Treatment well tolerated, with minimal myelosuppression
  - Vincristine added starting in third cycle
- Residual non-target 7 mm lung lesion excised after 6 months of therapy, leading to **surgical complete remission**
- Treatment ongoing, **no evidence of disease at >1.5 years on study**



Baseline

2 cycles single-agent TK216

All target lesions resolved



Meyers 2019 CTOS and data cutoff 8/13/2020
MSKCC = Memorial Sloan Kettering Cancer Center

Second Complete Response with TK216 in Patient with Metastatic Relapsed/Refractory Ewing Sarcoma

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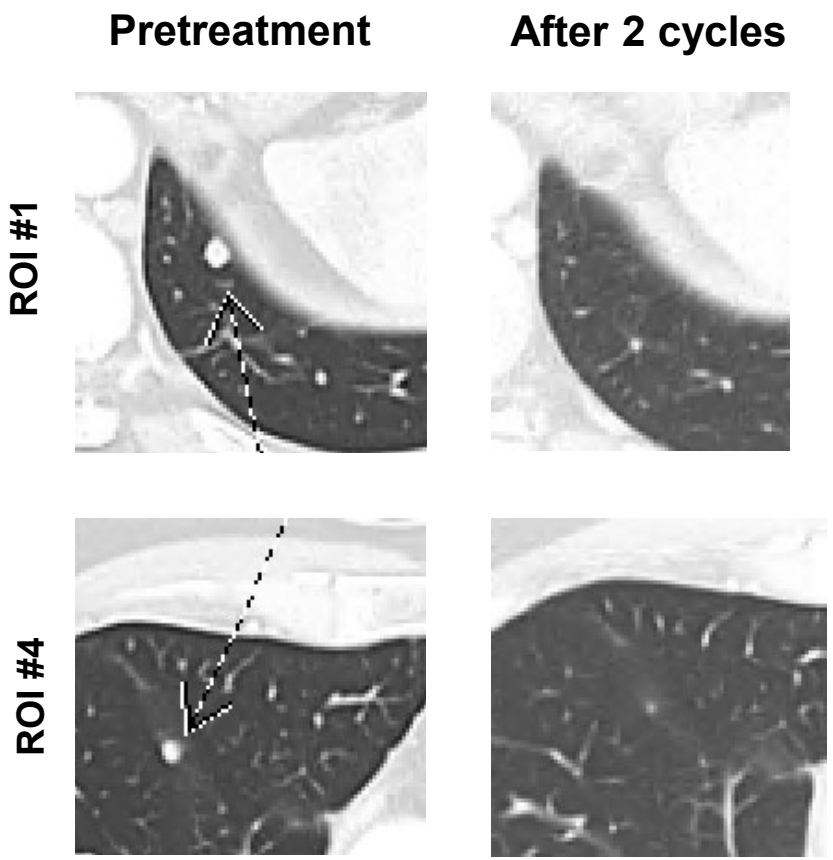
- **Patient:** 51-year-old with Ewing sarcoma diagnosed June 2018
  - 10-cm tumor near the right kidney and multiple lung metastases
- **Extensive prior treatment:**
  - Chemotherapy: vincristine/doxorubicin and ifosfamide (VAI), high-dose ifosfamide
  - Surgery: right nephrectomy and vascular reconstruction
- **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/m^2/day for 14 days + vincristine 0.75 mg/m^2 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**



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

Data Cutoff 8/13/2020

Unmet Medical Need
Relapsed / Refractory Ewing Sarcoma

ONCTERNAL therapeutics™

- 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.[(1)]
  - U.S. prevalence ~4,000 [(1)]
- 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

(1) Incidence 1.3 per million, prevalence 12 per million – SEER data "ICD-0-3/WHO 2008 Ewing Tumor", accessed January 3, 2020; NCI Ewing Sarcoma Treatment (PDQ), accessed September 11, 2019; Company analysis

Additional Opportunities for TK216 in Cancers with ETS Alterations

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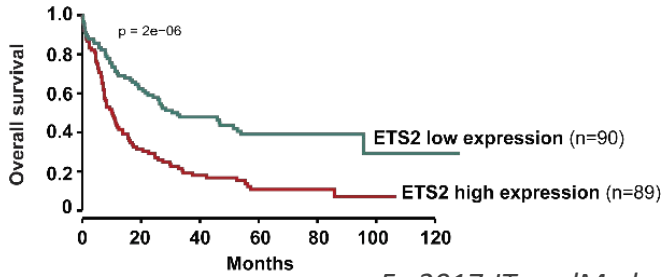
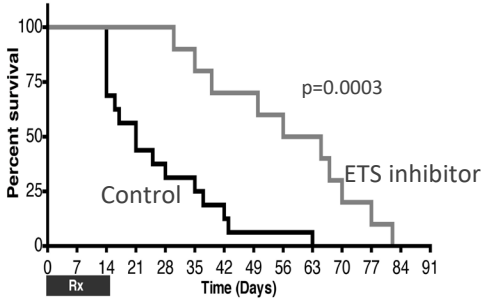
Acute Myeloid Leukemia (AML)

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



Fu 2017 JTranslMed

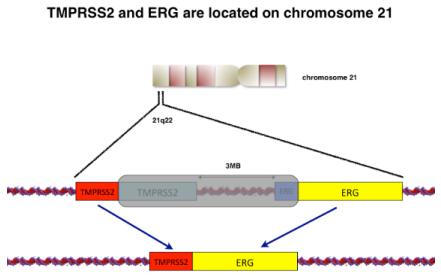
- Sensitivity of AML cell lines to TK216 was proportional to level of ETS overexpression
- ETS inhibition prolonged survival in EWS-FLI1 transgenic AML model



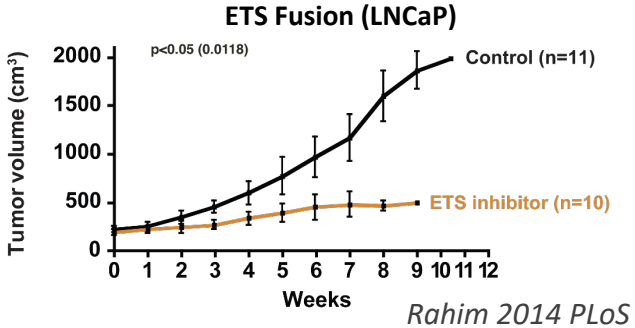
Minas 2015 Oncotarget

Prostate Cancer

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



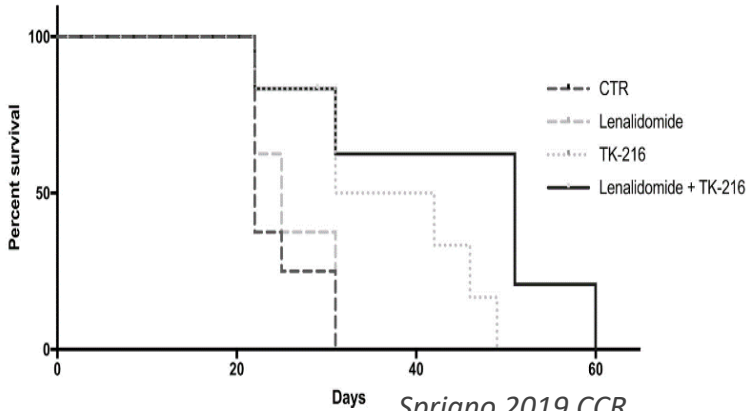
- ETS inhibition demonstrated anti-tumor activity in human prostate cancer xenograft model



Rahim 2014 PLoS One

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 model
- Anti-tumor activity demonstrated in xenograft models



Spriano 2019 CCR

ONCTERNAL therapeutics™

BUSINESS & FINANCIALS

Financial Information

ONCTERNAL therapeutics™

Ticker	ONCT (Nasdaq)
Cash & Cash Equivalents @ 9-30-20 Cash Runway into 2023[1]	$21.3M
Debt	$0.0M
Capitalization:	
Common Shares Outstanding[1]	48.8M
Options in the Money @ 9-30-20[2]	0.5M
Fully Diluted	49.3M
Non-Dilutive Support • CIRM Grant for CIRLL Study • Ibrutinib CTM for CIRLL Study	~$14M Expanded Supply Agreement

(1) Includes 26.4M shares issued in connection with $109M raised in Q4 2020 offerings
(2) Excludes out of the money options and warrants totaling ~7.8M, including warrants issued to the underwriter in connection with Q4 2020 offerings

Anticipated Pipeline Milestones

ONCTERNAL therapeutics™

- Cirmtuzumab
  - MCL clinical data update for ongoing Phase 1/2 — **1H 2021**
  - CLL clinical data update for ongoing Phase 1/2 — **1H 2021**
  - HER2-negative breast cancer clinical data update for ongoing Phase 1b — **1H 2021**
  - Preclinical data in additional ROR1 expressing tumors — **1H 2021**
- ROR1 CAR-T first-in-human dosing in China — **2H 2021**
- TK216
  - Ewing sarcoma Phase 1 expansion cohort data update — **1H 2021**
  - Preclinical data in additional ETS-driven tumors — **1H 2021**

Corporate Highlights

ONCTERNAL therapeutics™

THREE NOVEL ONCOLOGY PRODUCT CANDIDATES IN DEVELOPMENT

CIRMTUZUMAB: 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: PRECLINICAL DEVELOPMENT WITH CIRM AND SHANGHAI PHARMA

- Potential to improve on CAR-T efficacy and safety

TK216: TARGETED ETS INHIBITOR

- Two durable complete responses in patients with metastatic relapsed/refractory Ewing sarcoma in ongoing Phase 1/2
- Additional opportunities in other cancers with ETS alterations

MULTIPLE DATA CATALYSTS EXPECTED IN NEXT 12 MONTHS

- Clinical data updates expected in MCL, CLL, breast cancer and Ewing sarcoma
- ROR1 CAR-T expected to reach clinic in 2021 in China

EXPERIENCED MANAGEMENT AND BOARD OF DIRECTORS