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# **Corporate Highlights**

We are a clinical stage biotech company developing antibody therapeutics for cancer

LEAD ASSETS

CTX-009: DLL4 x VEGF-A bispecific antibody

CTX-471: CD137 agonist antibody

CTX-8371: PD-1 x PD-L1 bispecific antibody



StitchMabs™ platform designed to identify synergistic bispecific antibodies

Common Light Chain technology enables multi-specificity and manufacturability

Focus on Translational research



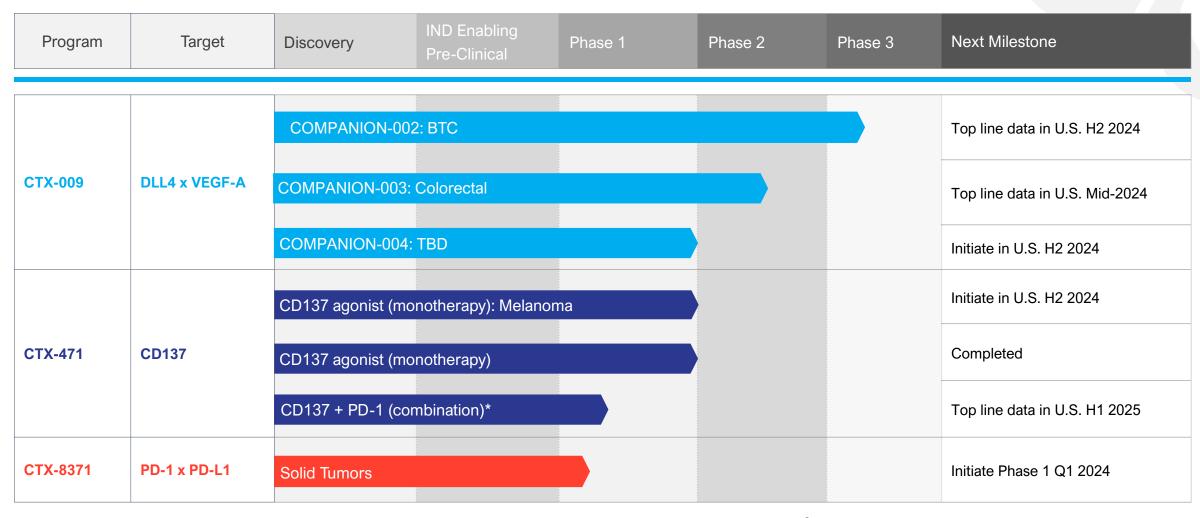
Cash runway into mid-2026 (YE 2023: \$152M)

Funded by leading life-science investors

~32 FTEs based in Boston, MA with experienced leadership team



# Focused Pipeline with Multiple Value Inflection Points



<sup>\*</sup>Clinical collaboration with Merck & Co. Inc., Rahway NJ USA in combination with anti-PD-1 therapy KEYTRUDA®



# Leadership Team Experienced in Drug Discovery and Development



Jon Anderman VP, Head of Legal



Vered Bisker-Leib, PhD, MBA CEO



lan Chia, PhD VP, Business Development



Bing Gong, PhD VP, Protein Sciences



**Karin Herrera**VP, Clinical Operations



James Kranz, PhD VP, CMC



Neil Lerner, CPA, MIM VP, Finance



Minori Rosales, MD, PhD SVP, Head of Clinical Development



Kris Sachsenmeier, PhD VP, Translational Science



Thomas J. Schuetz, MD, PhD
President of R&D and Vice Chairman



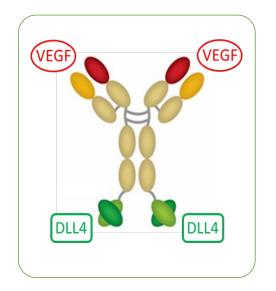
CTX-009

DLL4 X VEGF-A bispecific antibody

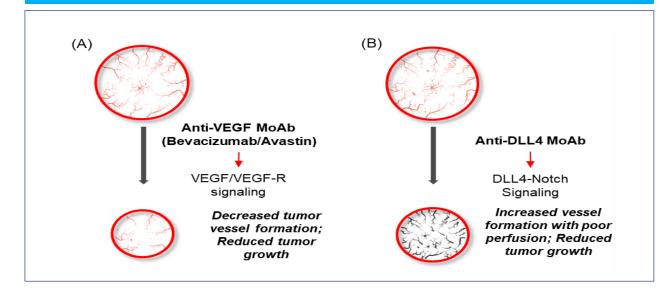


## **Overview of CTX-009**

- Bispecific antibody blocking DLL4 (Notch-1 ligand) and VEGF-A (soluble ligand)
- Does not lead to ADCC, Fc inactive
- Binds to its targets with 2:2 valency
- At 10 mg/Kg, CTX-009 has approximately the same VEGF-A capturing ability as bevacizumab (Avastin)
- ➤ The only DLL4 X VEGF bispecific that demonstrated monotherapy activity in the clinic in colorectal and gastric cancer
- Durable responses in patients with cholangiocarcinoma seen in Phase 1b study of CTX-009 in combination with paclitaxel



# Dual blockade of DLL4 and VEGF overcomes VEGF resistance





#### CTX-009 – Vision and Potential



# Best-in-class DLL4 x VEGF-A bispecific

- Phase 3 ongoing in BTC
- Phase 2 ongoing in CRC

#### Oncology

Has demonstrated compelling activity in the 3<sup>rd</sup> line and 4<sup>th</sup> line settings in patients with Cholangiocarcinoma, Colorectal Cancer, Gastric Cancer and Pancreatic Cancer

Could become front line therapy in multiple solid tumors

Other potential indications based on DLL4 expression such as Ovarian Cancer & Renal Cell

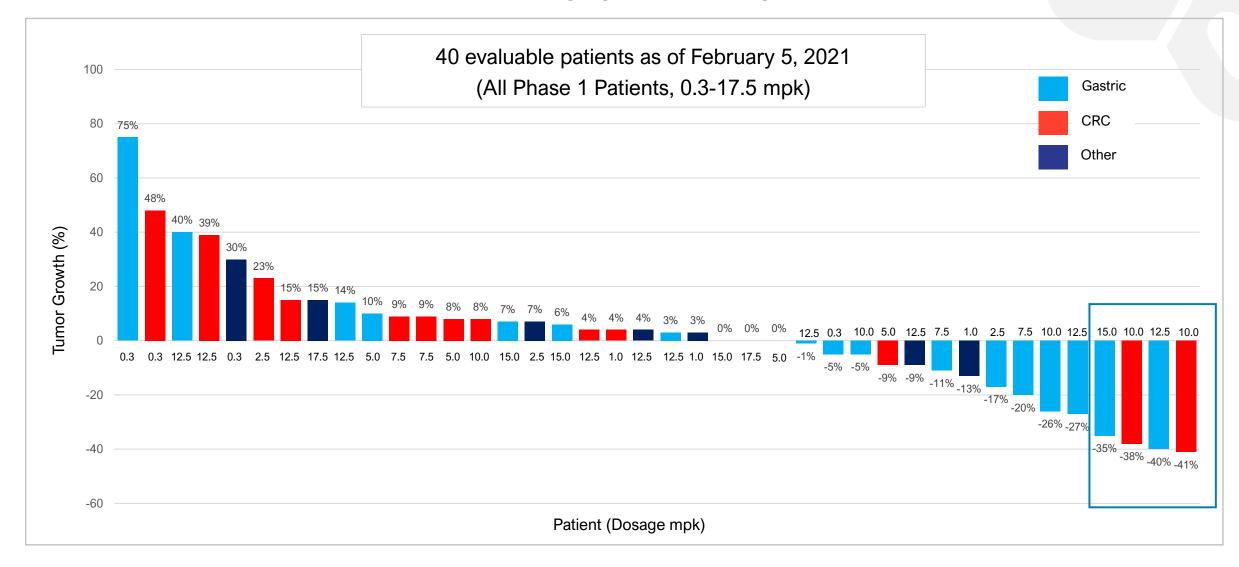
#### Ophthalmology

Potential to address AMD and DME based on mechanism

Consideration for partnership

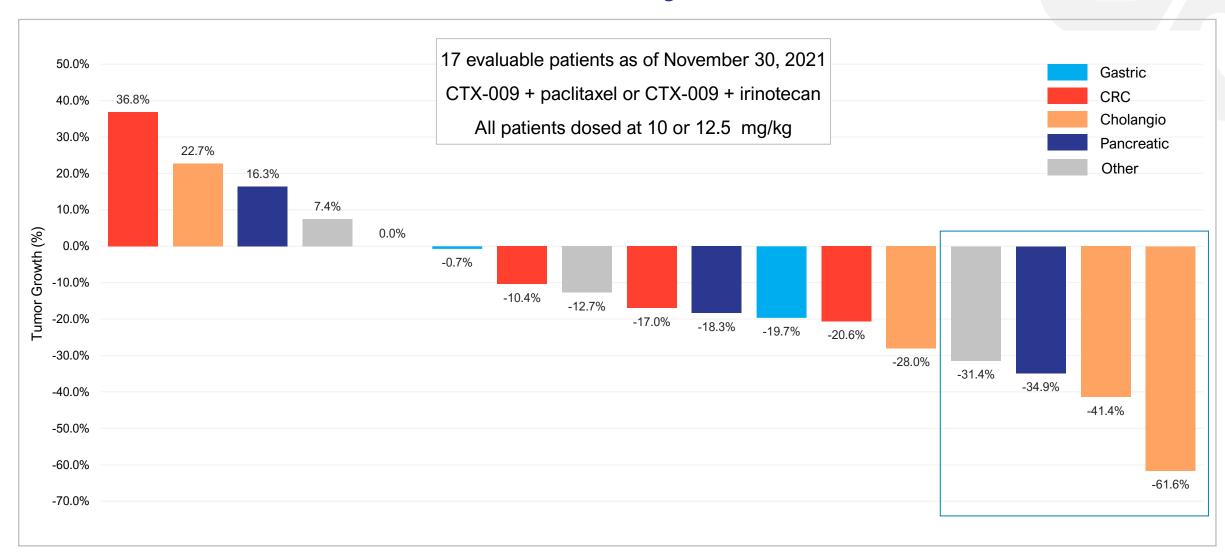


# Phase 1a CTX-009 Monotherapy (all doses)





# **Phase 1b CTX-009 Combination Study**





# **Phase 1 CTX-009 Safety Data**

#### **Phase 1a Monotherapy (n=45)**

Drug-related adverse events observed in > 5% of patients	Total (n)	Total (%)	Grade 3 (n)	Grade 3 (%)
Hypertension*	17	38	7	16
General disorders (fatigue, fever, asthenia, edema, etc.)	7	16	1	2
Nervous system disorders (headache, dizziness)	7	16	1	2
Gastrointestinal disorders (nausea, vomiting, etc.)	6	13	2	4
Pulmonary hypertension	4	9	0	0
Proteinuria	3	7	0	0

#### **Phase 1b Combination (n=17)**

Drug-related adverse events observed in > 1 patient	Total (n)	Total (%)	Grade 3 (n)	Grade 3 (%)
Hypertension	8	47	4	24
Nausea	8	47	1	6
Fatigue	6	35	1	6
Neutropenia** Anemia** Thrombocytopenia**	6 4 2	35 24 12	2 3 2	12 18 12
Diarrhea	5	29	0	0
Anorexia	5	29	0	0
Proteinuria	5	29	0	0
Pulmonary hypertension (all grade 1)	5	29	0	0
Dyspnea	4	24	0	0
Gingival edema (mucositis)	2	12	0	0
Anal hemorrhage	2	12	0	0

<sup>\*</sup> In clinical trials of bevacizumab, incidence of Grade 3-4 hypertension ranged between 5%-18% (Avastin label). It is typically managed by anti-hypertensive drugs



# **CTX-009 – Phase 1 Clinical Studies Summary**

Overall Response Rate at the Efficacious Dose

(10-12.5 mg/kg)

Monotherapy

18.8% ORR (3/16)

Combination

23.5% ORR (4/17)

Clinical Benefit Rate at the Efficacious Dose

(10-12.5 mg/kg)

Monotherapy

68.8% (11/16)

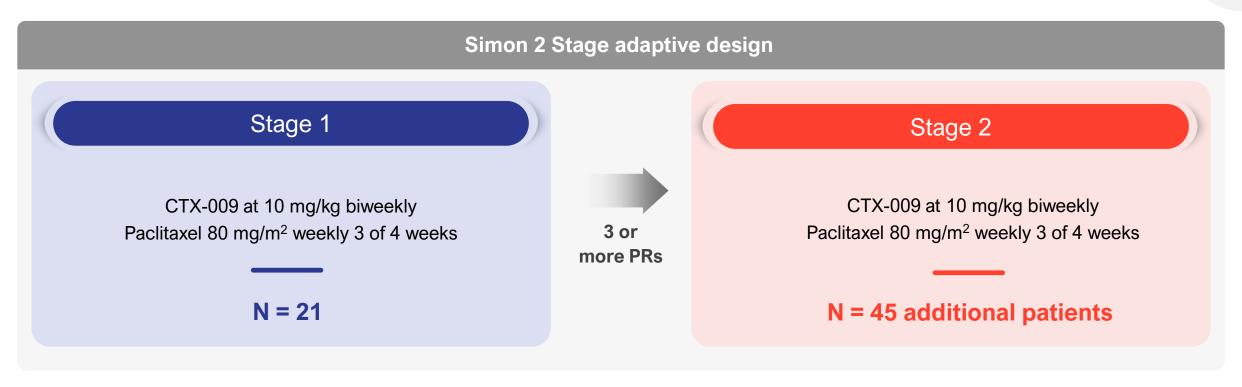
Combination

76.5% (13/17)



# Phase 2 CTX-009 Combination Study (S. Korea)

Patients with biliary tract cancers after one or two prior therapies

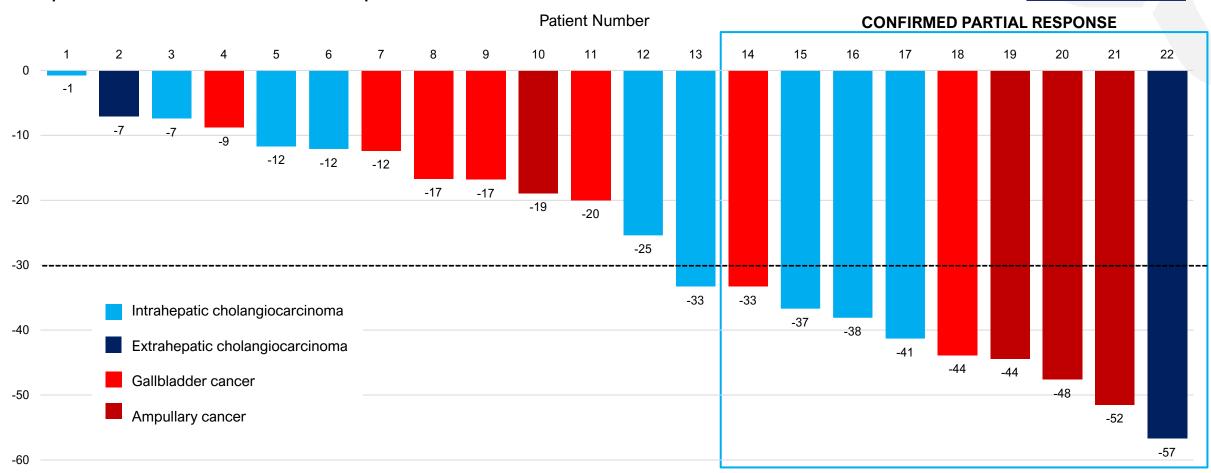




### Phase 2 CTX-009 Data

ORR = 37.5% CBR = 91.5%

Responses achieved across multiple BTC subclasses. Data as of November 9, 2022

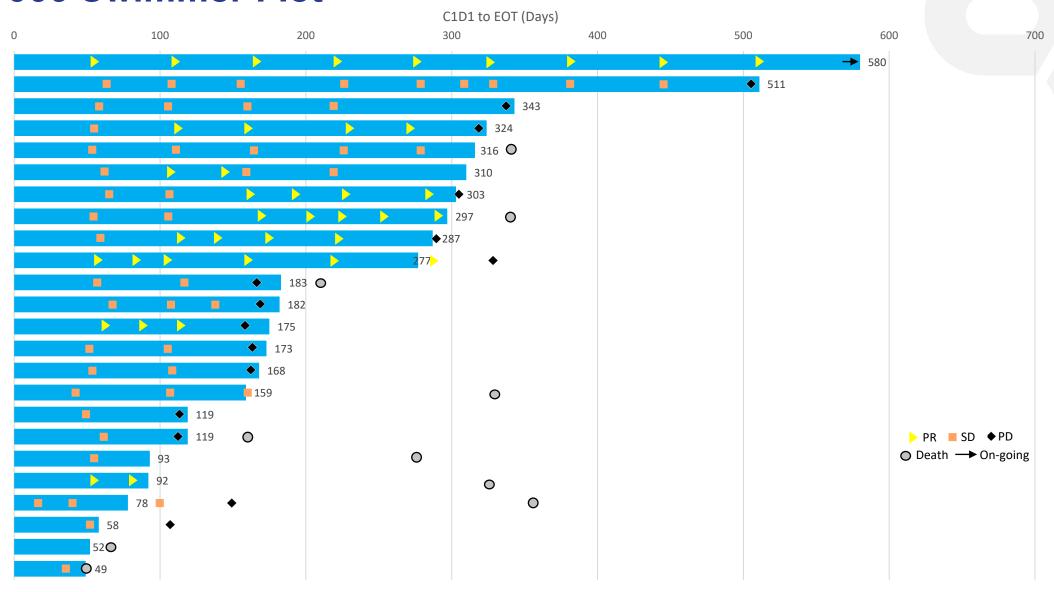


2 patients were not evaluable (one missing post baseline scan; one had a scan outside of protocol window)



Percent tumor decline

## **CTX-009 Swimmer Plot**





# CTX-009 Phase 2 Results (Median follow-up of 12.1 months)

- 24 patients enrolled and dosed
- 1 patient remains on study

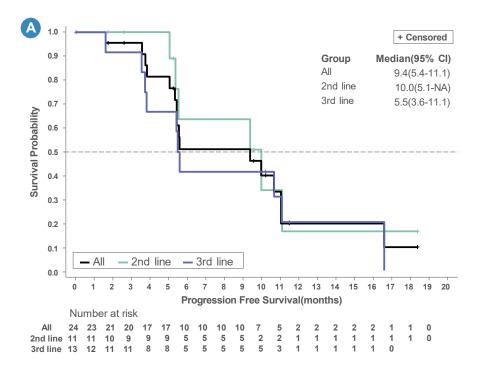
Endpoint	Value (95% CI)
Overall Response Rate (ORR)	37.5%
Stable Disease (SD)	54.2%
Progression Free Survival (PFS)	<b>9.4 m</b> (5.4 – 11.1)
Overall Survival (OS)	<b>12.5 m</b> (10.9 – NA)
Duration of Response	<b>6.9 m</b> (3.5 – NA)

Number of previous systemic therapies	ORR
Pts treated in the 2L [n=11]	7/11 (63.6%)
Pts treated in the 3L [n=13]	2/13 (15.4%)

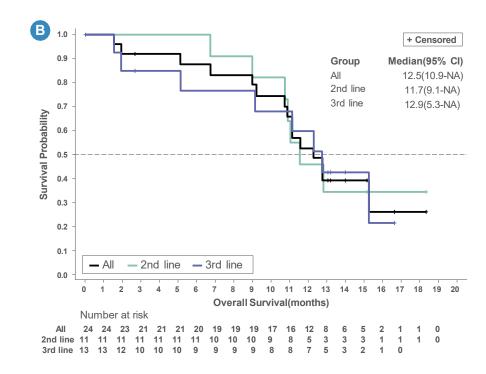


# **Secondary Endpoints: PFS and OS**

Median PFS: 9.40 m (5.4-11.1)



Median OS: 12.5 m (10.9-NA)





# **Treatment-Emergent ≥ Grade 3 Adverse Events** (>10% of patients)

#### Phase 2 BTC study of CTX-009 plus paclitaxel

Event	24 total Patients N (%)
Neutropenia	20 (83.3%)
Anemia	5 (20.8%)
Hypertension	4 (16.7%)
Thrombocytopenia	3 (12.5%)

TEAE leading to discontinuation: confusion, embolism, pneumonia (grade 5), biliary fistula, large intestine perforation, blood creatinine increased, and blood urea nitrogen increased

#### **Bevacizumab and paclitaxel label information**

Event	Bevacizumab (label)	Paclitaxel (label)
Neutropenia		52%
Hypertension	5-18%	
Anemia		16%
Thrombocytopenia		7%
	Additional events: GI perforation, wound healing complications, Proteinuria, hemorrhage	Additional events: Hypersensitivity reactions, infections, bleeding, neuropathy



# **How Does CTX-009 Data Compared to Other BTC Studies?**

Parameter	CTX-009 Mixed 2L and 3L	FOLFOX (ABC-06) <sup>1</sup> Only 2L	Gem/Cis <sup>2</sup> 1L	Gem/Cis + Durv <sup>3</sup> Only 1L
	N=24	N=81	N=204	N=341
ORR	37.5% [64% 2L; 15% 3L]	5%	26%	26.7%
os	12.5 m	6.2 m	11.7 m	12.9 m
PFS	9.4 m	4.0 m	8.0 m	7.2 m
Any AE	100%	99%	55%	99.4%
Gr 3/4 AEs	92%	60%	71%	74%
Deaths (as Gr 5)	1 (4%)	10 (12%)	17 (8%)	13 (4%)
AEs leading to discontinuation	25%	~ 12%	10%	13%

Lamarca D, Lancet Oncol 2021; March 30

Valle, J. et al., N ENGL J MED, 362; 14 Apr 8, 2010, p. 1273

# CTX-009 Phase 2 Study Summary

# 24 patients with BTC have been enrolled and dosed

9 partial responses (PRs) for a 37.5% ORR in patients treated in the second- and third-line settings (**64% ORR** of patients treated in the 2<sup>nd</sup> line setting)

Median PFS 9.4 months

Median OS 12.5 months

Adverse event profile similar to Phase 1 studies

#### Other regimens in BTC

**FOLFOX** (NCCN guidelines):

5% ORR in the second-line setting

4.0 month median PFS

6.2 month median OS

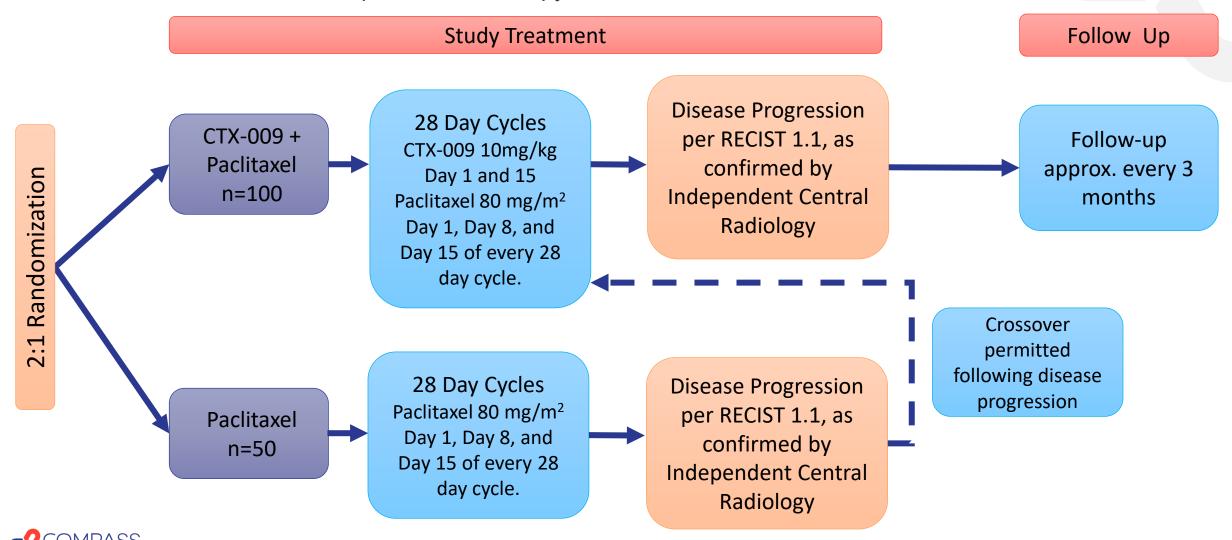
**TOPAZ-1** (Phase 3 study):

26.7% ORR for Gem/Cis/Durvalumab (anti PD-L1) in the first-line setting



# COMPANION-002: Phase 2/3 U.S. BTC Study

Patients who have received one prior line of therapy



# CTX-009: BTC Patient Demographics and Current Treatments

	us	EU5	Japan	Worldwide
Incident Cases	18,400 <sup>1</sup>	21,8002	14,329 <sup>2</sup>	>200,000³

#### **1L Treatment**

Doublet chemo of gemcitabine + cisplatin (ABC-02 study)

Or

Gemcitabine/cisplatin + durvalumab (recently approved for 1L)

#### 2L Treatment

OLFOX	FGFR2 mutation
% ORR	Pemigatinib
.9 Mos OS $\Delta$	(10-15% of CCA

<u>n</u>	IDH1 mutation
	Ivosidenib
A)	(1-3% of BTC)

MSI-H tumors
PD-1 Inhibitor
(<1% of BTC)

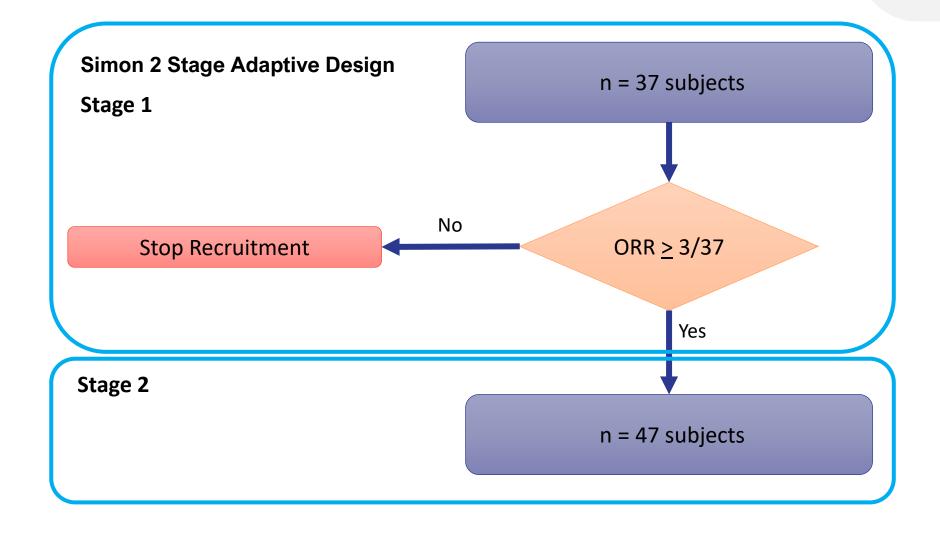
Clinical trial

1. NCI Surveillance, Epidemiology, and End Results (SEER) program

0

- 2. Delveinsight/company estimates
- 3. International Agency for Research on Cancer/GLOBOCAN

# COMPANION-003: Phase 2 U.S. Colorectal Cancer (CRC) Study





# CTX-009: CRC Patient Demographics and Current Treatments

	US	EU5	Japan	Worldwide
Incident Cases	153,020 <sup>1</sup>	246,734 <sup>2</sup>	148,505 <sup>2</sup>	1,931,590 <sup>2</sup>
~50% Metastatic <sup>3</sup> 50-70% reach 3L <sup>4</sup>	38,000-53,000 patients			

1L Treatment			2L Treatment		3L Treatment	
Chemotherapy FOLFOX/FOLFIRI	Bevacizumab or EGFR inhibitor +	Anti-PD-1 with MSI-H/dMMR	Bevacizumab or EGFR + chemo	BRAF/EGFR with V600E mutation	Regorafenib	Trifluridine/ tipiracil
	chemotherapy	mutation		5-8% of CRC	ORR 1%, Median PFS 2.0 months	ORR 1-2%
		~5% of CRC				Median PFS ~2 months

- 1. NCI Surveillance, Epidemiology, and End Results (SEER) program
- 2. International Agency for Research on Cancer/GLOBOCAN
- 3. L Biller, D Schrag, JAMA 2021 Feb 16
- 4. Bekaii-Saab, Clin advances in Hem and Onc, Supp Jan 2021

# The COMPANION (COMPASS ANTI-ANGIOGENESIS) Studies

Top-line H2 2024

COMPANION 002
Phase 2/3 Randomized
BTC study in the US

**Top-line H1 2024** 

COMPANION 003

Phase 2

study in third- and fourthline CRC in the US

Initiate H2 2024

COMPANION 004
Phase 2 study in 3<sup>RD</sup>
Solid Tumor Indication in the US

Evaluating additional indications for CTX-009 both as a monotherapy and in combination with chemotherapy



# **CTX-471** CD137 monoclonal antibody

# CTX-471: Potential Best-in-Class CD137 Agonist

#### CTX-471: next generation CD137 agonist

Fully human, IgG4, optimized affinity for agonistic antibody

Unique epitope: non-ligand blocking

#### Phase 1 Study Update

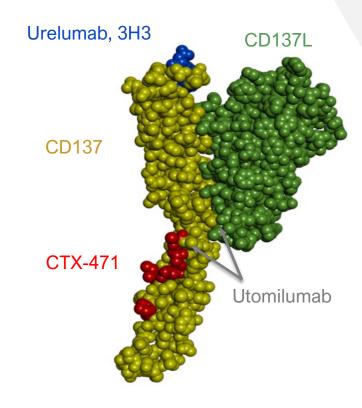
Monotherapy in post checkpoint inhibitor patients

Monotherapy Phase 1a multiple ascending dose study completed

MTD defined by immune thrombocytopenia

Monotherapy Phase 1b dose expansion study completed

- 1 CR: small cell lung cancer
- 4 PRs observed: melanoma (3 of 11) and mesothelioma (1 of 4)



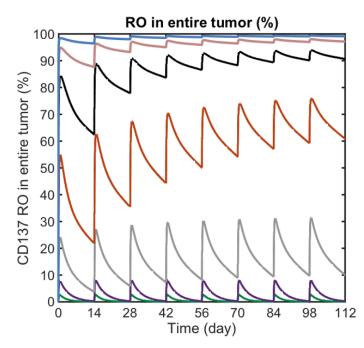
JCI Insight. 2020;5(5):e133647



# What is the Optimal Dose of an Agonist Antibody?

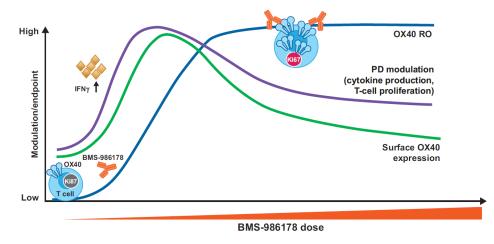
- Our dose selection is based on modeling of CD137 fractional receptor occupancy (RO)
- Modeling predicted human pk parameters based on preclinical data
- Preliminary Phase 1 PK data are consistent with the modeling

#### CTX-471 predicted %RO in humans



10 mg/kg Q2W for 16 weeks
3 mg/kg Q2W for 16 weeks
1 mg/kg Q2W for 16 weeks
0.3 mg/kg Q2W for 16 weeks
0.1 mg/kg Q2W for 16 weeks
0.03 mg/kg Q2W for 16 weeks
0.01 mg/kg Q2W for 16 weeks
0.01 mg/kg Q2W for 16 weeks

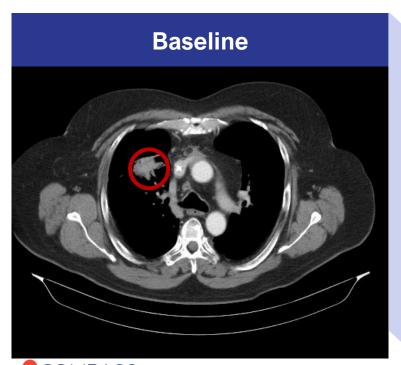
Maximal %RO may not lead to optimal response (Wang et al., Clinical Cancer Research, 2019)

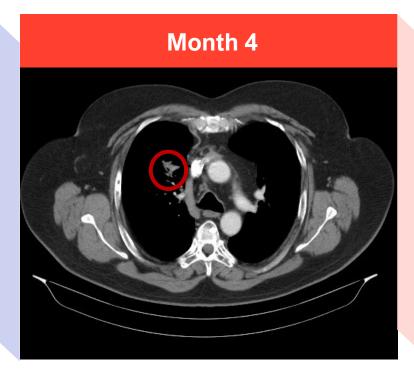


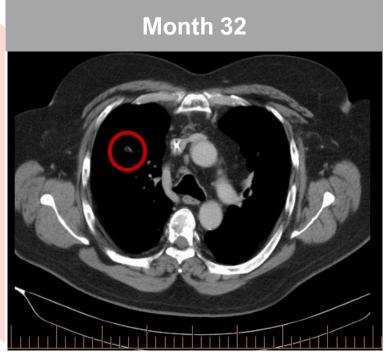
## CTX-471: Complete Response in a Patient with Small Cell Lung Cancer

After progression on atezolizumab/chemo and nivolumab

- >> 66 y.o. man with advanced SCLC: Carboplatin/etoposide plus atezolizumab first line; nivolumab second line
- Confirmed, complete response (CR) by PET ~ 3 years on therapy







# **CTX-471 Clinical Development Plans**

#### **Phase 1b Monotherapy Study**

Generally well tolerated

A complete response and four partial responses in the post PD-1/PD-L1 patient population

Small cell lung cancer, mesothelioma, and melanoma (three patients)

# Phase 1b of CTX-471 with KEYTRUDA® in collaboration with Merck

Abbreviated CTX-471 dose escalation into the PD-1 regimen, followed by a cohort expansion

Post PD-1/PD-L1 Salvage Study

Dose escalation complete, no DLT

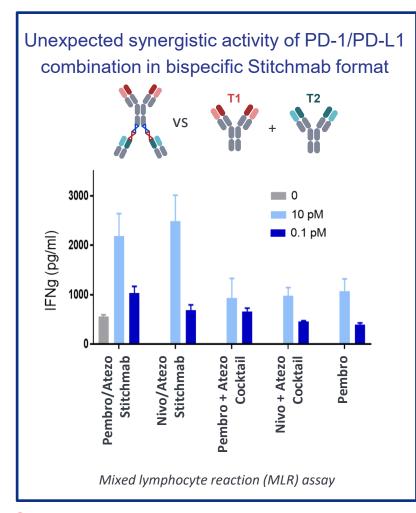
Dose expansion is ongoing



# CTX-8371

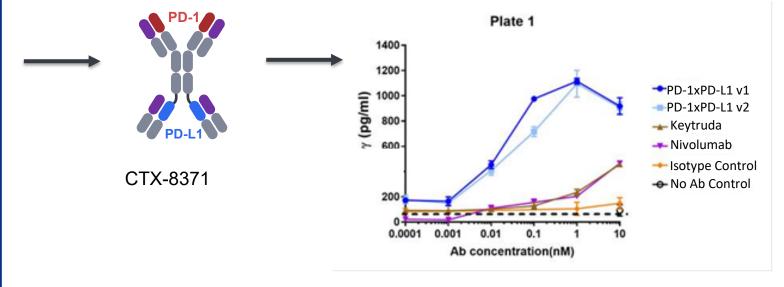
PD-1 x PD-L1 bispecific antibody

# StitchMabs<sup>TM</sup> Platform was Utilized to Identify CTX-8371



Common Light Chain bispecifics were generated to test therapeutic hypothesis

Our PD-1xPD-L1 bispecifics observed to outperform PD-1 blockers in T-cell activation assay

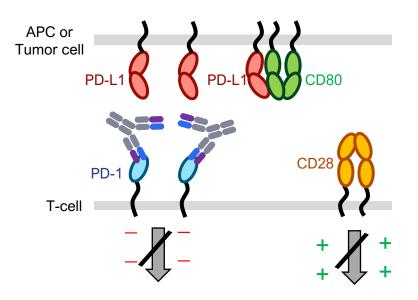




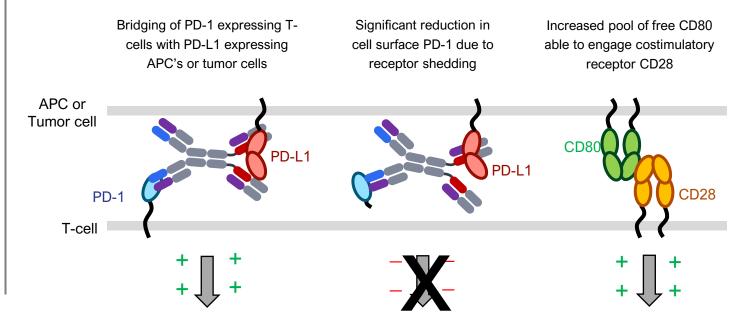
#### CTX-8371: Differentiated MoA Leads to Enhanced T-Cell Activation

Converting PD-1 positive T cells into PD-1 negative T cells

PD-1 blockers release brake but don't directly promote T-cell activation



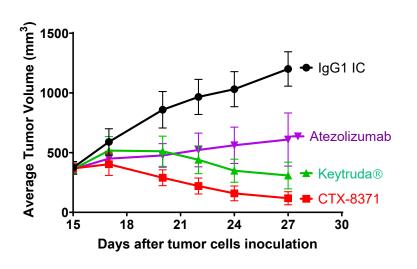
#### CTX-8371 activates T-Cells Through Multiple MOA's

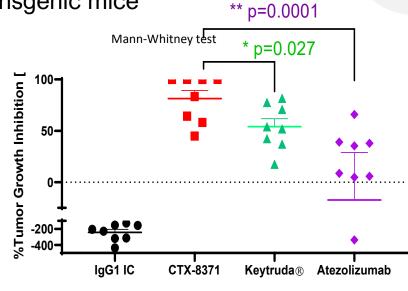


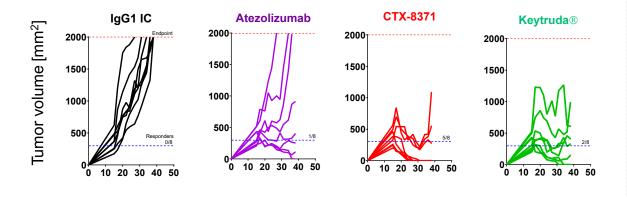


# **CTX-8371 Pre-Clinical Proof of Concept**

Activity in MC38-hPD-L1 model implanted in hPD-1/hPD-L1 transgenic mice







Group	% Cured	Tumor free / total
CTX-8371	62.5	5/8
Atezolizumab	12.5	1/8
IgG1 IC	0	0/8
Keytruda	25	2/8



Days post treatment

# **CTX-8371: Development Status**

IND was accepted

Currently opening clinical sites

First patient dosing expected in
1Q 2024

## Phase 1 study design

Multiple ascending dose, dose-escalation study

5 doses planned: 0.1, 0.3, 1.0, 3.0, and 10 mg/kg

Post PD-1 or PD-L1 patient population: Melanoma, NSCLC, HNSCC, Hodgkin's Lymphoma, TNBC

First patient dosing targeted for Q1 2024

Potential for proprietary combination regimens with CTX-009 and CTX-471



# **Compass Therapeutics**

Summary

# **Program Summary**

#### >>> CTX-009 Novel DLL4 x VEGF-A bispecific antibody with both combination and monotherapy activity

Phase 1: Dose response established – responses in multiple indications

BTC Phase 2 results: 24 patients: 37.5% ORR (2L/3L), 63.6% (2L), median PFS 9.4 months, OS 12.5 months

COMPANION-002: BTC Phase 3 randomized study ongoing; top-line data expected H2 2024

COMPANION-003: CRC Phase 2 monotherapy study ongoing; top-line data expected mid-2024

#### >>> CTX-471 Potential best-in-class CD137 agonist antibody with monotherapy activity

Phase 1 monotherapy study complete:

1 complete response (CR): small cell lung cancer (1 of 3), and 4 partial responses (PRs) in post PD-1 population: metastatic melanoma (3 of 11) and mesothelioma (1 of 4)

CTX-471 in combination with KEYTRUDA® dose escalation complete, dose expansion ongoing

#### >>>> CTX-8371 Next generation PD-1 x PD-L1 bispecific antibody

Unique MOA – enhances T-cell activation

IND cleared, currently opening clinical sites



# **Key 12 Month Milestones**

