DECEMBER 12, 2023

Exelixis R&D Day: Science & Strategy

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Agenda

- **Strategic Overview**
- **R&D for Commercial Impact**
- **Broadening Research Impact in Biotherapeutics & Small Molecules**
- Break – 10 Minutes
- **Zanzalintinib in Clear Cell RCC: Results from STELLAR-001**
- **Focused Execution Drives Long-term Value Creation**
- **Closing Remarks**
- Break – 10 Minutes
- **Q&A Session**

Lunch reception to follow the presentation next door in the foyer.

Safe Harbor Statement

This presentation, including any oral presentation accompanying it, contains forward-looking statements, including, without limitation, statements related to: Exelixis' belief it is positioned to be a global biotech leader in oncology R&D; Exelixis' overall strategy and commitment to value creation in the short-, middle- and long-term horizon by helping more patients with cancer; potential new market opportunities for the cabozantinib franchise in mCPRC and NET, should Exelixis obtain regulatory approvals for cabozantinib in those indications; Exelixis' commercial strategy to build oncology franchises across the GU, GI, Lung/H&N and GYN/breast core disease areas, and Exelixis' belief that the breadth and depth of its pipeline is well-positioned to build on success in GU and GI while delivering growth in new disease areas; the commercial potential of zanzalintinib, XB002, XL309 and the rest of the Exelixis pipeline, and Exelixis' belief that a future multi-product portfolio could eventually treat up to 13 tumors and serve over ten times the current addressable patient population for cabozantinib; Exelixis' drug discovery strategy to expand the pipeline with development candidates that have potential for differentiated clinical profiles, and Exelixis' expectation it will build a consistent flow of development candidates and target two new INDs per year; Exelixis' preclinical development plans for and beliefs regarding the therapeutic potential of its biotherapeutics development candidates, including XB010, XB628, XB371 and XB064, as well as its small molecule development candidates, including XL495 and EXEL-7871; Exelixis' clinical development plans for and beliefs regarding the therapeutic potential of zanzalintinib, XB002 and XL309; Exelixis' plans for future data presentations, including from CONTACT-02, and Exelixis' overall vision for development execution; and Exelixis' anticipated long-term milestones to drive value creation in 2023, in 2024 through 2027, and in 2028 and beyond. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of these risks and uncertainties, which include, without limitation: the degree of market acceptance of CABOMETYX and other Exelixis products in the indications for which they are approved and in the territories where they are approved, and Exelixis' and its partners' ability to obtain or maintain coverage and reimbursement for these products; the effectiveness of CABOMETYX and other Exelixis products in comparison to competing products; the level of costs associated with Exelixis' commercialization, research and development, in-licensing or acquisition of product candidates, and other activities; Exelixis' ability to maintain and scale adequate sales, marketing, market access and product distribution capabilities for its products or to enter into and maintain agreements with third parties to do so; the availability of data at the referenced times; the potential failure of cabozantinib, zanzalintinib and other Exelixis product candidates, both alone and in combination with other therapies, to demonstrate safety and/or efficacy in clinical testing; uncertainties inherent in the drug discovery and product development process; Exelixis' ability to identify strategic opportunities to enhance its pipeline and to consummate the necessary transactions; Exelixis' dependence on its relationships with its collaboration partners, including their pursuit of regulatory approvals for partnered compounds in new indications, their adherence to their obligations under relevant collaboration agreements and the level of their investment in the resources necessary to complete clinical trials or successfully commercialize partnered compounds in the territories where they are approved; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' continuing compliance with applicable legal and regulatory requirements; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating cabozantinib and other Exelixis product candidates; Exelixis' dependence on third-party vendors for the development, manufacture and supply of its products and product candidates; Exelixis' ability to protect its intellectual property rights; market competition, including the potential for competitors to obtain approval for generic versions of Exelixis' marketed products; changes in economic and business conditions; and other factors detailed from time to time under the caption "Risk Factors" in Exelixis' most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q, and in Exelixis' other future filings with the Securities and Exchange Commission (SEC). All forward-looking statements in this presentation are based on information available to Exelixis as of the date of this presentation, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein, except as required by law.

Strategic Overview

Michael M. Morrissey, Ph.D.
President and CEO

EXEL 2024: Positioned to Be Global Biotech Leader in Oncology R&D

- Cabozantinib: Blockbuster VEGFR TKI franchise
- Deep pipeline targets 10x more patients than cabo
- Conviction to pursue differentiation in Phase 3
- Disciplined R&D efforts in line with revenue peers
- Urgency, focus & excellence define our work

EXEL R&D – Improve SOC for cancer patients with a pipeline of differentiated drugs

SOC = standard of care
TKI = tyrosine kinase inhibitor

Value Creation Driven By Singular Focus on Cancer Patients

#1 launch in biotech oncology (2016)

54% sales* CAGR from 2016 – 2022

NET, mCRPC drives potential near-term growth in new indications

1 Strong Returns from CABO

2 Focused Strategy

R&D strategy in **solid tumor oncology**

Singular focus on improving standard of care for patients with cancer

Robust pipeline of differentiated small molecule and biotherapeutics programs

Next generation clinical stage programs **(ZANZA, XB002)** drive mid-term growth

3 Innovative Pipeline

4 Big, Small Biotech Culture

Execute at the level of **big pharma** and with the agility of **small biotech**

Culture of collaboration – internal and external – maximizes impact and ROI

Exelixis is committed to creating value in the short-, mid- and long-term horizon by helping more patients with cancer

CAGR = compound annual growth rate
NET = neuroendocrine tumors
ROI = return on investment
mCRPC = metastatic castration-resistant prostate cancer

**Global net product revenue*

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Cabozantinib Franchise Success Provides Blueprint for Pipeline Strategy

CABOMETYX® (cabozantinib) tablets

COMETRIQ® (cabozantinib) 80 mg and 20 mg capsules

Unique Target Profile

Targets MET, VEGFRs, TAMKs and other kinases implicated in tumor growth

Active in >20 Tumor Types

CRPC, breast cancer, urothelial cancer and others

6 Approvals, >20k Patients Treated per Quarter

Approved in MTC, DTC, RCC (3) and HCC

Superior Clinical Activity in RCC

Compared to sunitinib in head-to-head trials

Global "Blockbuster" Status

Net global revenues of ~$2.2B (LTM)

#1 TKI in aRCC
and
#1 TKI + IO Combination in 1L aRCC

Cabozantinib's clinical and commercial success achieved by improving SOC for cancer patients

CRPC = castration-resistant prostate cancer
MTC = medullary thyroid cancer
DTC = differentiated thyroid cancer
aRCC = advanced renal cell carcinoma
HCC = hepatocellular carcinoma
TKI = tyrosine kinase inhibitor
IO = immunotherapy
1L = first-line
SOC = standard of care
LTM = last twelve months
OS = overall survival

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Commercial Success Results from Disciplined R&D Investments

17

Cabozantinib Pivotal Trials, with 14 Trials Read Out

- 14 of 17 trials focused on GU & GI cancers

71%
(10/14)

Pivotal Trials with Positive Primary Endpoint

- vs. Industry Average of **53%**[1]

8th VEGFR TKI Launched*

#1 in VEGFR TKI Sales

GU = Genitourinary
GI = Gastrointestinal
TKI = tyrosine kinase inhibitor

**in the U.S.*
[1] *Trialtrove Analysis of Solid Tumor Phase 3 Trials Jan 2013 – Nov 2023 (n = 461 trials)*

Collaborate to Succeed: Risk-Sharing Maximizes Optionality & Impact

Combination	Phase 3 Study	Partners	Commercial Impact
Cabozantinib + Nivolumab	**CheckMate -9ER** 1L aRCC	Bristol Myers Squibb™ IPSEN Innovation for patient care Takeda	Doubling of cabozantinib franchise global annual net product revenue from **~$1B in 2020 to ~$1.9B in 2022**
Cabozantinib + Atezolizumab	CONTACT-01 NSCLC CONTACT-02 mCRPC CONTACT-03 RCC	Roche IPSEN Innovation for patient care Takeda	Positive results from **CONTACT-02** announced

~25% Study Costs Funded by Exelixis

Pursuing similar risk-sharing collaborations for zanza and other pipeline programs enables the development of novel combinations to meaningfully improve SOC for patients

1L = first-line
aRCC = advanced renal cell carcinoma
NSCLC = non-small cell lung cancer
mCRPC = metastatic castration-resistant prostate cancer
SOC = standard of care

[1] *Exelixis JPM Presentation, Jan 2020*

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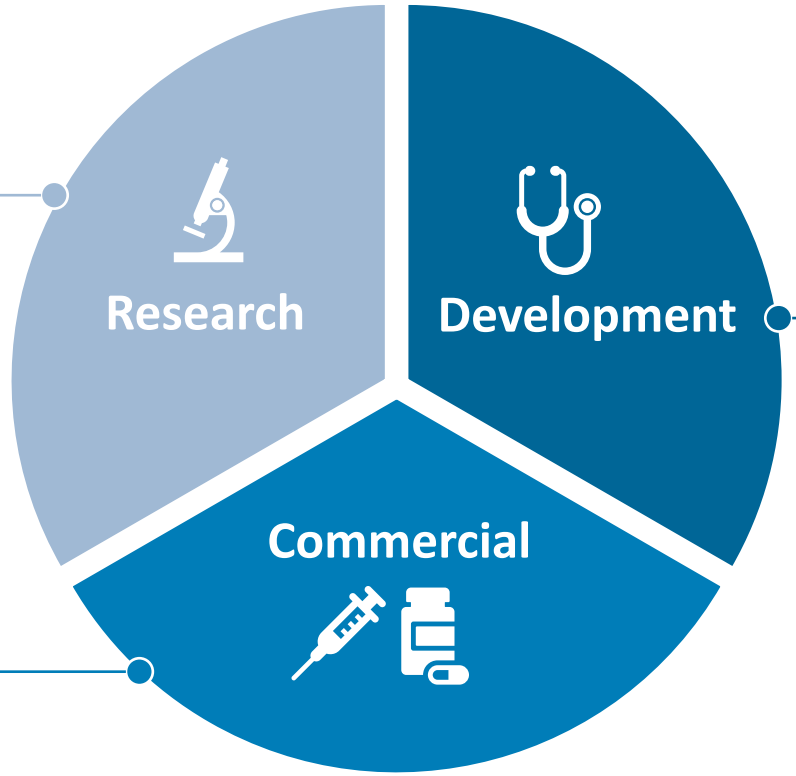
End-to-End Integration of Research, Development and Commercial

- **Multi-modal approach** to reduce target/biology risk
- Prioritization of programs with potential for **clinical differentiation**



- Balance the optimization of **probability of success, speed and value** across pipeline
- **Novel combinations** in earlier lines
- **Efficiency** in execution

- **Maximize patient impact** in large solid tumor populations
- Strong & early focus on **competitive differentiation**

Integration of R&D with commercial provides a complementary and balanced approach to driving science & strategy

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Exelixis Biotherapeutics & Small Molecule Pipeline

Pre-IND	Phase 1	Phase 1b/2	Pivotal
XB010: 5T4-MMAE	**XB002:** TF-MTI	**Zanzalintinib:** MET/VEGFR/AXL *Multiple solid tumors*	**Zanzalintinib:** *3L+ CRC*
XB628: PD-L1-NKG2A	**XL309:** USP-1		**Zanzalintinib:** *nccRCC*
XB371: TF-TOPOi	**ADU-1805:** SIRPα	**XB002:** TF-MTI *Multiple solid tumors*	**Zanzalintinib:** *SCCHN*
XL495: PKMYT1	**CBX-12:** TOPOi PDC		
XB064: ILT2			

2023 Discontinuations

XB014: PD-L1-CD47 (PC)	**XL114:** FABP5 (Ph1)
	XL102: CDK7 (Ph1)

Drug Modality

- Small Molecule
- Monoclonal Antibody
- Bispecific Antibody
- Antibody/Peptide Drug Conjugate

Combination Partner

- PD-L1
- Novel ICI (e.g., LAG-3, TIGIT)
- Other (e.g., VEGF, HIF2α)

MMAE = monomethyl auristatin E
TF = tissue factor
3L = third-line
CRC = colorectal carcinoma
PD-L1 = programmed death-ligand 1
NKG2A = natural killer cell receptor group 2A
USP-1 = ubiquitin specific peptidase 1
nccRCC = non-clear cell renal cell carcinoma
SIRPα = signal-regulatory protein alpha
SCCHN = squamous cell carcinoma of head and neck
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
MTI = auristatin-based microtubulin inhibitor
TOPOi = topoisomerase inhibitor
PDC = peptide drug conjugate
ILT2 = Ig-like transcript 2
CD47 = cluster of differentiation 47
LAG-3 = lymphocyte-activation gene 3
CDK7 = cyclin-dependent kinase 7
ICI = immune checkpoint inhibitor
HIF2α = hypoxia-inducible factor 2 alpha

Strategic Vision for Building Multiple Franchises Across Portfolio

Maximize speed and impact of development and commercialization activities for zanzalintinib, XB002, XL309 and rest of pipeline

SOC = standard of care

Today's Speakers

PJ Haley
EVP, Commercial

- **R&D for Commercial Impact**

Dana T. Aftab, Ph.D.
EVP, Discovery & Translational Research and CSO

- **Broadening Research Impact in Biotherapeutics & Small Molecules**

Sumanta Pal, M.D., FASCO
Professor, Department of Medical Oncology & Therapeutics Research, City of Hope Cancer Center

- **Zanzalintinib in Clear Cell RCC: Results from STELLAR-001**

Amy Peterson, M.D.
EVP, Product Development & Medical Affairs and CMO

- **Focused Execution Drives Long-term Value Creation**

RCC = renal cell carcinoma

R&D for Commercial Impact

PJ Haley
EVP, Commercial

Pipeline Commercial Focus Through the Cabo Lens

Cabozantinib Lens

- **$2.2B** in Global Net Product Revenue (2023 LTM)
- **#1 TKI** in aRCC and 2L HCC – tumors with multiple TKIs approved
- **#1 TKI + IO** in 1L aRCC – multiple TKI + IO combinations marketed; approved 20 months after pembrolizumab + axitinib

Pipeline Focus

- **Solid Tumor Focus:** address unmet need that exists across solid tumors and stay on the forefront of evolving landscapes
- **Maximize Patient Impact:** advance standard of care to move the needle for large patient populations
- **Best-in-class Target Product Profiles:** clinical differentiation drives commercial success, even in competitive markets

1L = first-line
2L = second-line
LTM = last twelve months
TKI = tyrosine kinase inhibitor
aRCC = advanced renal cell carcinoma
HCC = hepatocellular carcinoma
IO = immunotherapy

Potential New Market Opportunity: mCRPC

2023 Estimated Drug-Treatable Incidence:	Current Therapeutic Options:
1L: ~33k	▪ NHT ▪ Docetaxel
2L: ~26k	▪ NHT ▪ Docetaxel
3L+: ~18k	▪ JEVTANA ▪ PLUVICTO ▪ Docetaxel

Cabozantinib Opportunity in mCRPC

- Low 5-year survival rate of 15%
- Majority of mCRPC patients are NHT-experienced:
  - 1L: >50% patients, 2L: almost all patients
- Significant need for chemotherapy free treatment options for patients progressing from NHTs
- Excitement for new mechanisms of action in mCRPC
- **If approved, cabozantinib + atezolizumab represents a compelling option for patients who have progressed from NHT and want to delay chemotherapy**
- Synergy with existing commercial infrastructure and customers

Potential to be the first and only TKI + IO combination in mCRPC

1L = first-line
2L = second-line
3L = third-line
mCRPC = metastatic castration-resistant prostate cancer
NHT = novel hormonal therapy
TKI = tyrosine kinase inhibitor
IO = immunotherapy

Sources:
Estimated drug-treatable incidence (2024): DRG, 10/2023;
Post-novel hormonal therapy: BrandImpact, July 2023

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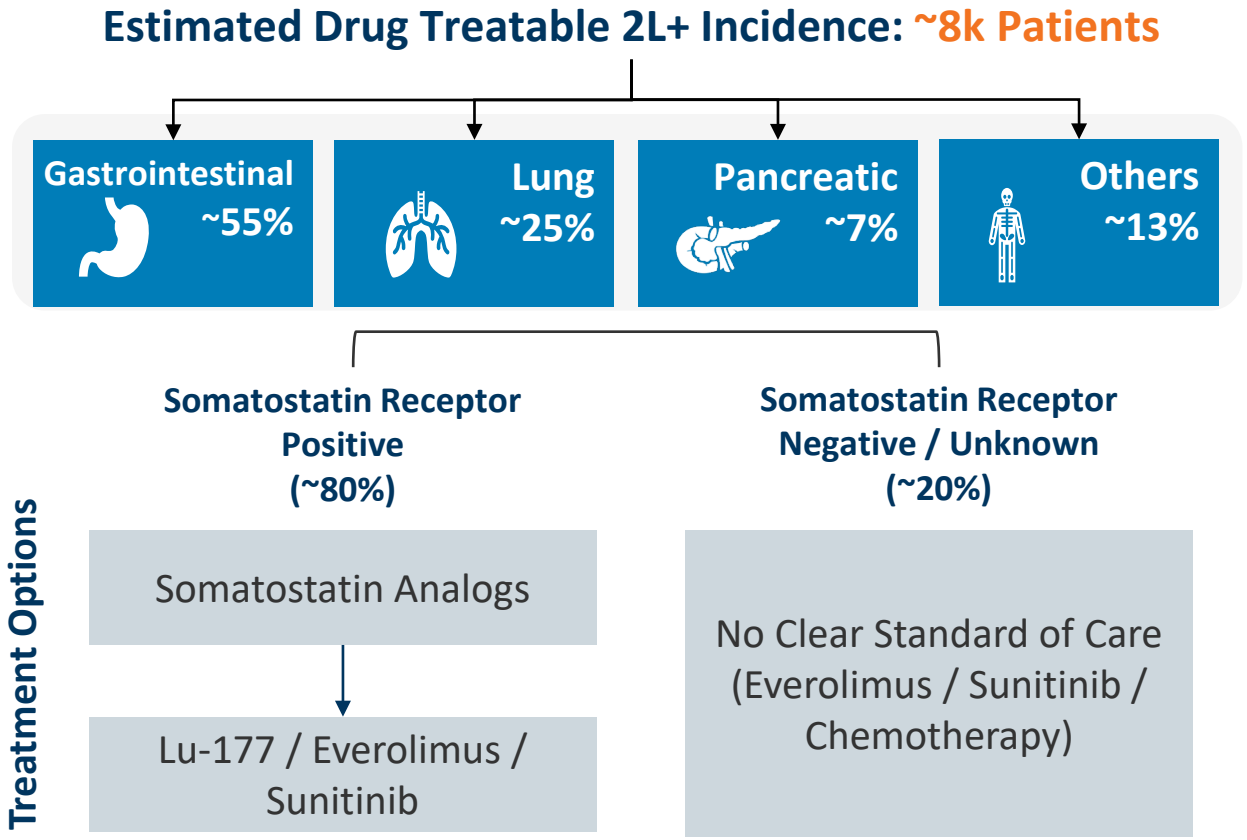
Potential New Market Opportunity: NET



Cabozantinib Opportunity in NET

- Neuroendocrine tumors are a heterogenous group of malignancies generally considered to be indolent
- NETs represent a significant prevalent population (>5x incidence), as most patients progress through multiple lines of therapy
- Increasing incidence with improved detection
- Significant opportunity exists, as patients have limited treatment options
- **Cabozantinib potentially represents a treatment option for all previously treated NET patients, regardless of tumor location and SSTR status**

Potential to be a new standard of care in 2L+ neuroendocrine tumors

NET = neuroendocrine tumors
2L = second-line
SSTR = somatostatin receptor

Sources:
NET Landscape Assessment Research (2023): Canadian Cancer Society; Cancer.net; Zihan et al. JAMA, 2021; Lung-NET are less likely to be SSTR+ (40-60%), across all NET are 80-90% SSTR+; hang & Kunz, JCO 2021; Haq et al., Best Pract Res Clin Endocrinol Metab, 2023; Al-Toubah et al., J Nucl Med. 2023; Kaemmerer et al., J Clin Endo & Meta, 2015

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Strategy to Build Franchises Across Four Core Disease Areas

Maximize patient impact and chance of success in solid tumor oncology

1 Strengthen Leadership and Innovation in Exelixis Current Disease Areas

GU

GI

Strengthen leadership in RCC through expansive development of zanzalintinib

Expand presence in genitourinary & gastrointestinal cancers through development in new indications and combinations

2 Expand into New Disease Areas Using Our Strengths as a Guide

Lung/H&N

GYN/Breast

Establish foothold in head & neck and non-small cell lung cancers through zanzalintinib and XB002

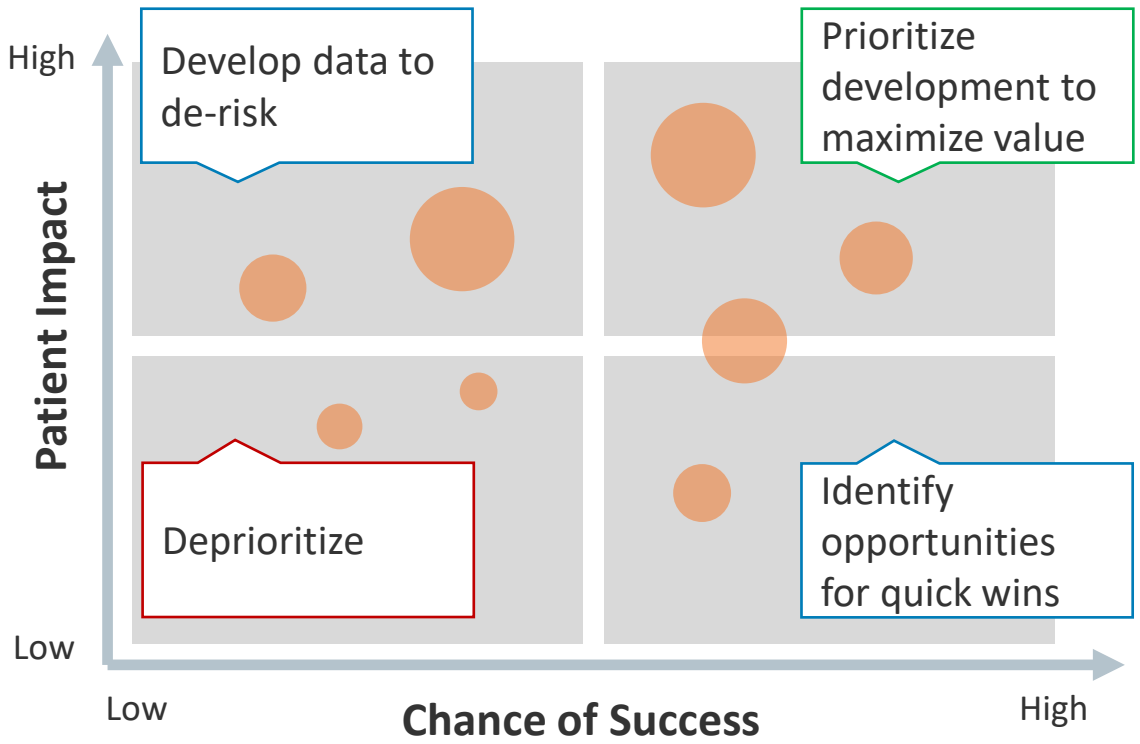
Leverage diverse pipeline to develop the right treatment approaches for patients who will benefit the most

GU = genitourinary cancers
GI = gastrointestinal cancers
H&N = head & neck cancers
GYN = gynecological cancers
RCC = renal cell carcinoma

Portfolio Planning Maximizes Value and Drives Focus

Portfolio Prioritization Through the Lens of Patient Impact and Chance of Success

- Market Size
- Unmet Need
- Competitive Landscape



- Clinical Proof of Concept
- Development/Regulatory Risk

Bubble size represents rNPV

Disease Areas/Tumors of Interest

	Addressable Patients (US)*
Genitourinary *Kidney, Prostate*	~100k
Gastrointestinal *Liver, Colorectal, Pancreatic*	~220k
Lung/H&N *Non small cell lung, Head & neck*	~330k
Gynecological/Breast *Endometrial, Breast*	~140k

rNPV = risk-adjusted net present value
H&N = head and neck cancers

**2023 Drug treatable patients across lines of therapy in the advanced/metastatic setting. Source: DRG*

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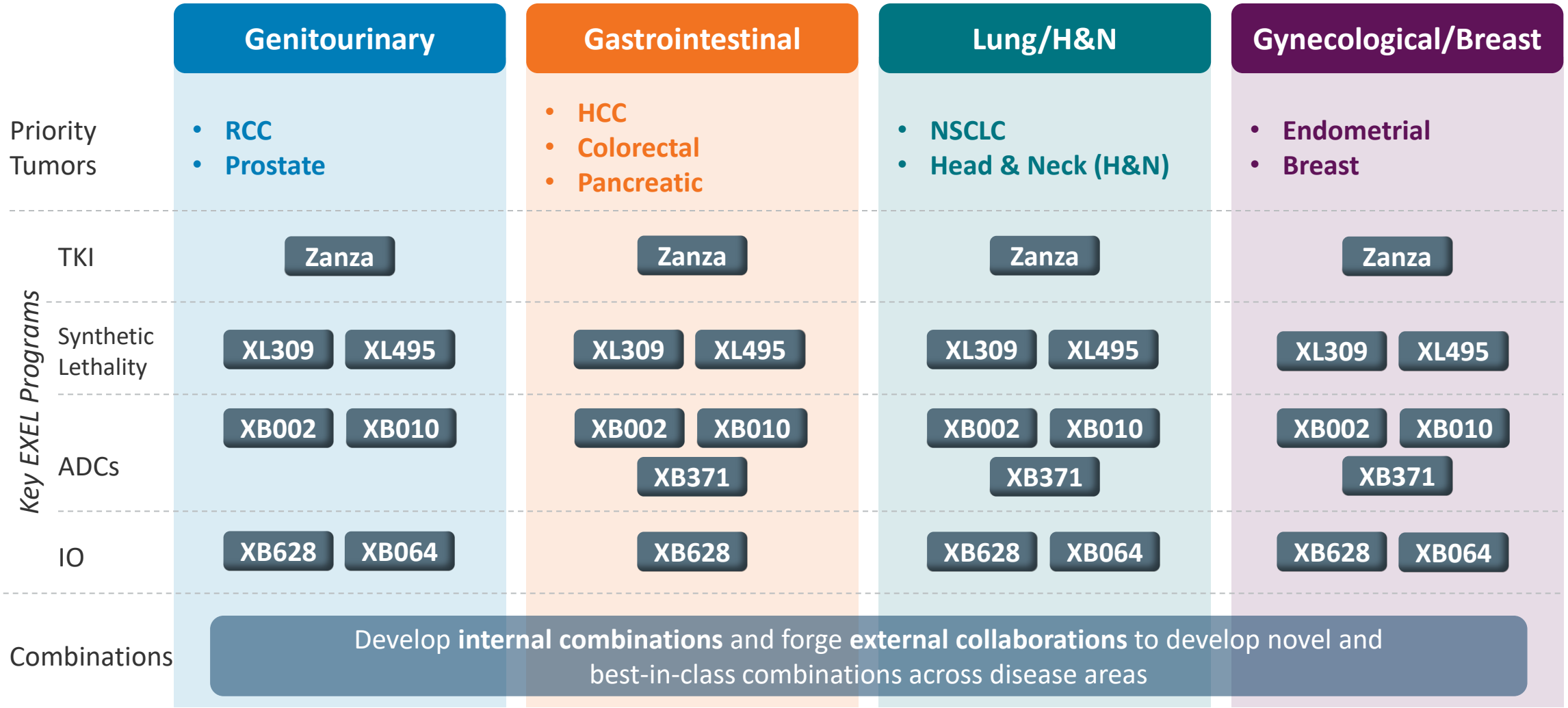
Pipeline Is Well Positioned to Build on Success in GU and GI, while Delivering Growth in New Disease Areas



GU = genitourinary cancers
GI = gastrointestinal cancers
RCC = renal cell carcinoma
HCC = hepatocellular carcinoma
NSCLC = non-small cell lung cancer
TKI = tyrosine kinase inhibitor
ADC = antibody-drug conjugate
IO = immunotherapy
H&N = head & neck

**2023 drug treatable patients across lines of therapy in the advanced/metastatic setting. Source: DRG*

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Zanzalintinib: VEGFR TKI Combination Partner of Choice

Strategic Focus

1. **Accelerate development** in high unmet need indications
2. **Expand TKI footprint** in indications where IO is approved
3. **Develop new standards of care** in novel combinations

Competitive Differentiation

+ **Favorable benefit/risk profile** vs. other VEGFR TKIs
+ Builds on Cabo's key drivers of commercial success
+ **VEGFR TKI combination partner of choice**

Commercial Potential

	Addressable Pts (US)*	Commercial Drivers for Zanza
3L+ CRC	~31k	• Large market with high unmet need • Opportunity in both NLM & LM
nccRCC	~7k	• First industry-sponsored RCT in ncc • Continued commitment to RCC
1L SCCHN (PD-L1+)	~13k	• Similar market size to RCC • Limited advancements in SOC

Disease Areas of Interest:

GU	GI	Lung/H&N	GYN/Breast
✓	✓	✓	✓

TKI = tyrosine kinase inhibitor
NLM = non-liver metastases
LM = liver metastases
IO = immunotherapy
RCC = renal cell carcinoma
nccRCC = non-clear cell RCC
CRC = colorectal cancer
RCT = randomized controlled trial
1L/3L = first-/third-line
SCCHN = head & neck squamous cell carcinoma
PD-L1 = programmed cell death-ligand
GI = gastrointestinal cancers
SOC = standard of care
H&N = head & neck cancers
GYN = gynecological cancers
GU = genitourinary cancers

**Clarivate DRG drug-treatable patients (2023) in the advanced/metastatic setting*

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XB002 & XB371: Best-in-class Tissue-Factor (TF) ADC Franchise

Strategic Focus

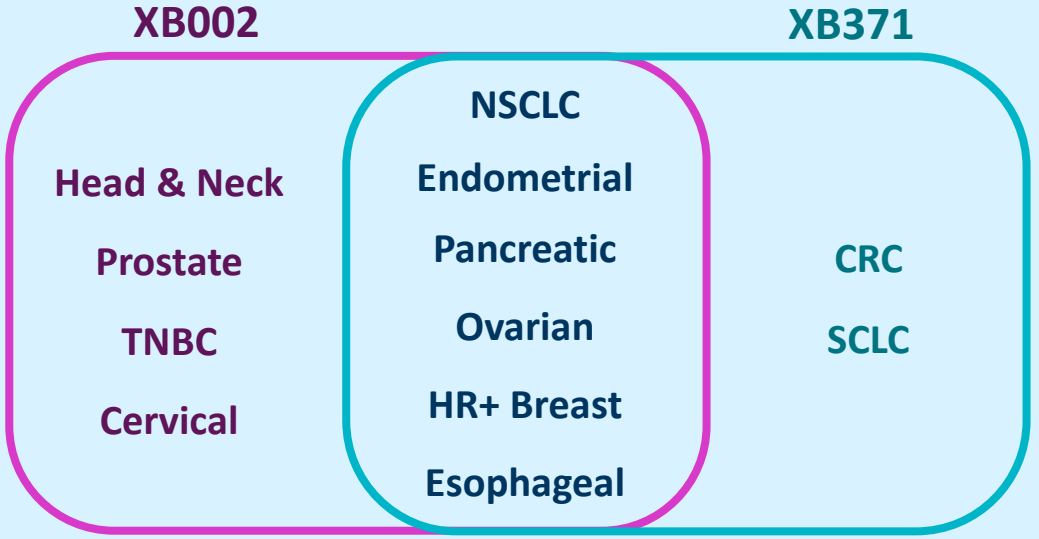
1. **Leverage differentiated profiles** to improve outcomes and compete effectively
2. **Accelerate development** in markets with FIC potential
3. **Access new indications** with XB371 (TOPO1i payload)

Competitive Differentiation

+ **XB002: Potentially best-in-class** safety and efficacy
+ **XB371: First-in-class** Tissue Factor (TF) TOPO1i ADC

Commercial Potential

Tissue Factor ADC Franchise leverages a complementary approach to maximize optionality and drive value for patients



Disease Areas of Interest:

GU	GI	Lung/H&N	GYN/Breast
✓	✓	✓	✓

ADC = antibody-drug conjugate
FIC = first-in-class
TOPO1i = topoisomerase 1 inhibitor
TNBC = triple-negative breast cancer
HR+ = hormone receptor positive
CRC = colorectal cancer
SCLC = small cell lung cancer
GU = genitourinary tumors
GI = gastrointestinal tumors
H&N = head & neck
GYN = gynecologic tumors
NSCLC = non-small cell lung cancer

**Clarivate DRG drug-treatable patients (2023) in the advanced/metastatic setting across specified tumors*

XL309: Best-in-class USP1i with Potential to Build and Expand on PARPi

Strategic Focus

1. **Accelerate development** in PARPi-refractory patients
2. **Advance standard of care** in combination with PARPi
3. **Expand** beyond existing PARPi market

Competitive Differentiation

+ Potentially **differentiated safety profile** vs. competition
+ **Improved combinability** with PARPi, chemo and internal & external synthetic lethality targeting programs

Commercial Potential

XL309 Has the Potential to Build and Expand Upon the Existing Attractive PARP Inhibitor Market

PARPi Approved Tumors	Mutation Rate^	Addressable Pts (US)*	2022 PARPi US Sales
♀ Ovarian	HRD+ ~50%	~20k	>$1.6B
Breast	gBRCAm ~10%	~40k	
♂ Prostate	HRRm ~30%	~21k	

Initial Disease Areas of Interest:

GU	GI	Lung/H&N	GYN/Breast
✓			✓

USP1i = ubiquitin specific protein 1 inhibitor
PARPi = poly ADP ribose polymerase inhibitor
GU = genitourinary cancers
GI = gastrointestinal cancers
HRD+ = homologous recombination deficiency positive
gBRCAm = germline BRCA mutation
HRRm = homologous recombination repair mutated
GYN = gynecological cancers
H&N = head & neck

**Clarivate DRG drug-treatable patients (2023) in the advanced/metastatic setting*
^ Shao et al. Environ Mol Mutagen. 2022;63:308–316.

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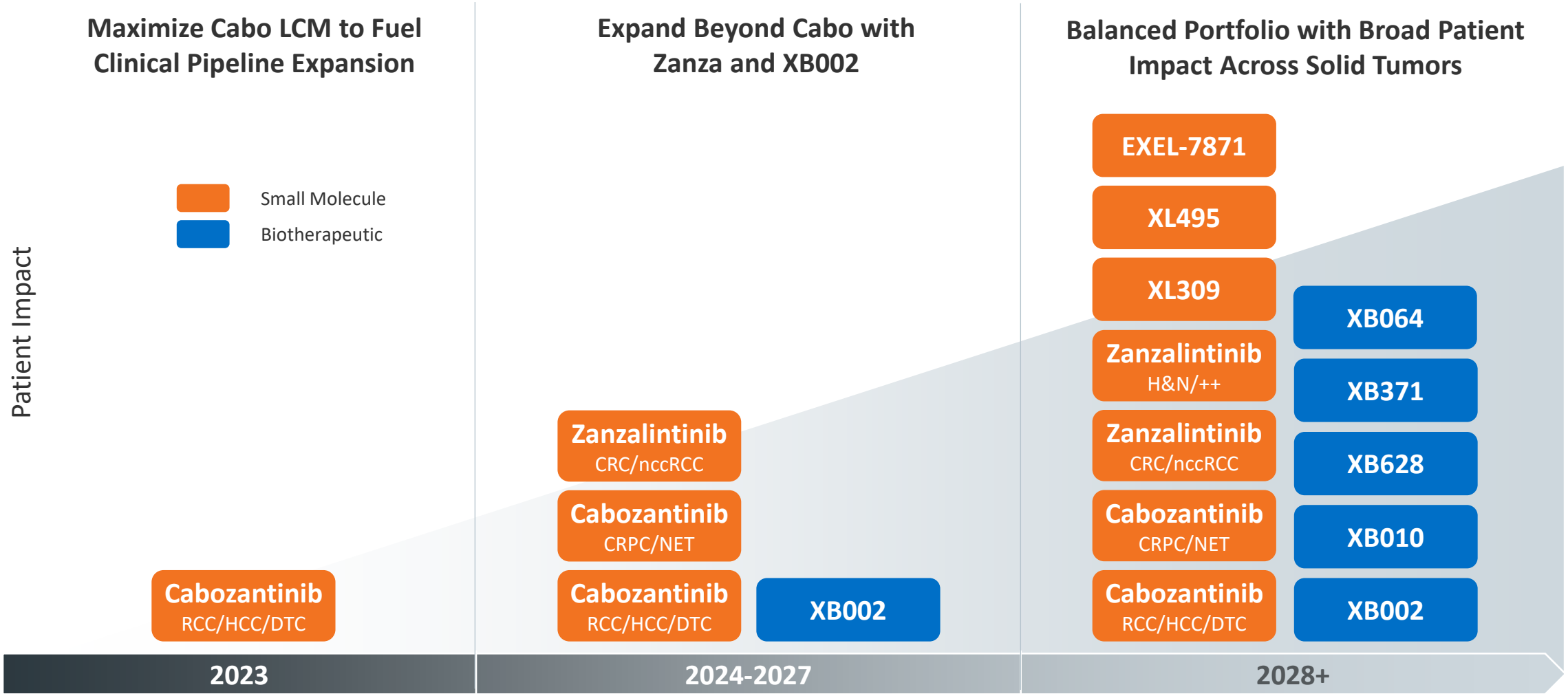
Exelixis Commercial Vision: Multi-Product, Multi-Modal Solid Tumor Portfolio



RCC = renal cell carcinoma
HCC = hepatocellular carcinoma
DTC = differentiated thyroid cancer
CRC = colorectal cancer
NET = neuroendocrine tumors
H&N = head & neck
CRPC = castration-resistant prostate cancer
nccRCC = non-clear cell renal cell carcinoma
LCM = life-cycle management

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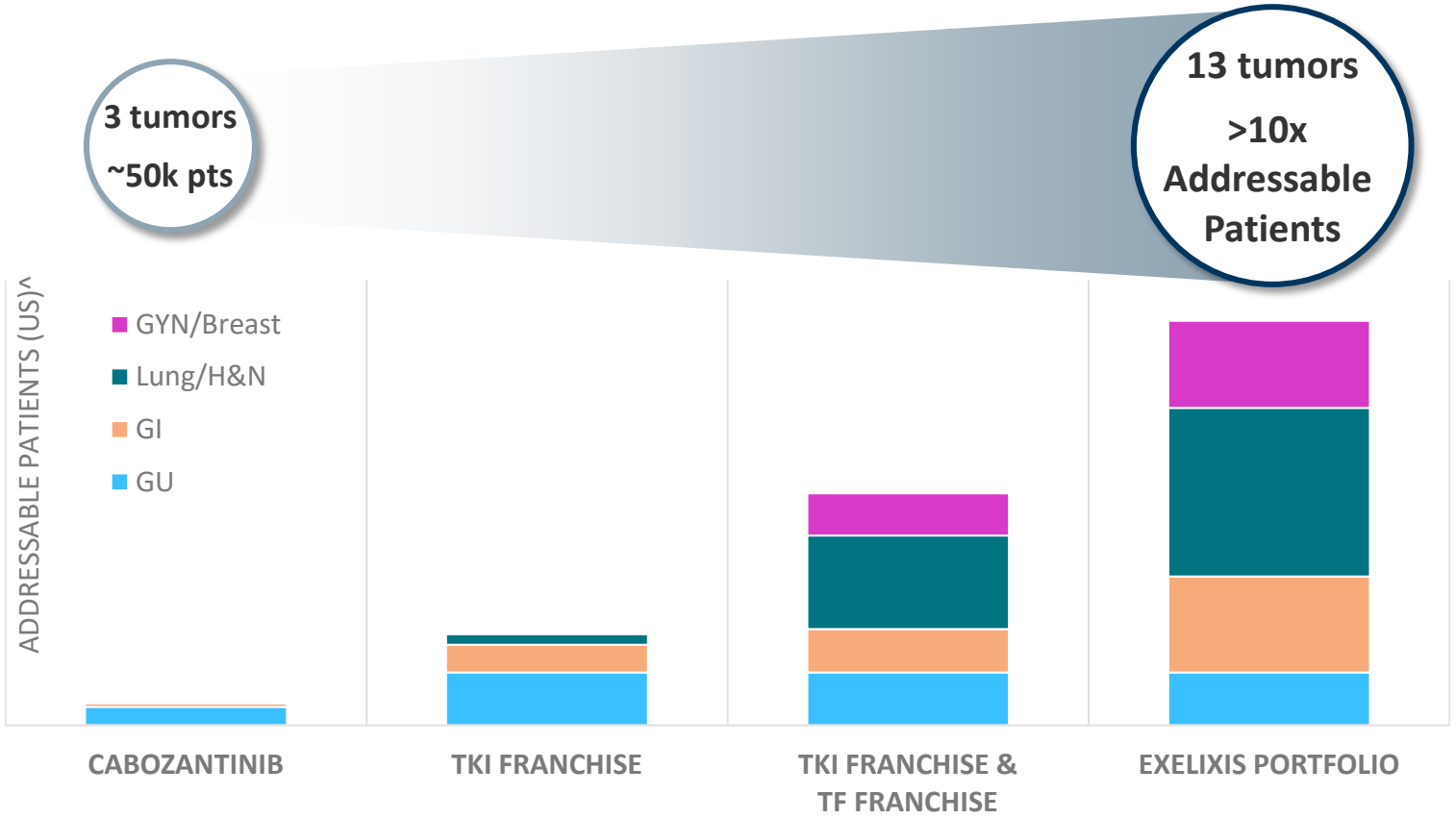
Exelixis R&D Strategy Enables Us to Deliver on Our Mission

Small Molecules	Biotherapeutics
Cabozantinib RCC/HCC/DTC/ CRPC*/NET*	XB002
Zanzalintinib RCC/CRC/H&N/++	XB010
XL309	XB628
XL495	XB371
EXEL-7871	XB064



Multiple franchises across solid tumors with significant potential to improve the lives of cancer patients

RCC = renal cell carcinoma
HCC = hepatocellular carcinoma
DTC = differentiated thyroid cancer
CRC = colorectal cancer
NET = neuroendocrine tumors
H&N = head & neck
CRPC = castration-resistant prostate cancer
GYN = gynecologic tumors
GI = gastrointestinal tumors
GU = genitourinary tumors
TKI = tyrosine kinase inhibitor
TF = tissue factor

**Not yet approved*
^2023 drug treatable patients in indications/tumors of interest across lines of therapy in the advanced/metastatic setting. Source: DRG

Broadening Research Impact in Biotherapeutics & Small Molecules

Dana T. Aftab, Ph.D.
EVP, Discovery & Translational Research
and CSO

Pipeline Discovery: Focus through the Cabozantinib Lens

Pipeline Focus

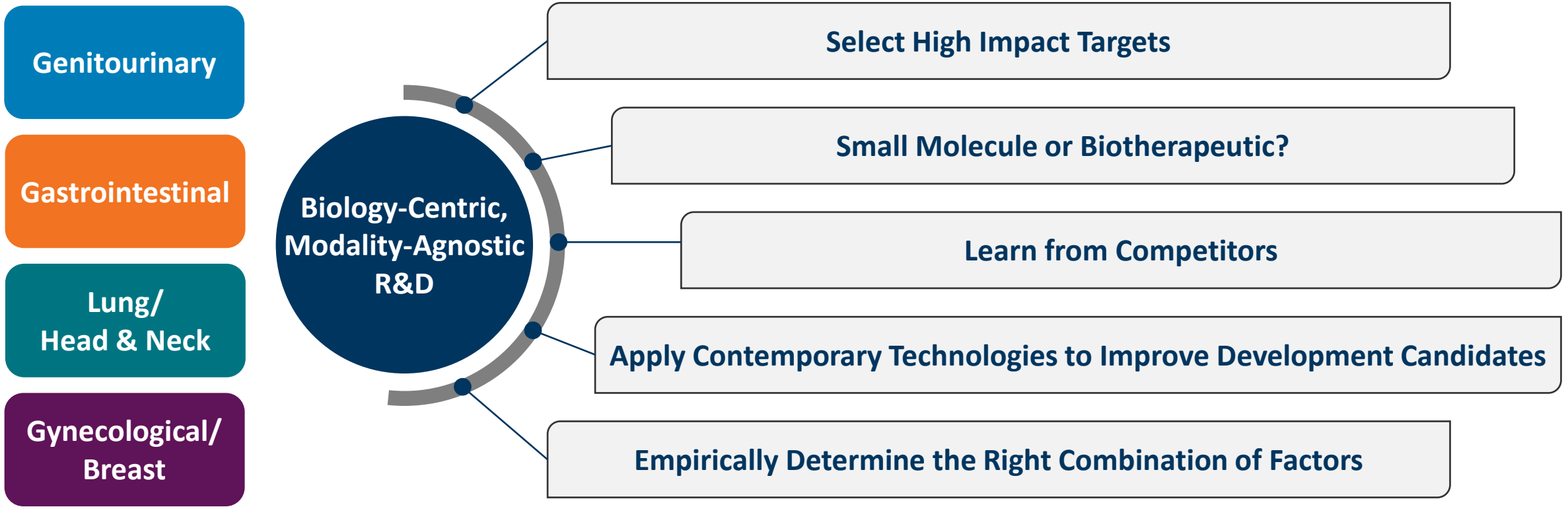
- **Expand pipeline** with development candidates that have potential for **differentiated clinical profiles**
- **Biotherapeutics strategy:** focus on next-generation ADCs, monoclonal antibodies and bispecifics
- **Small molecule strategy:** focus on synthetic lethality and the tumor microenvironment

Cabozantinib Lens

- **Leveraging learnings & expertise** in drug discovery and development to design **next-generation compounds**
- **Deep focus on tumor biology** drives drug design strategy
- **Broadly applicable** drug candidates with activity across **multiple tumor types**

ADC = antibody drug conjugate

Discovering Next Generation Molecules with Best-In-Class Potential



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Collaborative Platforms Enable Rapid Biotherapeutics Discovery

Exelixis Expertise

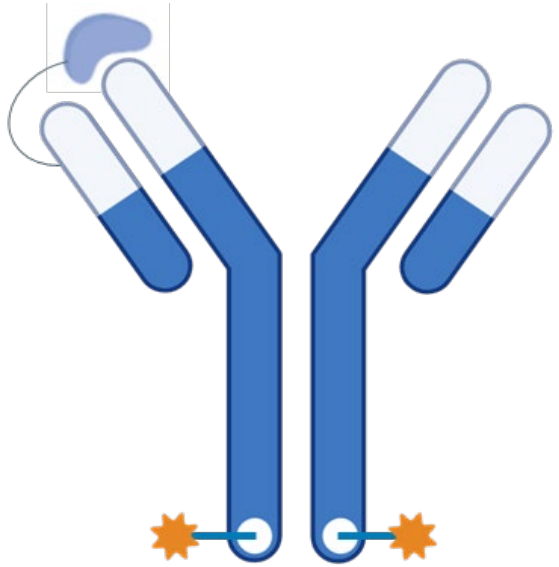
- Scientific leadership
- Project management
- Specialized lab functions

Antibody Discovery

invenra

WuXi Biologics
Global Solution Provider

GAMAMABS PHARMA



Platforms / Technologies

Catalent	**SMARTag®** (ADCs)
invenra	**B-Body®** (bispecifics)
ADAGENE	**SAFEbody®** (masking)
NBE therapeutics Innovating medicines	**SMAC-Technology™** (ADCs)
Aj AJINOMOTO	**AJICAP®** (ADCs)

Payloads

- Auristatins
- TOPO1 inhibitors
- STING agonists
- Anthracyclines

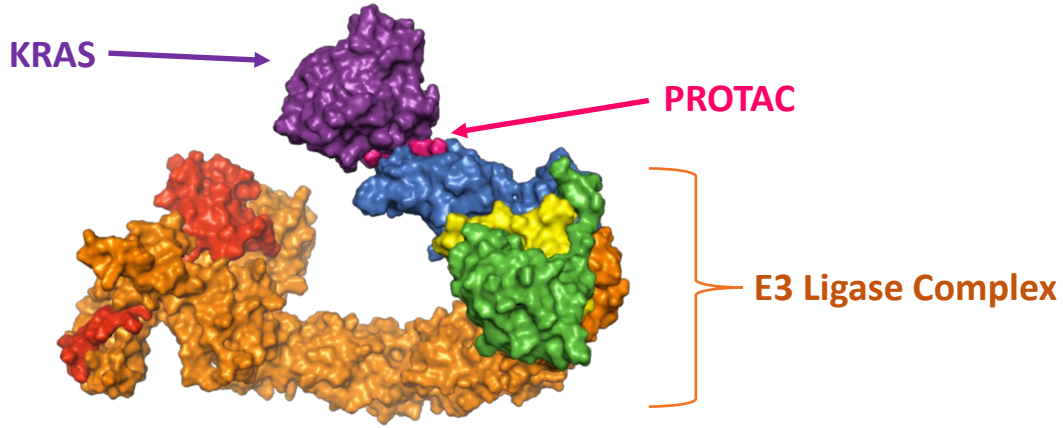
Scalable model - maximizes optionality, innovation and speed

ADC = antibody-drug conjugate
TOPO1 = topoisomerase 1

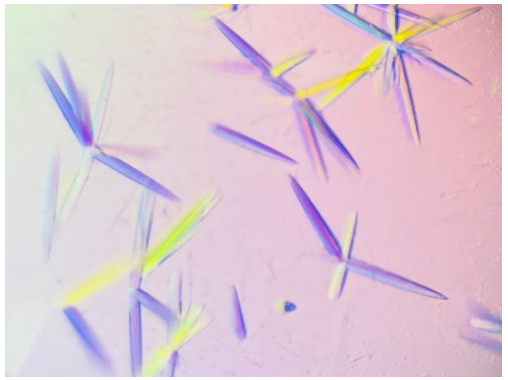
Technologies Drive Differentiated Approaches in Small Molecule Discovery

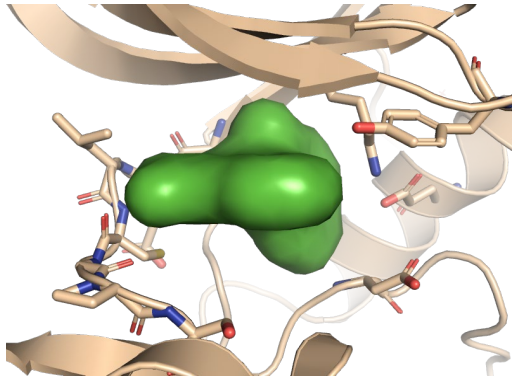
High-resolution structures solved at project initiation – yield vectors for design of more selective/potent molecules

CryoEM Structure of Chimeric Degrader Bound to KRAS + E3 Ligase

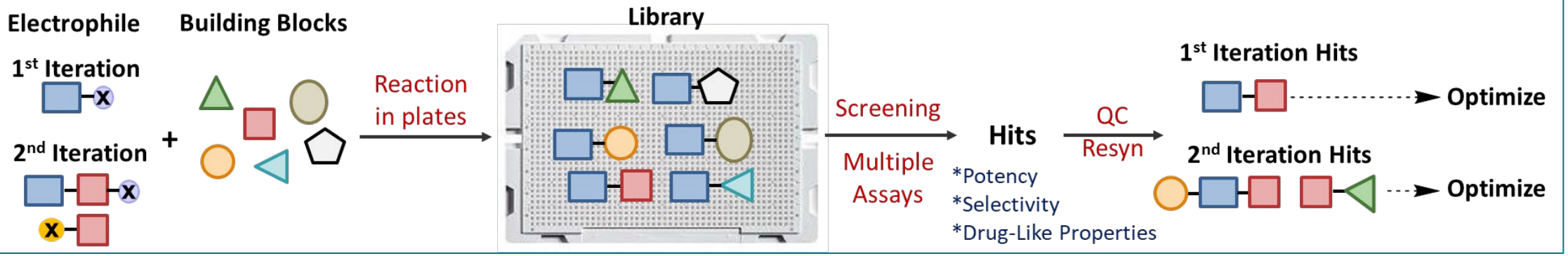


X-ray Crystal Structure of Inhibitor Bound to PKMYT1 (1.43 Å)





Rapid library construction enables a multiplexed approach to optimize potency, selectivity and properties

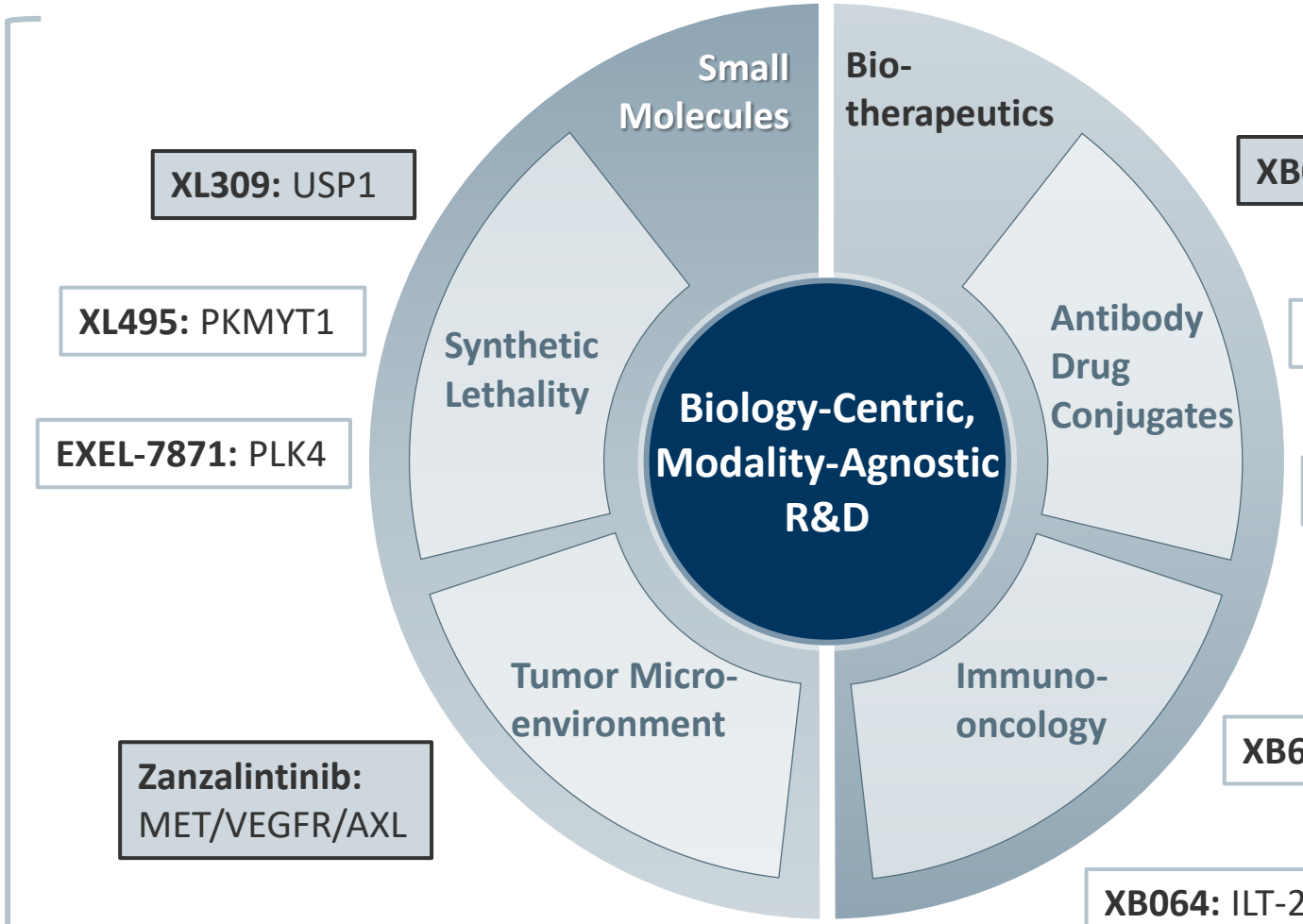


CryoEM = cryogenic electron microscopy
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
QC = quality control

EXELIXIS®

Modality-Agnostic Discovery Strategy: Focus on Differentiation

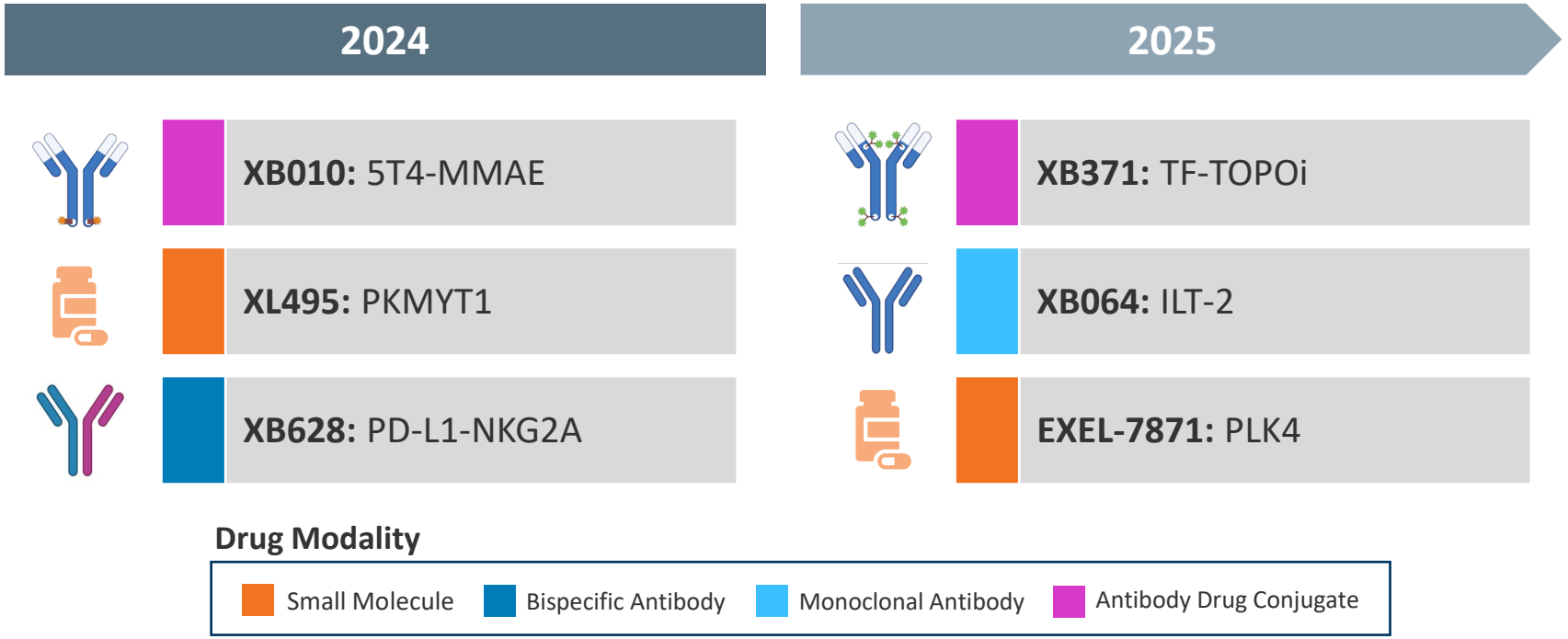
- Genitourinary
- Gastrointestinal
- Lung/Head & Neck
- Gynecological/ Breast



USP1 = ubiquitin specific peptidase 1
TF = tissue factor
MMAE = monomethyl auristatin E
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
MTI = auristatin-based microtubulin inhibitor
NKG2A = natural killer cell receptor group 2A
PLK4 = polo-like kinase 4
ILT-2 = ILT2 = Ig-like transcript 2
TOPOi = topoisomerase inhibitor
PD-L1 = programmed death-ligand 1

EXELIXIS®

Productive Discovery Engine Has Created a Deep IND Pipeline



Consistent flow of development candidates targeting 2 INDs/year

Generating portfolio of molecules, all with potential for clinical differentiation

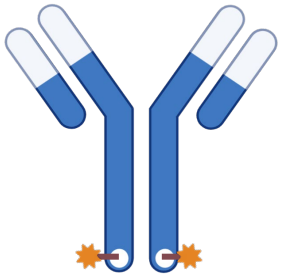
MMAE = monomethyl auristatin E
TF = tissue factor
ILT-2 = Ig-like transcript 2
IND = Investigational New Drug application
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
PD-L1 = programmed death-ligand 1
NKG2A = natural killer cell receptor group 2A
PLK4 = polo-like kinase 4
TOPOi = topoisomerase inhibitor

Biotherapeutics Pipeline

Biotherapeutics with Potential for Differentiating Clinical Activity

2024 INDs

XB010



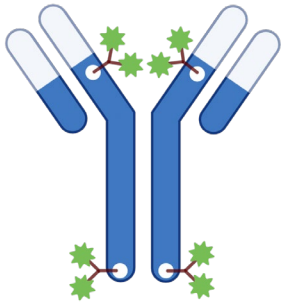
- 5T4-MMAE ADC, DAR = 2
- High expression in breast/GYN and lung/H&N tumors

XB628

- PD-L1 + NKG2A bispecific antibody
- Blocks inhibition of NK cell activation by tumor HLA-E, while relieving PD-L1 mediated T-cell checkpoint
- Acts as NK cell engager

2025 INDs

XB371



- TF-TOPOi ADC, DAR = 8
- Broadens reach of TF franchise beyond XB002 to include tumors not responsive to tubulin inhibitors

XB064

- ILT2 monoclonal antibody
- Blocks inhibition of T-cells, macrophages, and NK cells by tumor HLA-G
- Associated with resistance to PD-1/L1 inhibitors

IND = Investigational New Drug application
ADC = antibody-drug conjugate
MMAE = monomethyl auristatin E
TF = tissue factor
DAR = drug-to-antibody ratio
NK = natural killer
PD-L1 = programmed death-ligand 1
NKG2A = natural killer cell receptor group 2A
HLA-E/G = human leukocyte antigen E/G
H&N = head & neck cancers
GYN = gynecological cancers
TOPOi = topoisomerase inhibitor
ILT2 = Ig-like transcript 2
PD-1 = programmed cell death protein 1

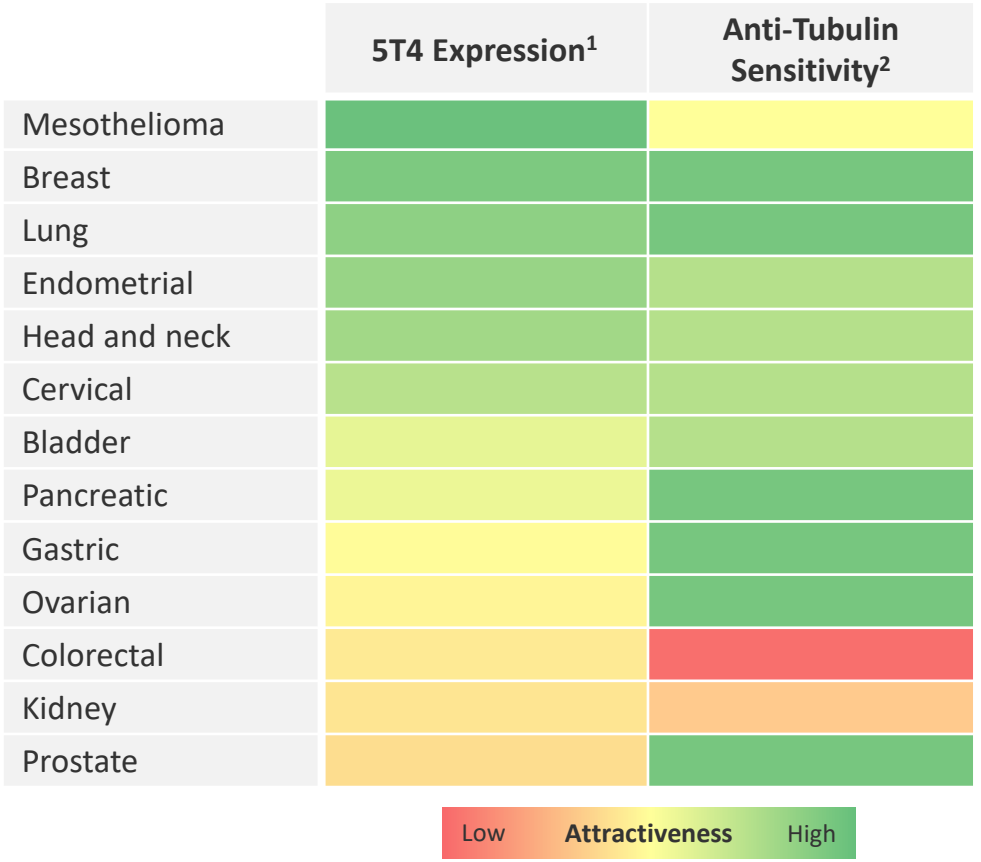
XB010

5T4-MMAE Antibody-Drug Conjugate

5T4 is an Optimal Target for an Antibody-Drug Conjugate Approach

5T4 is overexpressed in several cancer types with limited expression in normal adult tissues	
Function	• 5T4 is associated with cancer stem cells (CSCs), cell adhesion, epithelial-to-mesenchymal transition, and pathways that promote CSC mobilization
Healthy Adult Tissue Expression Profile	• Syncytiotrophoblast membrane in normal placenta
Solid Tumor Tissue Expression Profile	• Breast, lung, endometrial, head and neck, cervical, and others • Expression seen by immunohistochemistry in ~50% of circulating tumor cells in NSCLC patients

5T4 Expression & Anti-Tubulin Sensitivity



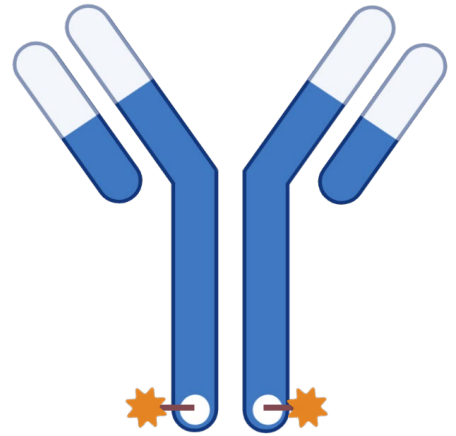
NSCLC = non-small cell lung cancer

[1] Exelixis IHC data; composite score based on percentage and intensity scores by pathologist
[2] Based on NCCN guidelines for anti-tubulin drugs

EXELIXIS®

First-in-Class Potential for a 5T4-Targeted ADC with Anti-Tubulin Payload

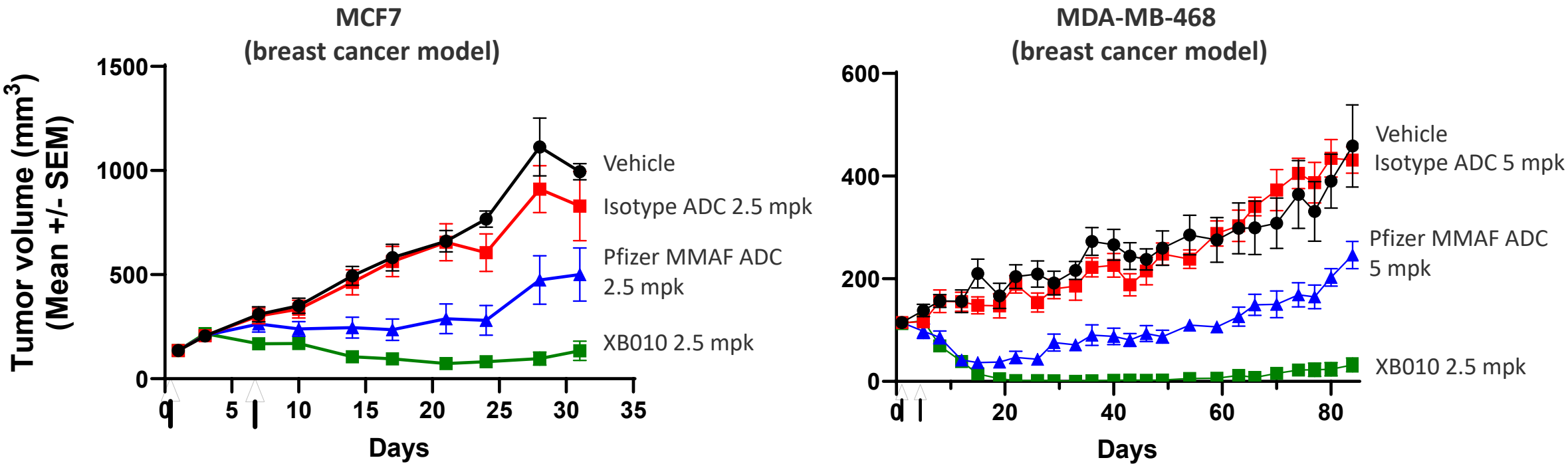
- High affinity 5T4 monoclonal antibody conjugated to MMAE
- Site-specific conjugation:
  - Nominal Drug Antibody Ratio (DAR) = 2
- Proprietary linker technology:
  - Requires two tandem cleavage events for payload release
- Highly potent and efficacious in preclinical models



Potential for broad impact across a range of tumor types

ADC = antibody-drug conjugate
MMAE = monomethyl auristatin E

XB010 Demonstrates Superior Efficacy in Xenograft Models



Arrows on x-axis indicate i.v. dosing

Efficacy observed across a range of PDX models including breast, lung, and endometrial cancers

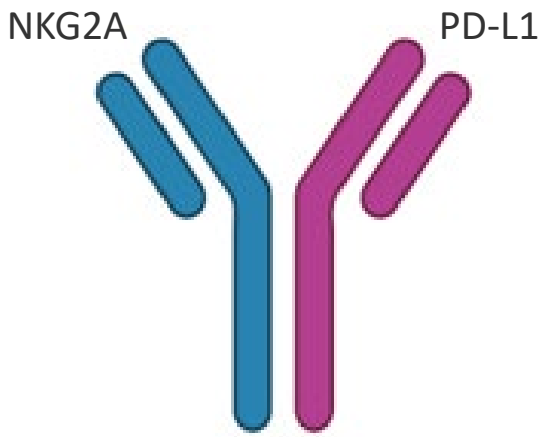
ADC = antibody-drug conjugate
PDX = patient derived xenograft
SEM = standard error of mean

XB628

PD-L1-NKG2A Bispecific Antibody

XB628 Simultaneously Targets Adaptive & Innate Immune Checkpoints

- High affinity PD-L1 & NKG2A binders formatted into a bispecific antibody
- Simultaneous inhibition of adaptive & innate immune checkpoints
- Acts as an NK cell engager, co-localizing NK and tumor cells
- Highly efficacious in tumor cell kill models *in vitro*
- B-Body® platform: high yield and efficient purification using conventional methods



XB628

First-in-class potential for a bispecific targeting PD-L1 and NKG2A simultaneously

PD-L1 = programmed cell death ligand 1
NKG2A = natural killer cell receptor group 2A
NK = natural killer

A Bispecific Targeting PD-L1 & NKG2A is a Differentiated Approach

Advantages of a bispecific over combination therapy

- Engager to co-localize/redirect NK and T cells to tumor cells for enhanced tumor killing
- Potential for improved dosing and PK/PD with bispecific compared to combination therapy

NKG2A/HLA-E

- NKG2A is an immune inhibitory checkpoint, expressed on NK cells and $CD8^+$ tumor infiltrating lymphocytes (TILs), that binds HLA-E
- HLA-E expression is upregulated on tumor cells and acts as a potential resistance mechanism to PD-1/L1 blockade

PD-L1

- PD-L1 is overexpressed in multiple tumors
- Antibodies targeting this pathway are extensively validated, with demonstrated success in the clinic

Phase 2 COAST (JCO 2022)[1]

Treatment Arm	No. of Events/ Total No. of Patients (%)	mPFS, Months (95% CI)	12-month PFS Rate, % (95% CI)	HR, % (95% CI)
Durvalumab + monalizumab	21/62 (33.9%)	15.1 (13.6 to NE)	72.7 (58.8 to 82.6)	0.42 (0.24 to 0.72)
Durvalumab	38/67 (56.7%)	6.3 (3.7 – 11.2)	33.9 (21.1 to 47.1)	-

Durvalumab in combination with monalizumab prolonged PFS vs. Durvalumab alone in patients with unresectable stage III non-small cell lung cancer

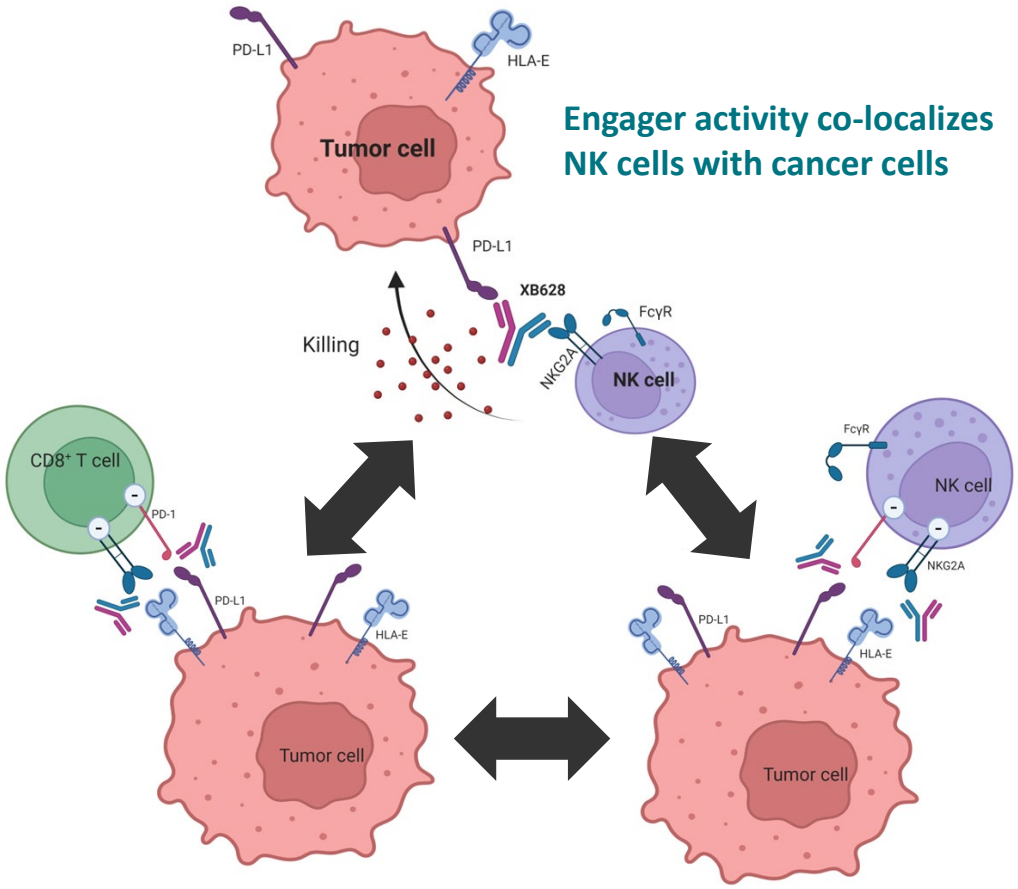
Simultaneous inhibition of adaptive and innate immune checkpoints with engager activity

PD-L1 = programmed cell death ligand 1
NKG2A = natural killer cell receptor group 2A
NK = natural killer
PK = pharmacokinetics
PD = pharmacodynamics
HLA-E = human leukocyte antigen E
PD-1 = programmed cell death protein 1
PFS = progression-free survival
HR = hazard ratio

[1] *Herbst et al. JCO 2022*

EXELIXIS®

Synergistic MOAs + Recruitment for Direct Killing = Potential for High Impact



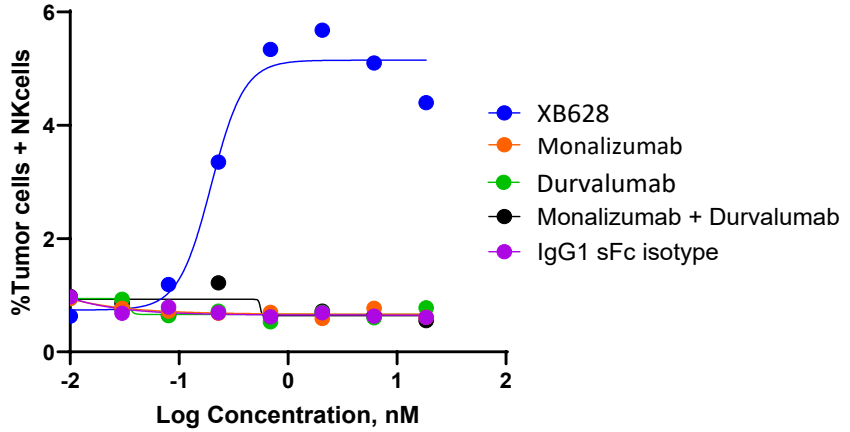
Engager activity co-localizes NK cells with cancer cells

Relieve inhibitory PD-L1/PD-1 checkpoint (adaptive immunity)

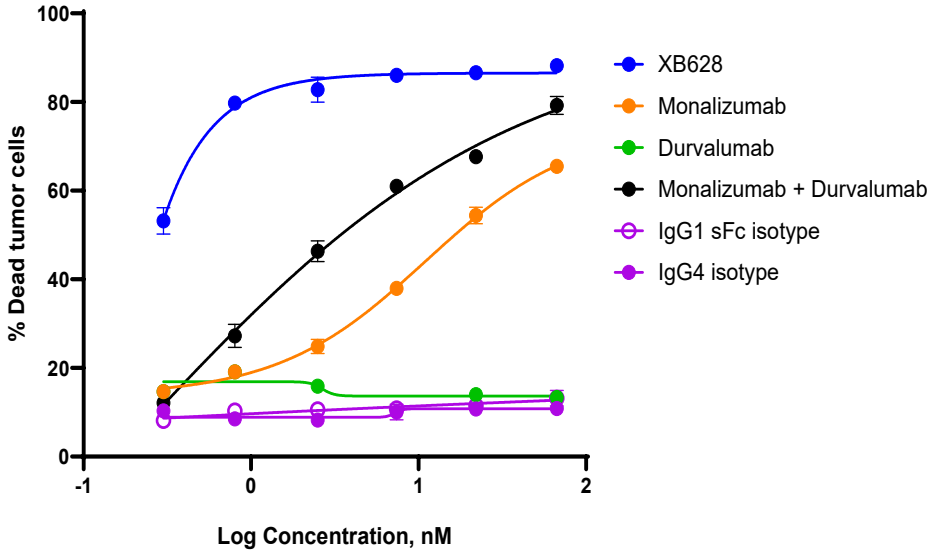
Relieve inhibitory HLA-E/NKG2A checkpoint (innate immunity)

Created with BioRender.com

Dose-Dependent Co-localization



Increased NK-Mediated Tumor Cell Killing Compared to Separate mAbs



PD-L1 = programmed cell death ligand 1
NKG2A = natural killer cell receptor group 2A
NK = natural killer
MOA = mechanism of action
PD-1 = programmed cell death protein 1
HLA-E = human leukocyte antigen E
mAb = monoclonal antibody

XB371

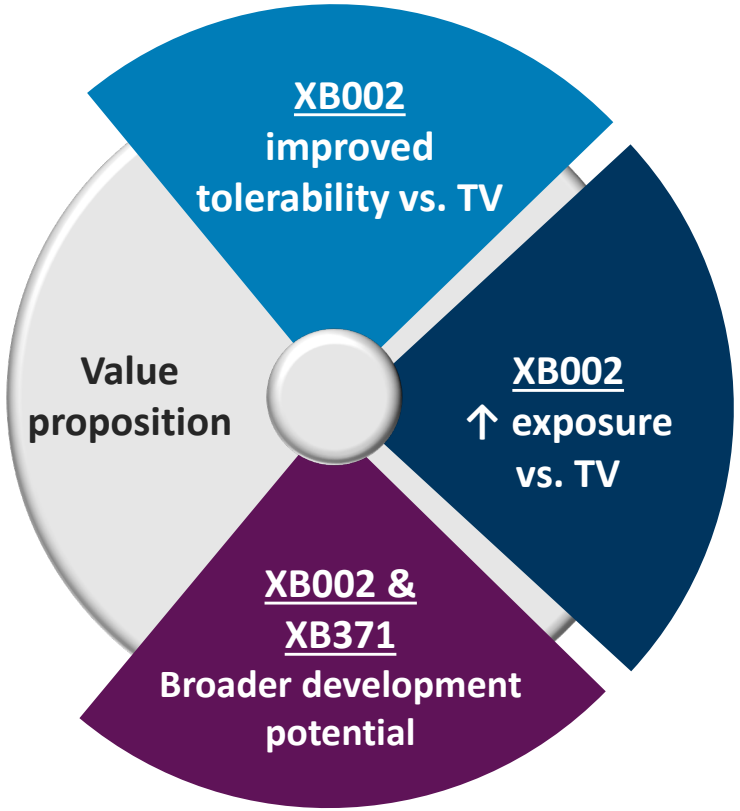
Tissue Factor-TOPOi Antibody-Drug Conjugate

Building a Tissue Factor ADC Franchise: XB002 and XB371

Tisotumab Vedotin (TV)

AEs of Special Interest	Bleeding, Neuropathy, Ocular Toxicity
Tumors in Active Development	Cervical, SCCHN, Pancreatic, NSCLC, CRC
Combination Potential	IO, Chemo, Bev: Significant toxicity in combinations

Exelixis Tissue Factor Franchise



XB002 potentially differentiates from TV on tolerability, exposure, and combinability
XB371 is complementary, providing optionality and unlocking access to additional markets

ADC = antibody-drug conjugate
AE = adverse event
IO = immunotherapy
SCCHN = squamous cell carcinoma of head & neck
NSCLC = non-small cell lung cancer
CRC = colorectal cancer

TF Franchise Has Broad Applicability Across Solid Tumors

Expected Payload Sensitivity for XB002 and XB371 Across Key Tumors

Potential applicability to EXEL TF Franchise

- XB002
- XB371
- XB002 & XB371

XB002 (TF-MTI ADC) and XB371 (TF-TOPOi ADC) are applicable across a range of solid tumors

Two distinct payload approaches provide optionality in several attractive markets

TF = tissue factor
ADC = antibody-drug conjugate
SCLC = small cell lung cancer
TOPOi = topoisomerase inhibitor
NSCLC = non-small cell lung cancer
MTI = auristatin-based microtubulin inhibitor

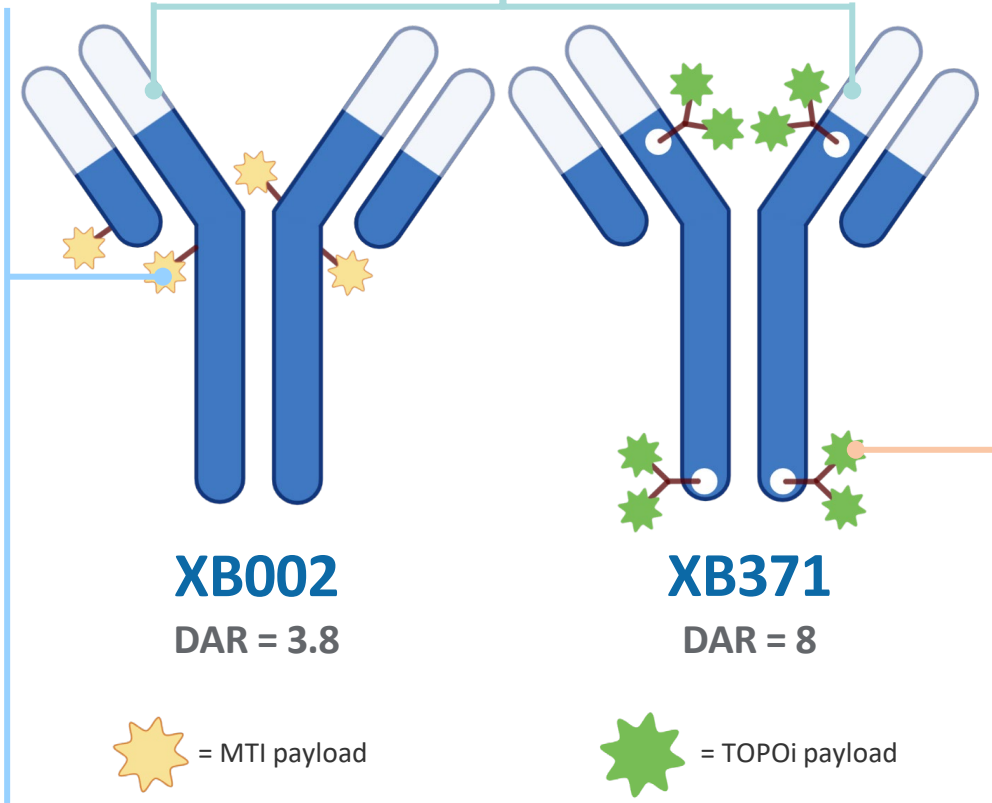
EXELIXIS®

XB002 & XB371 Utilize Next-Generation Technology

XB002 & XB371 utilize a novel mAb that recognizes a TF epitope that **does not interfere with Factor VII binding**

- Payload uses a **novel auristatin-based drug-linker** that is more hydrophilic than traditional MMAE-based drug-linkers
- Potential for **improved properties** compared first gen, MMAE-based ADCs

FIH Study (JEWEL-101) ongoing

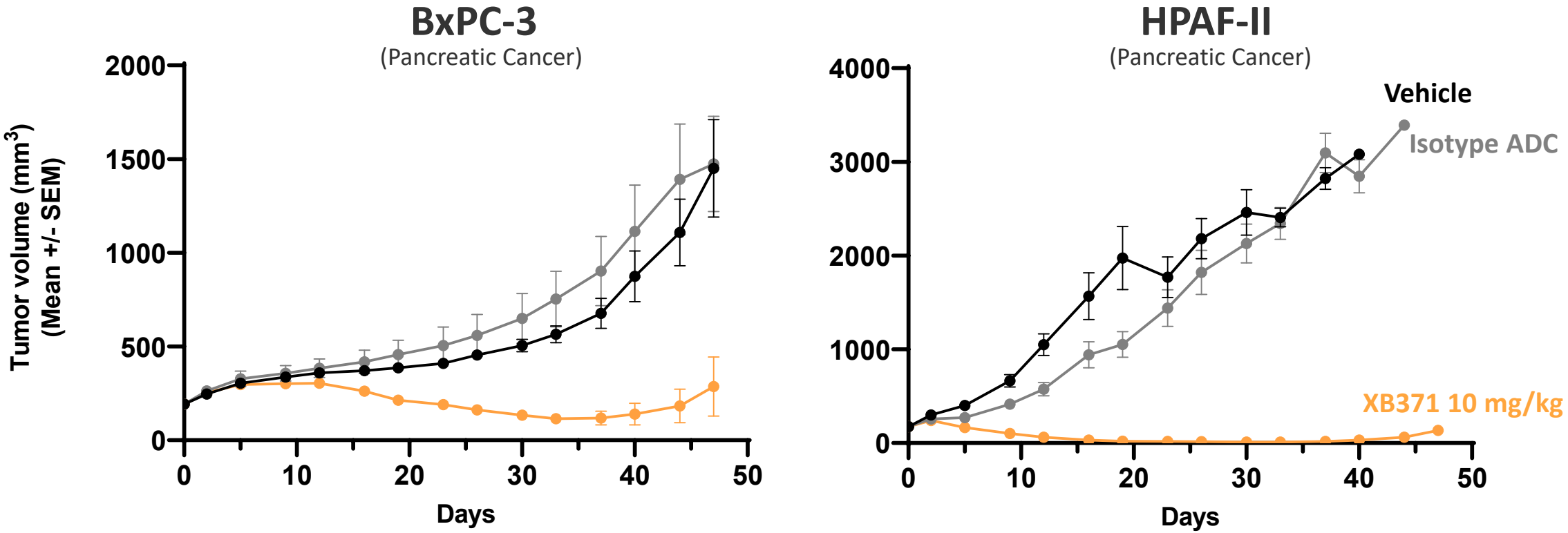


- **Site-specific conjugation** and proprietary tandem dual cleavage linker technology
- **Topoisomerase inhibitor payload** demonstrates potent efficacy and increased bystander effect

IND filing 2025

mAb = monoclonal antibody
TF = tissue factor
ADC = antibody-drug conjugate
MMAE = monomethyl auristatin E
FIH = first-in-human
DAR = drug antibody ratio
TOPOi = topoisomerase inhibitor
MTI = auristatin-based microtubulin inhibitor
IND = Investigational New Drug application

Potent Anti-Tumor Activity After Single XB371 Dose in Xenograft Models



Excellent tolerability in dose range finding non-GLP tox

SEM = standard error of mean
ADC = antibody-drug conjugate
GLP = good laboratory practice

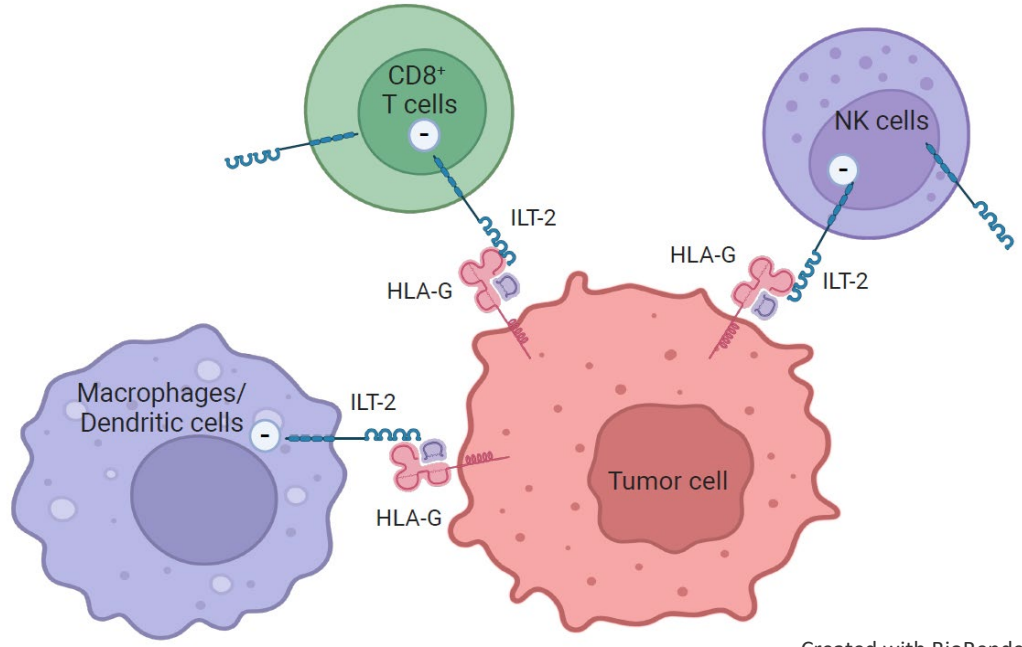
XB064

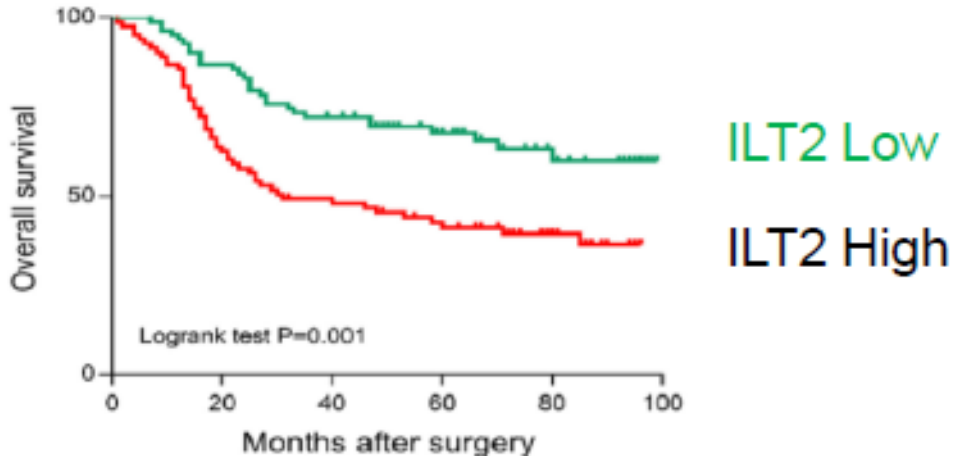
ILT2 Monoclonal Antibody

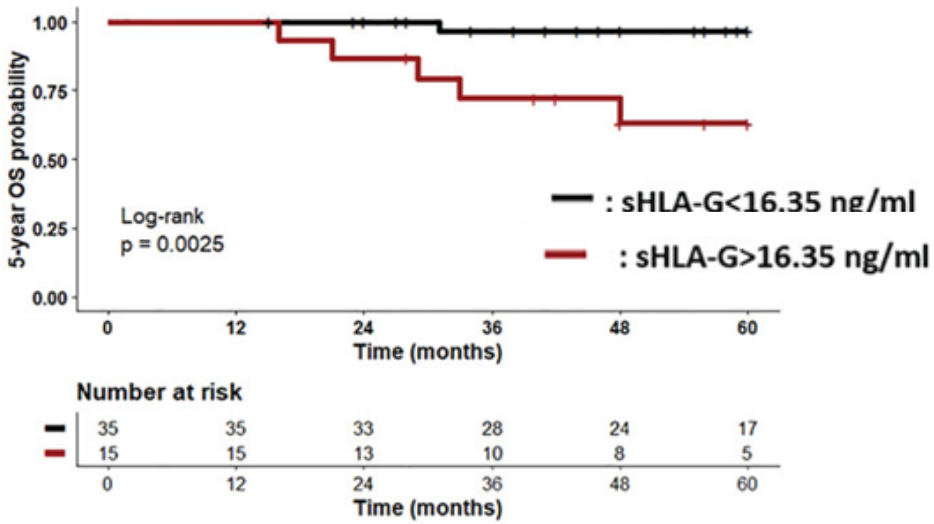
ILT2: Immune Checkpoint Potentially Associated with Resistance to Anti-PD-1

Binding of tumor cell HLA-G to ILT2 on immune cells impairs:

- Proliferation
- Cytotoxicity
- Phagocytosis
- Differentiation
- Cytokine secretion
- Chemotaxis







ILT2 = Ig-like transcript 2
PD-1 = programmed cell death protein 1
HLA-G = human leukocyte antigen G
NK = natural killer
CD8 = cluster of differentiation 8

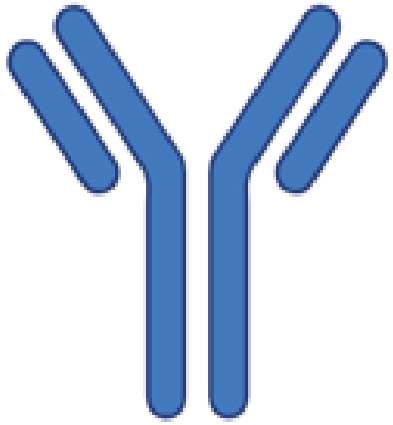
Mandel et al., J Immunother Cancer, 2022
Hoffman et al., Front. Immunol., 2023

EXELIXIS®

XB064: ILT2 Monoclonal Antibody

High affinity ILT2 mAb with best-in-class potency and activity in preclinical models

- Immune modulating checkpoint present in myeloid cells, NK cells, and T-cells
- Associated with resistance to PD-1 pathway inhibitors
- Ligand (HLA-G) highly expressed in clear cell RCC
- Opportunities to combine broadly with internal pipeline and approved IO agents

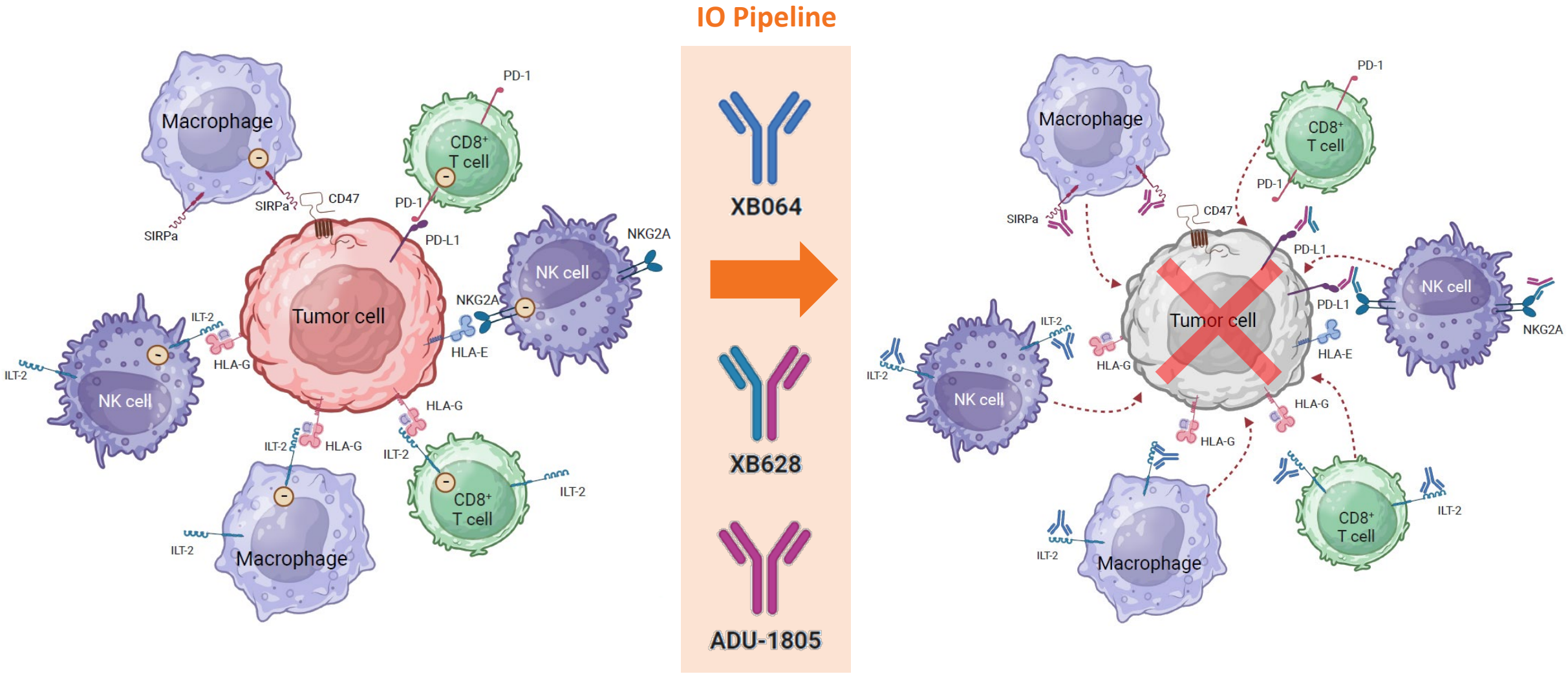


XB064

Building IO franchise with complementary mechanisms of action

ILT2 = Ig-like transcript 2
PD-1 = programmed cell death protein 1
HLA-G = human leukocyte antigen G
mAb = monoclonal antibody
NK = natural killer
RCC = renal cell carcinoma
IO = immunotherapy

XB064 Complements Our Immuno-Oncology Portfolio



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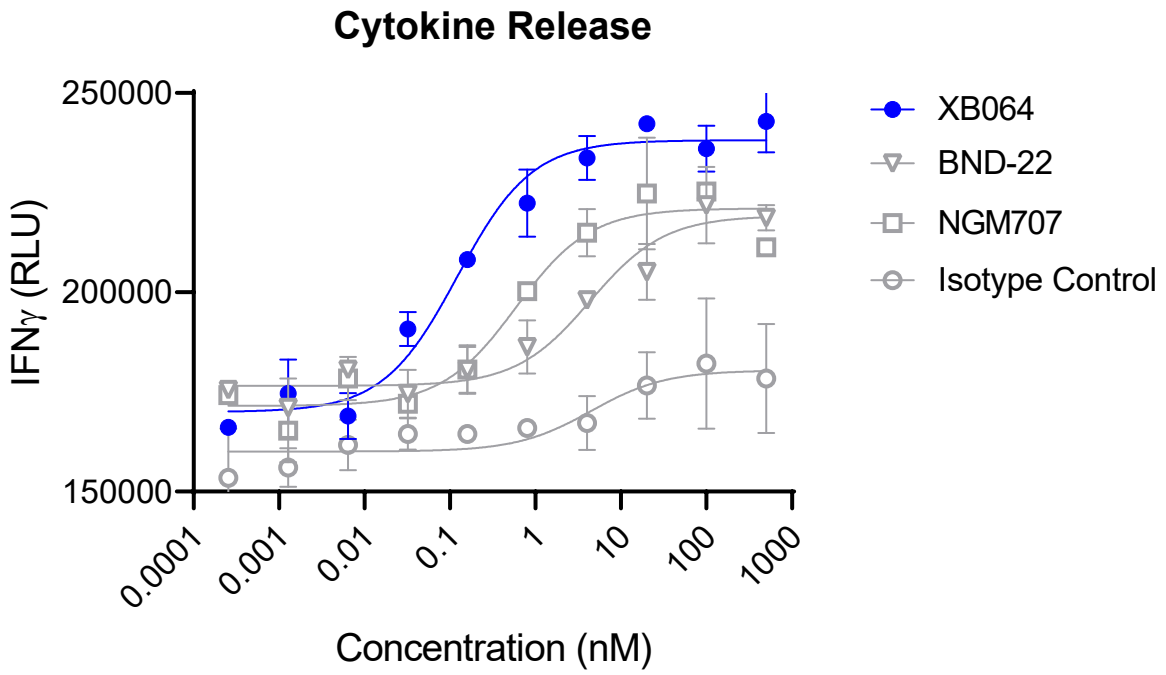
ILT2 = Ig-like transcript 2
PD-1 = programmed cell death protein 1
HLA-G/E = human leukocyte antigen G/E
mAb = monoclonal antibody
NK = natural killer
CD8 = cluster of differentiation 8
IO = immunotherapy
CD47 = cluster of differentiation 47
PD-L1 = programmed cell death ligand 1
NKG2A = natural killer cell receptor group 2A
SIRPa = signal-regulatory protein alpha

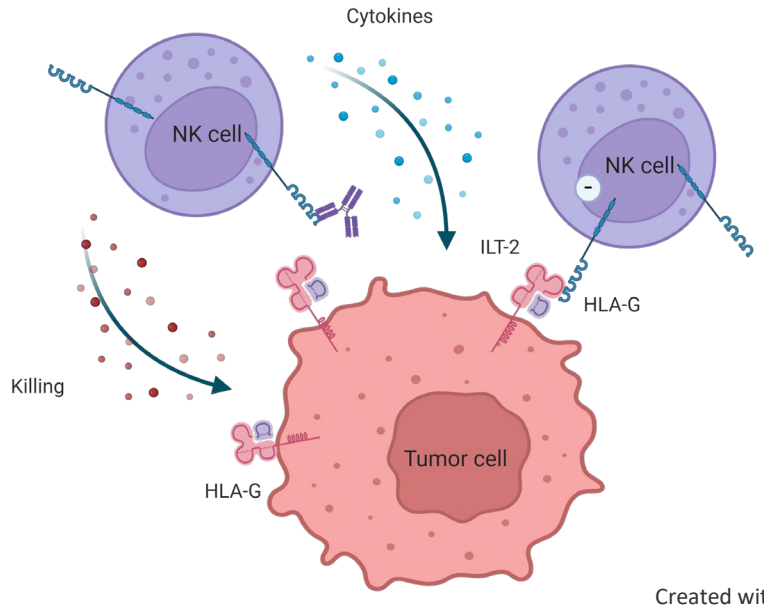
EXELIXIS®

XB064: Superior Activity in Functional Models Compared to Benchmarks



Compound	IC50 (nM)	
	IFNγ Release	NK-Mediated Cytotoxicity
XB064	0.1	0.03
NGM707	0.6	0.4
BND-22	4	1

Higher potency and magnitude of effect with XB064 compared to clinical benchmarks



Created with BioRender.com

IC50 = half-maximal inhibitory concentration
IFNγ = interferon gamma
NK = natural killer cell

EXELIXIS®

Small Molecule Pipeline

Small Molecules with Potential for Differentiating Clinical Activity

2023 IND

XL309

Synthetic Lethality: **USP1**

- USP1 inhibition shows synthetic lethality with BRCA1/2 mutations
- Potential superiority in safety pharmacology, toxicology, and DDIs
- Preclinical anti-tumor activity in BRCA-mutant and BRCA-wildtype

2024 IND

XL495

Synthetic Lethality: **PKMYT1**

- PKMYT1 inhibition results in death of cancer cells with unstable genomes
- XL495 has best-in-class potential with improved selectivity and PK
- High combination potential, including with chemotherapy, PARPi and XL309

2025 IND

EXEL-7871

Synthetic Lethality: **PLK4**

- PLK4 inhibition shows synthetic lethality with TRIM37 amplification
- EXEL-7871 is optimized for improved potency & selectivity with structure-based scaffold evolution

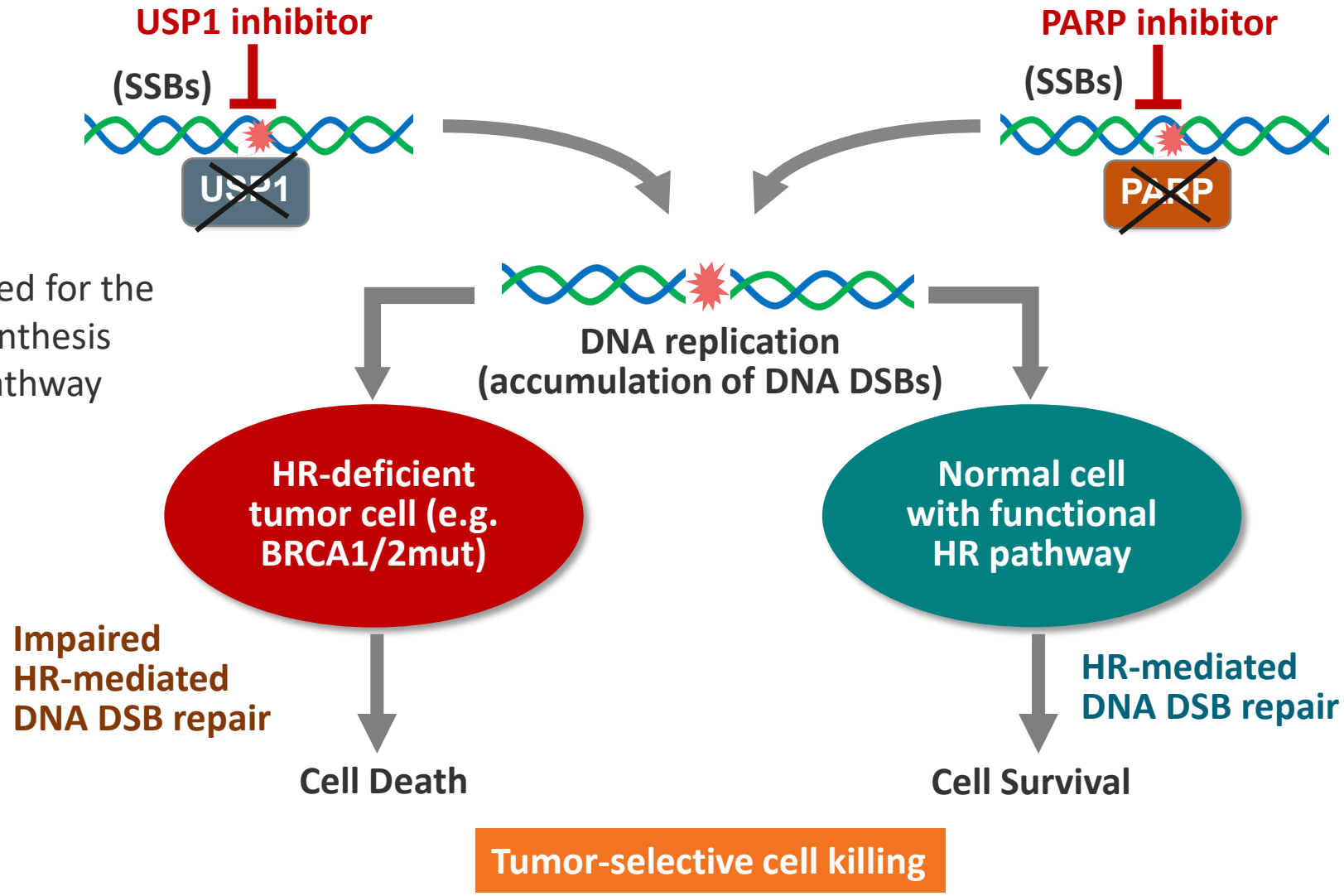
USP1 = ubiquitin-specific protein 1
PARPi = poly ADP ribose polymerase inhibitor
DDI = drug-drug interactions
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
PLK4 = polo-like kinase 4
TRIM37 = Tripartite Motif Containing 37 gene

XL309

USP1 Inhibitor

USP1 Inhibitors: Synthetic Lethality with BRCA1/2 Mutation

USP1 is required for the Translesion Synthesis DNA Repair Pathway



USP1 = ubiquitin-specific protein 1
PARP = poly ADP ribose polymerase
SSB = single-strand break
DSB = double-strand break
HR = homologous recombination

XL309 Differentiates from KSQ-4279 in Key Parameters

Parameter	XL309	KSQ-4279
USP1 IC_{50} (μM)	0.02	0.07
Cellular EC_{50} (μM)	0.02	0.02
CYP Induction (<10 μM)		CYP1A2 and 3A4
CYP Inhibition (<10 μM)	CYP2C8	CYP2C8
Solubility @ pH 6.8 / 1.0 (mg/mL)	0.04 / >18	< 0.001 / 0.005
Toxicology: exposure at MTD in rats vs efficacy exposure in mice	Dose-limiting tox observed at 18x (mono) and 50x (+ olaparib)	Dose-limiting tox observed at 6x (mono) and 13x (+ olaparib)

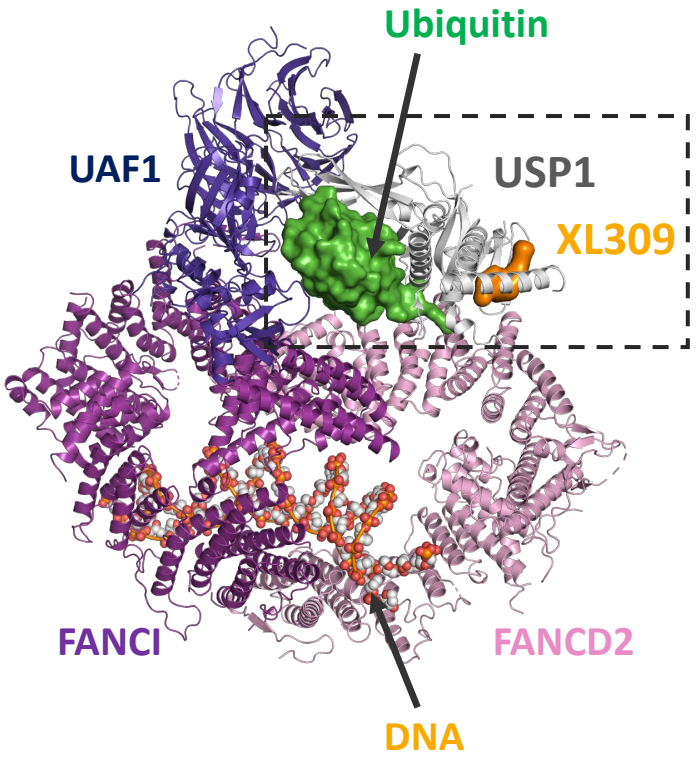
Safety Screen Panel (Ligand displacement @ 10 μM)	XL309	KSQ-4279
Adenosine transporter		
$Alpha_{1A}$ adrenergic receptor		
$Alpha_{2B}$ adrenergic receptor		
μ-opioid peptide receptor		
Platelet-activating factor receptor		
$5\text{-}HT_{2B}$ receptor		
L-type Ca^{2+} channel		
COX2		
PDE4D2		

XL309 superior in safety pharmacology & toxicology, drug-like properties and DDI potential

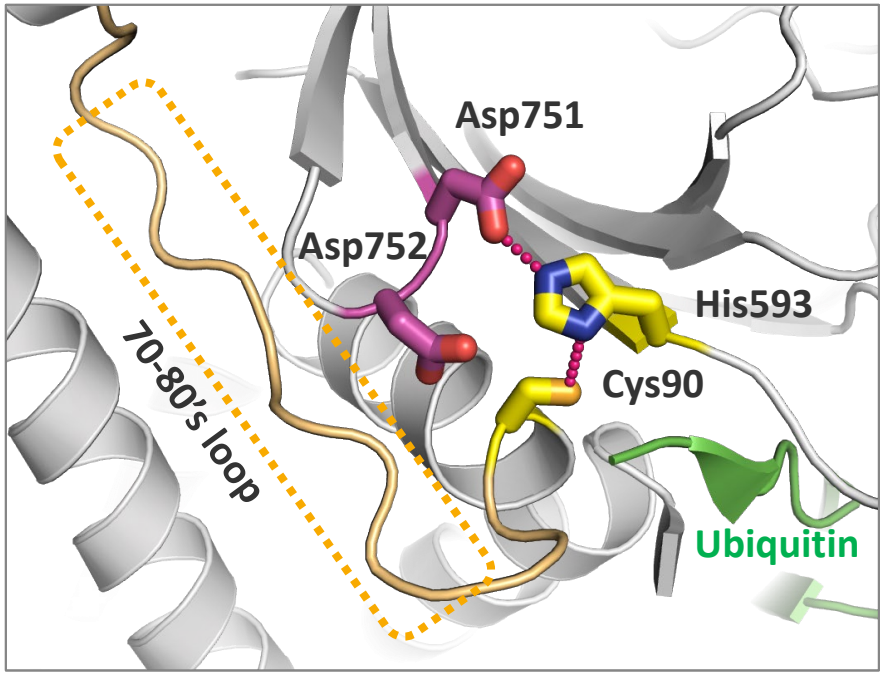
USP1 = ubiquitin-specific protein 1
IC50 = half-maximal inhibitory concentration
EC50 = half maximal effective concentration
CYP = cytochrome p450
MTD = maximum tolerated dose
DDI = drug-drug interactions

XL309-USP1 Cryo-EM Structure Provides MOA Insight

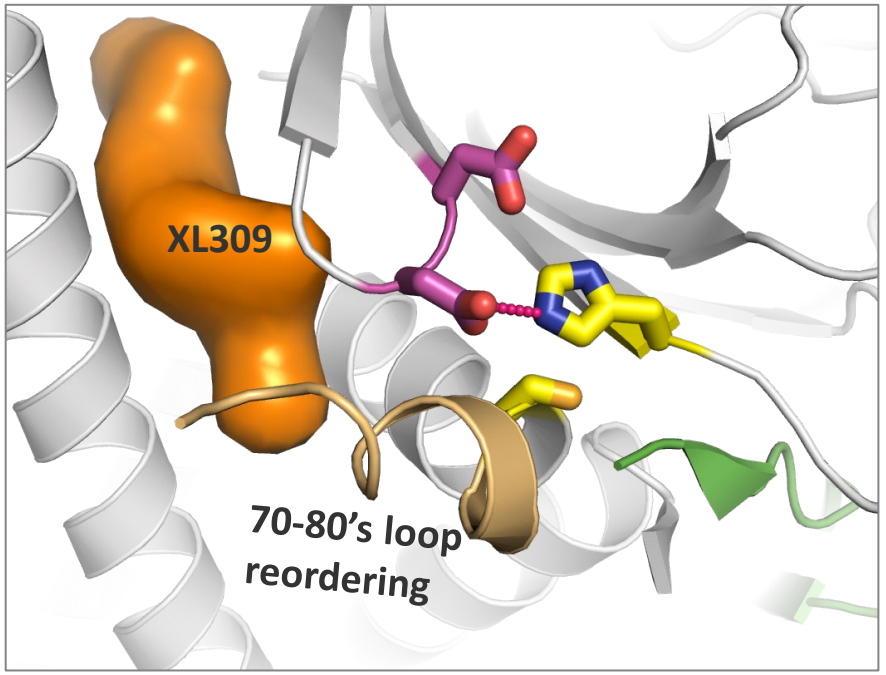
XL309-USP1-Ub FANCI/D2 complex



Catalytically competent complex



Inhibited complex (XL309 bound)



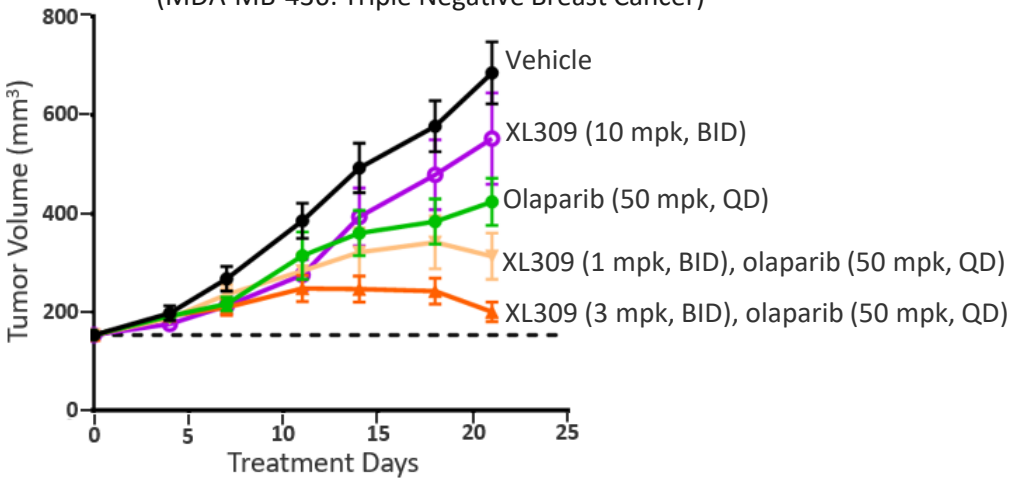
Provides insight on potential resistance mechanisms and vectors for design of next-generation inhibitors

USP1 = ubiquitin-specific protein 1
Cryo-EM = cryogenic electron microscopy
MOA = mechanism of action
UAF1 = USP1-associated factor 1
FANCI = Fanconi anemia, complementation group I
FANCD2 = Fanconi anemia group D2 protein

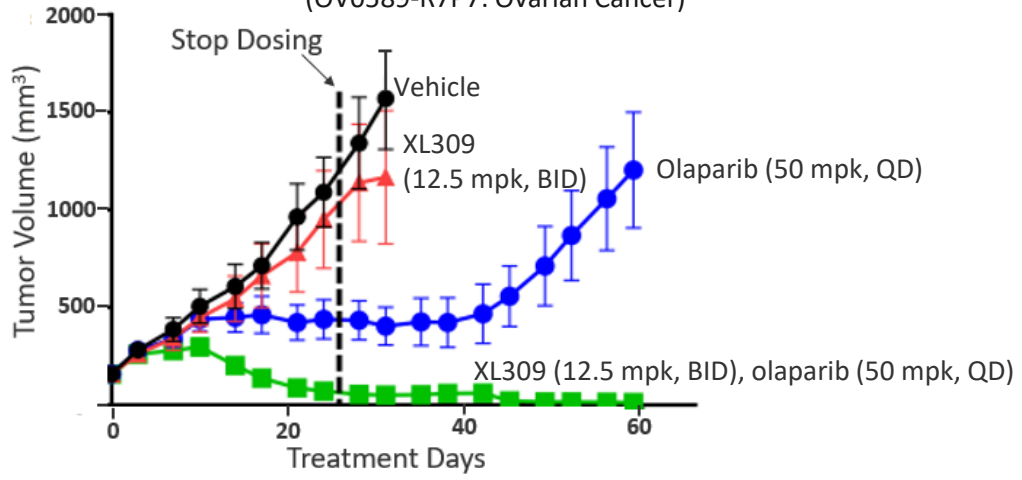
Anti-Tumor Activity with XL309 in BRCA-mt & BRCA-wt Xenografts

BRCA1-mutant

BRCA1-mutant Xenograft Model
(MDA-MB-436: Triple Negative Breast Cancer)

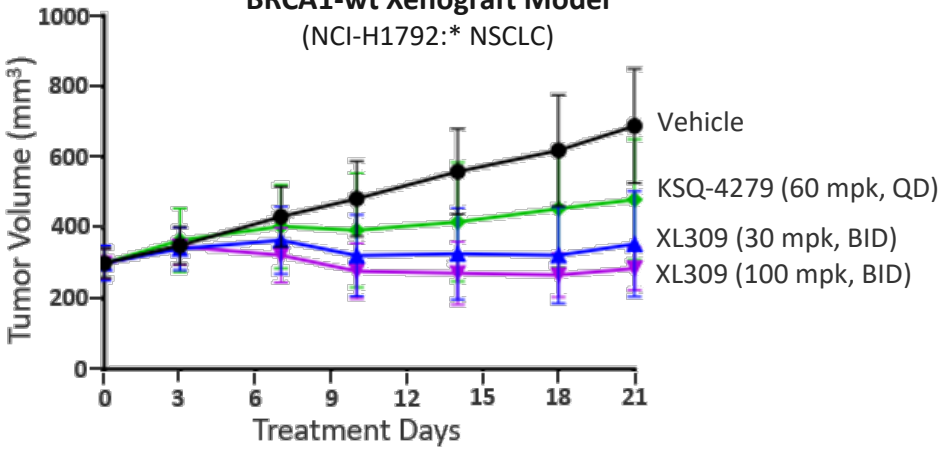


BRCA1-mutant Patient-Derived Xenograft Model
(OV0589-R7P7: Ovarian Cancer)

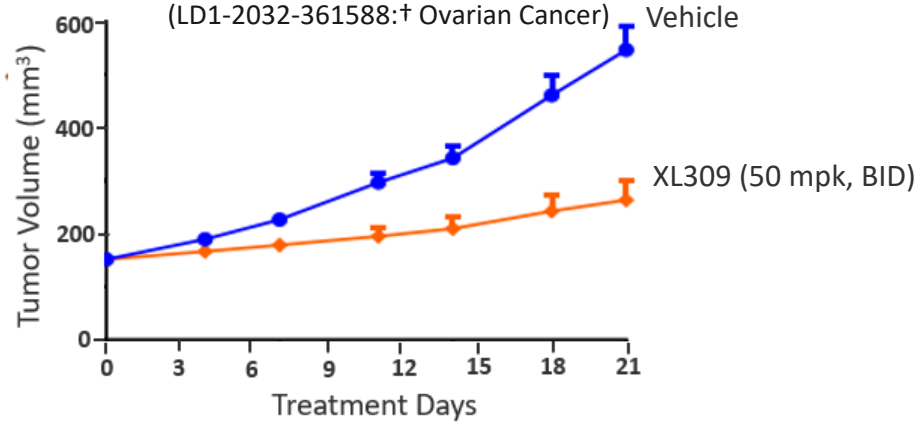


BRCA1-wt

BRCA1-wt Xenograft Model
(NCI-H1792:* NSCLC)



BRCA1-wt, Patient-Derived Xenograft Model
(LD1-2032-361588:† Ovarian Cancer)



mt = mutant
wt = wild-type
NSCLC = non-small cell lung cancer
QD = daily dosing
BID = twice daily dosing

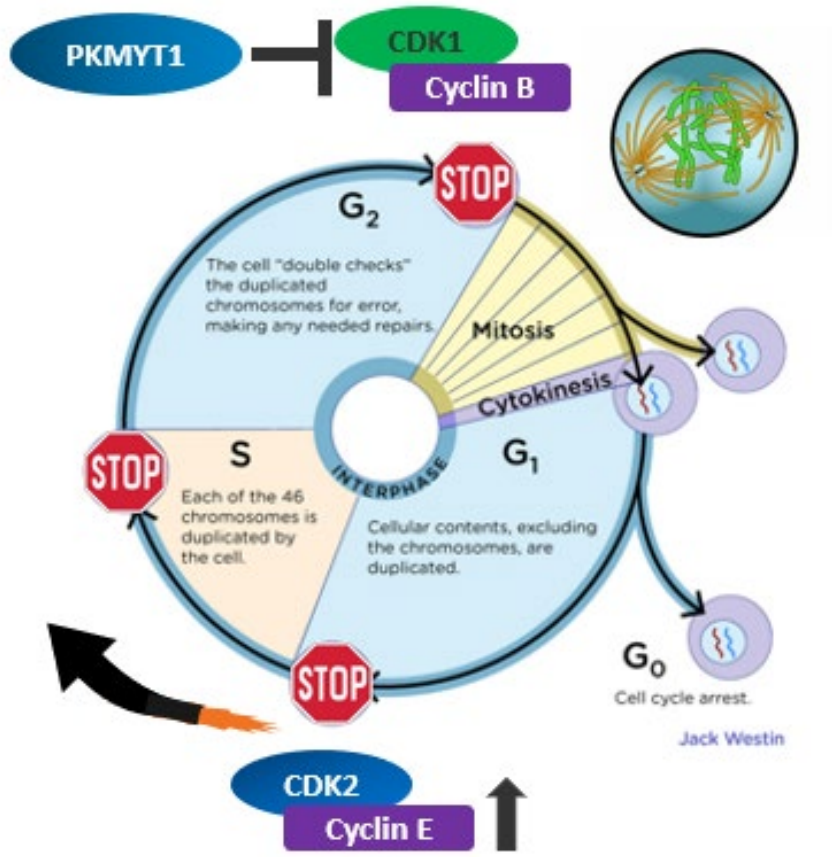
*NCI-H1792 cells are BRCA1/2-WT
†LDI-2032-361588 tumor is BRCA1-WT/BRCA2-mutant

EXELIXIS®

XL495

PKMYT1 Inhibitor

PKMYT1 Inhibition Results in Death of Cancer Cells with Unstable Genomes



PKMYT1

- PKMYT1 inhibits CDK1, preventing mitotic entry for damaged genomes
- Increased Cyclin E levels cause genome instability and DNA damage across a wide range of tumors including ovarian, endometrial, and colorectal
- Inhibition of PKMYT1 in cancer cells with high Cyclin E allows mitosis before completion of DNA synthesis, with catastrophic consequences
  - Synthetic lethality with CCNE1 amplification, or mutations in FBXW7 or PPP2R1A

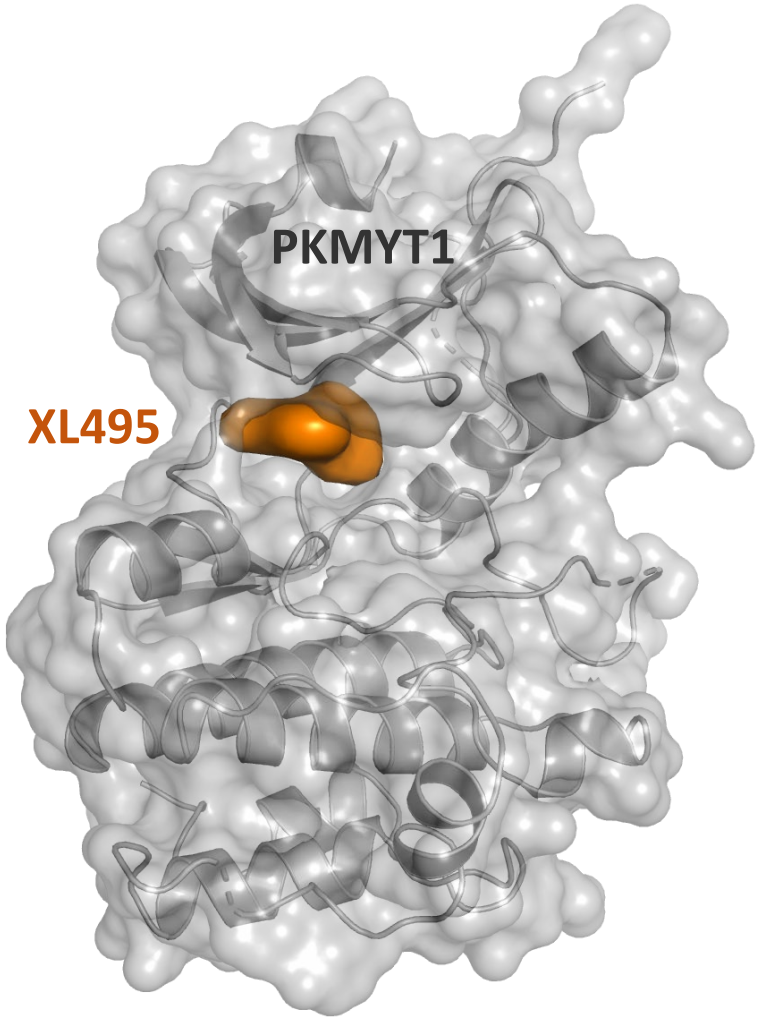
Incidence

- CCNE1 amplification: 40% uterine sarcomas, 15-20% ovarian cancers,~10% endometrial, esophageal and stomach cancers
- FBXW7 mutation: 38% uterine sarcomas, 15-20% endometrial cancers, and 15% colorectal cancers
- PPP2R1A mutation: ~8% of endometrial cancers

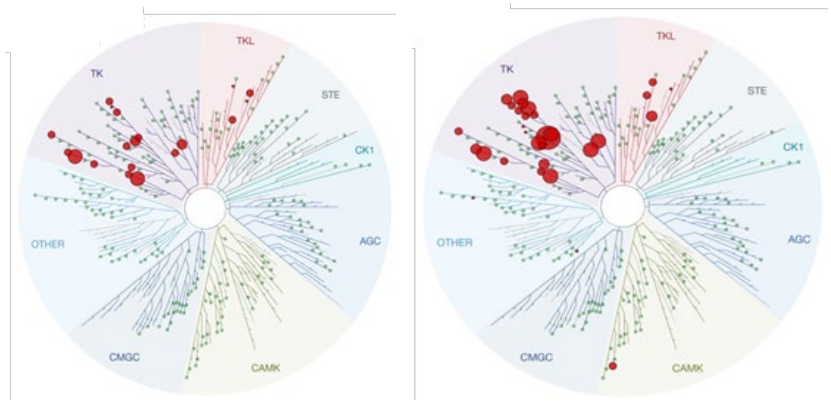
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
FBXW7 = F-Box And WD Repeat Domain Containing 7 gene
PPP2R1A = Protein Phosphatase 2 Scaffold Subunit A alpha gene
CDK1 = cyclin-dependent kinase 1
CCNE1 = Cyclin E1 gene

Cell Cycle Image: https://jackwestin.com/

XL495: A Potent Inhibitor of PKMYT1 with Best-in-Class Potential



Potency / Parameter	XL495	RP-6306
Cellular TE EC_{50} (nM)	16	2
Cellular pCDK1 IC_{80} (nM)	340	73
In vivo PD (pCDK1 EC_{75}, nM)	340	180
Kinome selectivity	19/374	30/374
Hepatocyte stability (human)	8% liver blood flow	56% liver blood flow
Predicted human $t_{1/2}$	17 h	2 h
Solubility pH 6.8 (mg/mL)	0.51	0.014
Oral bioavailability (rat)	76%	38%



Kinases inhibited at 100x cellular TE EC_{50}

PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
IC = inhibitory concentration
EC = effective concentration
PD = pharmacodynamics
pCDK1 = phospho-cyclin-dependent kinase 1

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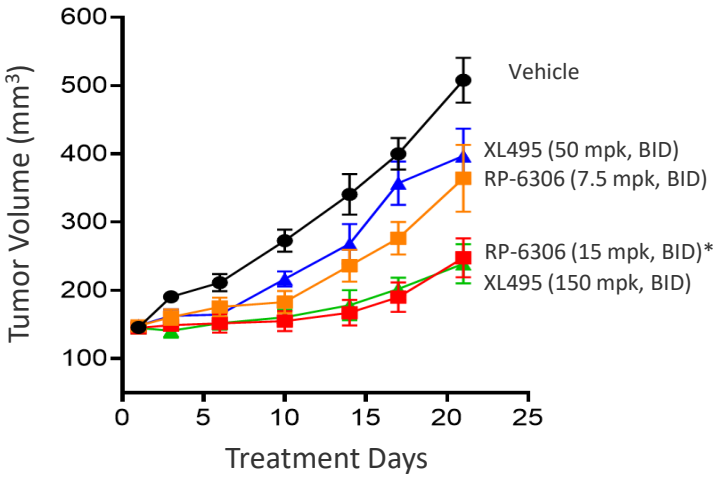
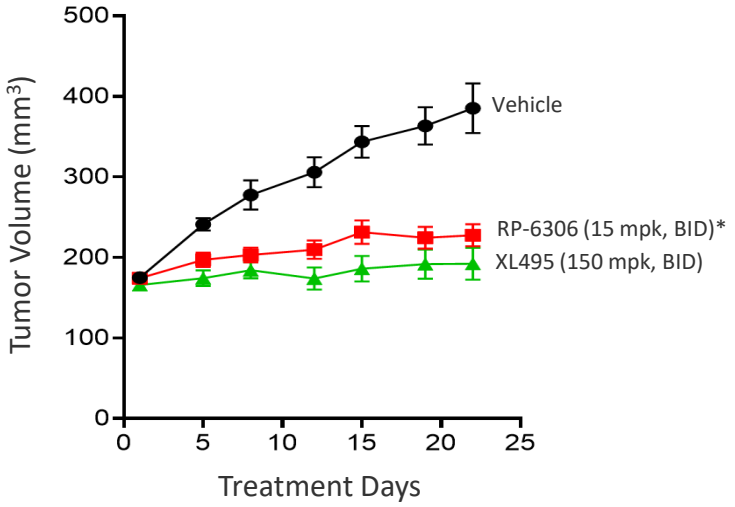
XL495: Comparable or Better Efficacy vs RP-6306 *In Vivo*

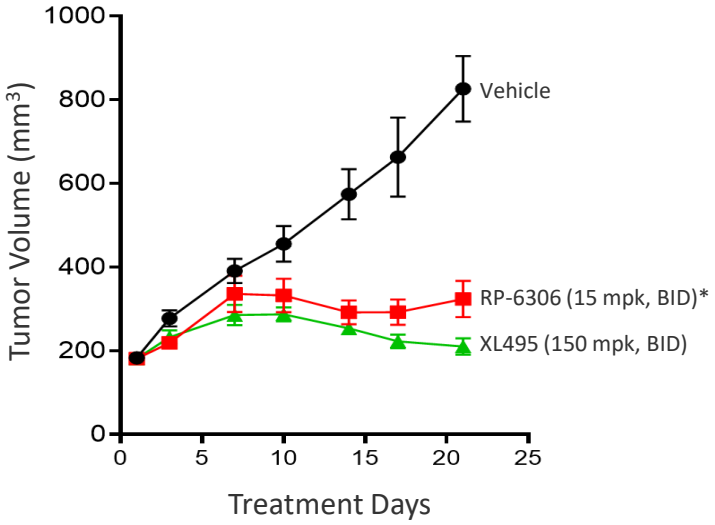
CCNE1 Amplified Mouse Xenograft
(HCC1569 - Primary Ductal Breast Carcinoma)



FBXW7 Mutated Mouse Xenograft
(SW837 – Colorectal Adenocarcinoma)



FBXW7 Mutated Mouse Xenograft
(SW1463 – Colorectal Adenocarcinoma)



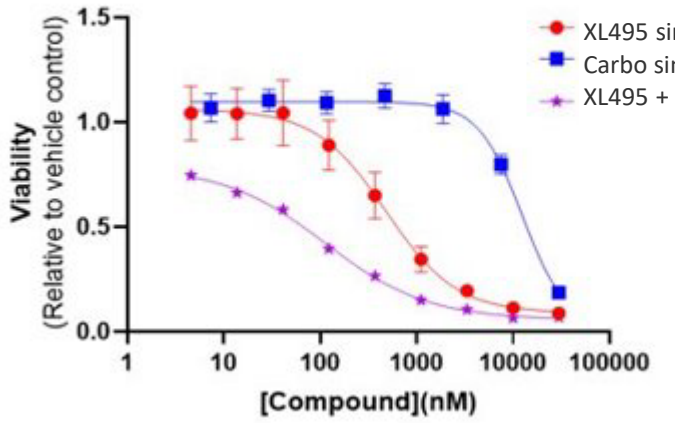
* RP-6306 not tolerated at 30 mpk BID

- XL495 is predicted to have **significantly improved pharmacokinetics** in humans
- Dose projections in humans predict complete target coverage with **once-daily dosing** of XL495

FBXW7 = F-Box And WD Repeat Domain Containing 7 gene
CCNE1 = Cyclin E1 gene
BID = twice daily dosing

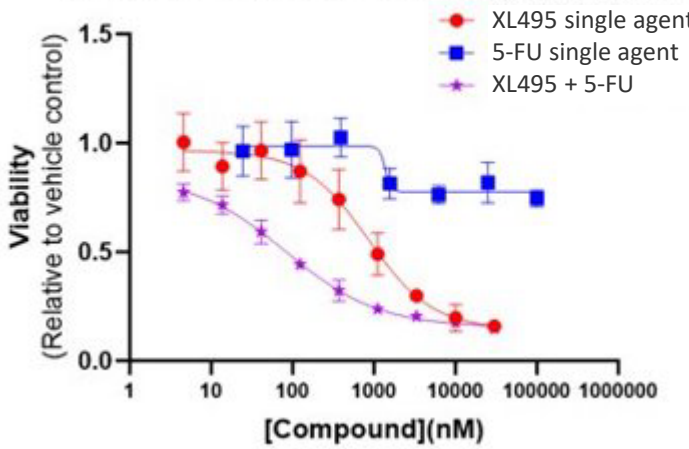
XL495 Demonstrates High Potential for Combination Therapy

XL495 in Combination with Carboplatin



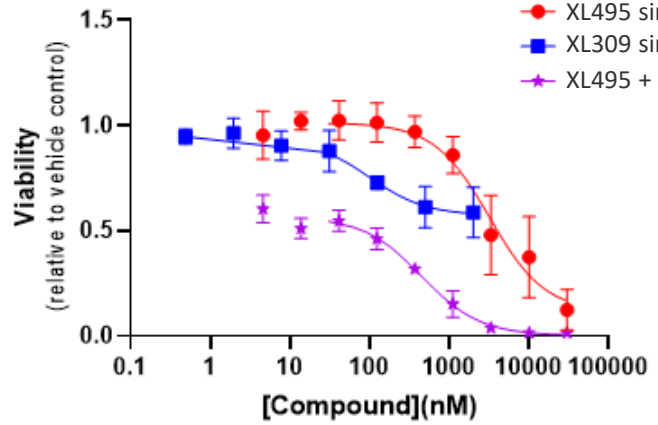
HCC1569
CCNE1-amp

XL495 in Combination with 5-Fluorouracil



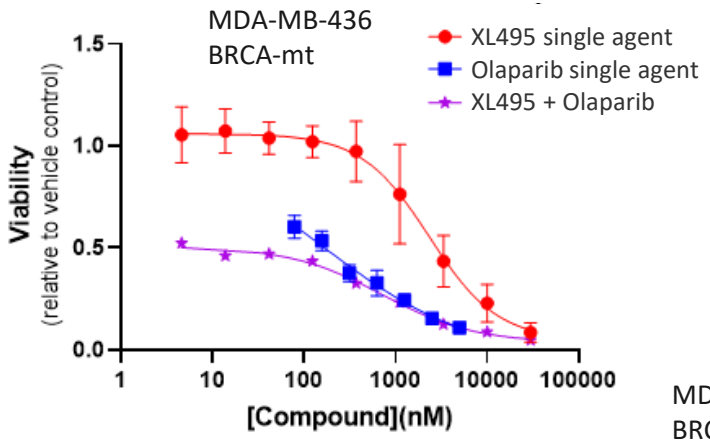
HCC1569
CCNE1-amp

XL495 in Combination with XL309 (USP1i)



MDA-MB-436
BRCAmt

XL495 in Combination with Olaparib



MDA-MB-436
BRCAmt

USP1i = ubiquitin-specific protein 1 inhibition
CCNE = Cyclin E gene
mt = mutant

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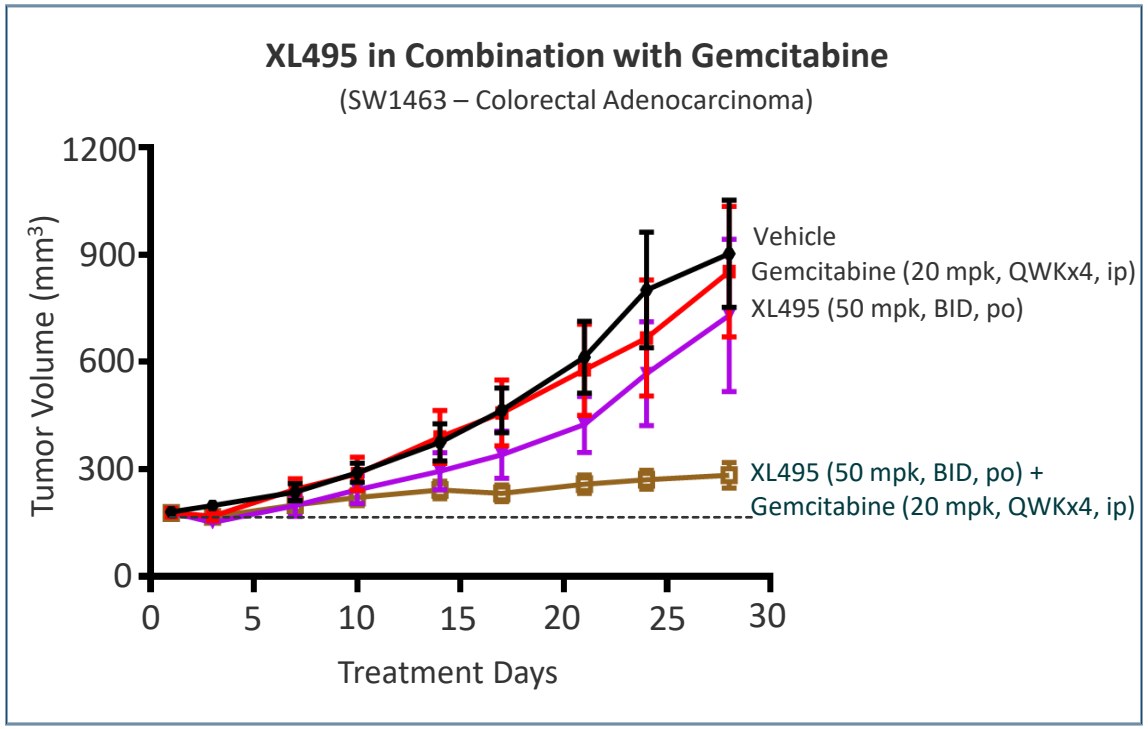
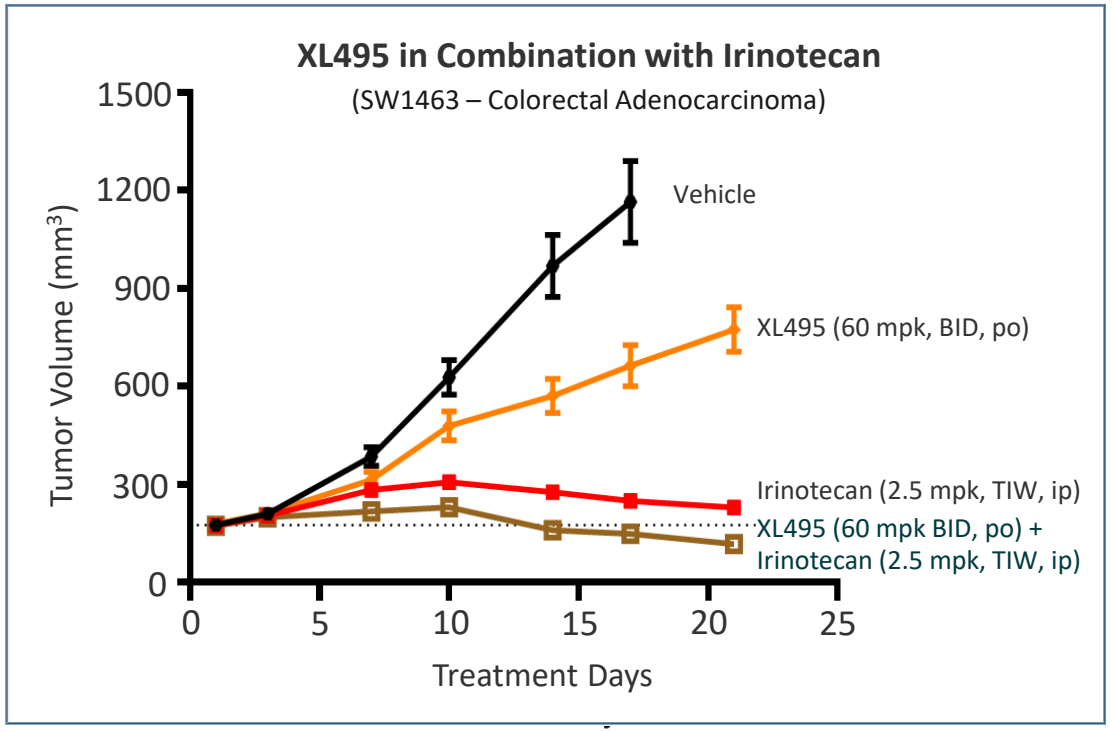
XL495 is Active in Combination with Gemcitabine & Irinotecan *In Vivo*





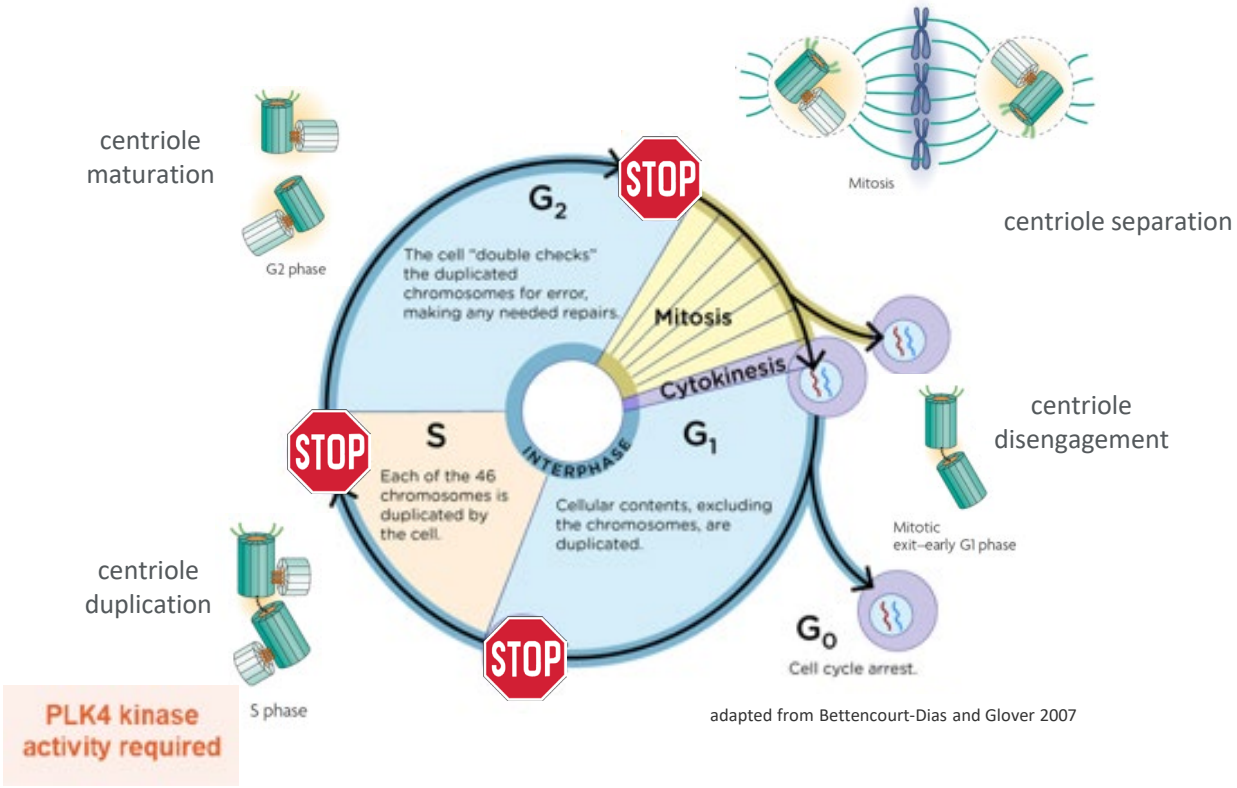
Selectivity and PK will drive differentiation of XL495 as a superior combination partner

PK = pharmacokinetics
BID = twice daily dosing
TIW = three times per week dosing
QWKx4 = once-weekly for 4 weeks dosing

EXEL-7871

PLK4 Inhibitor

PLK4 Inhibitors: Synthetic Lethality with TRIM37 Amplification



adapted from Bettencourt-Dias and Glover 2007

PLK4

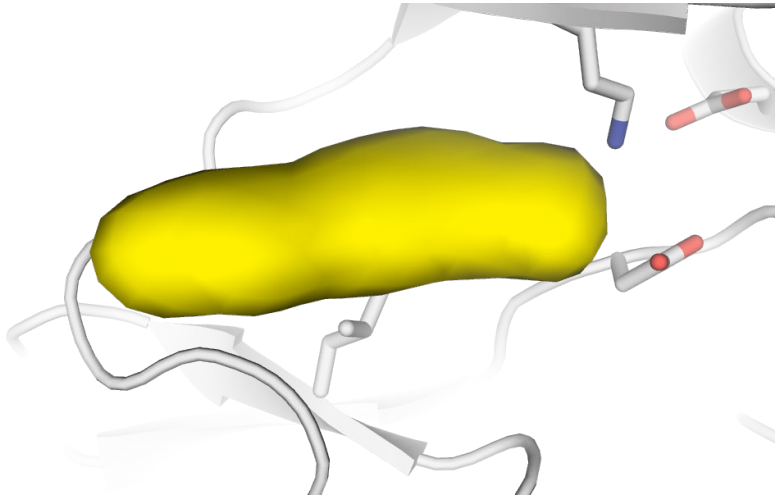
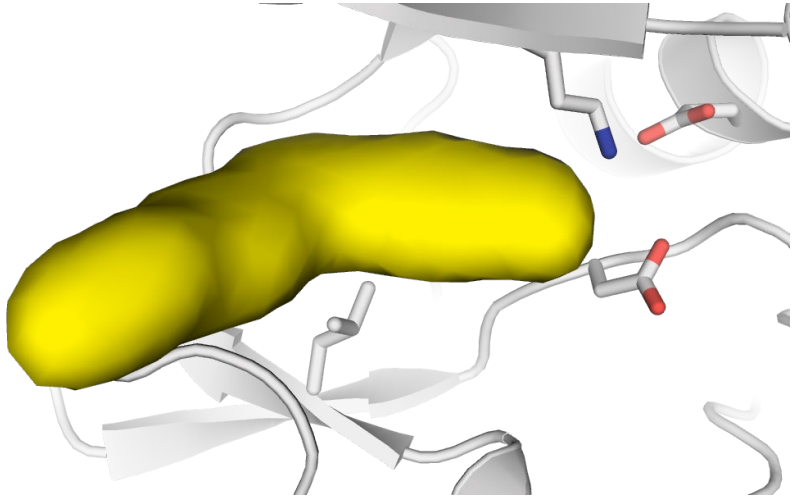
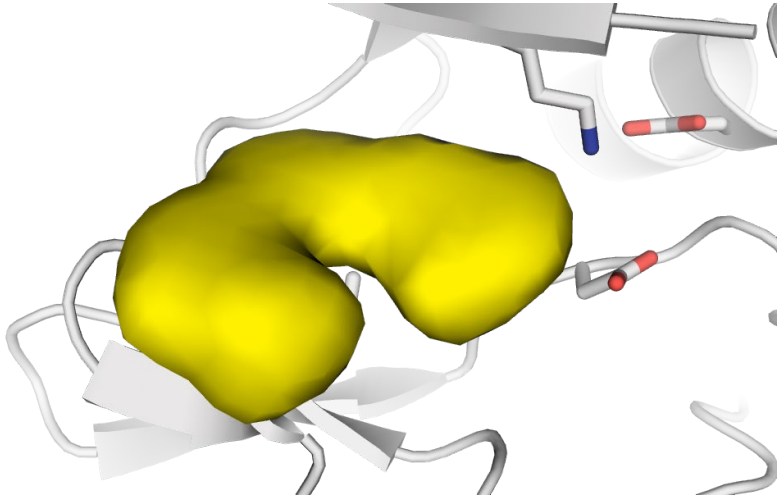
- PLK4 is a cell-cycle kinase that controls centriole duplication during S-phase
- Without centriole duplication, cell division occurs with delayed, acentrosomal spindle assembly that is highly reliant on pericentriolar material (PCM)
- TRIM37 amplification reduces PCM and inhibits acentrosomal spindle assembly, which leads to mitotic catastrophe when PLK4 is inhibited

TRIM37 is amplified in a significant proportion of neuroblastoma, breast, and lung tumors

PLK4 = polo-like kinase 4
TRIM37 = Tripartite Motif Containing 37 gene

Cell Cycle Image: https://jackwestin.com/

Improved Potency & Selectivity with Structure-based Scaffold Evolution

	Compound A (2.35 Å)	Compound B (2.53 Å)	Compound C (2.6 Å)
			
PLK 4 Cellular Assay (EC_{50})	>20,000 nM	6090 nM	74 nM

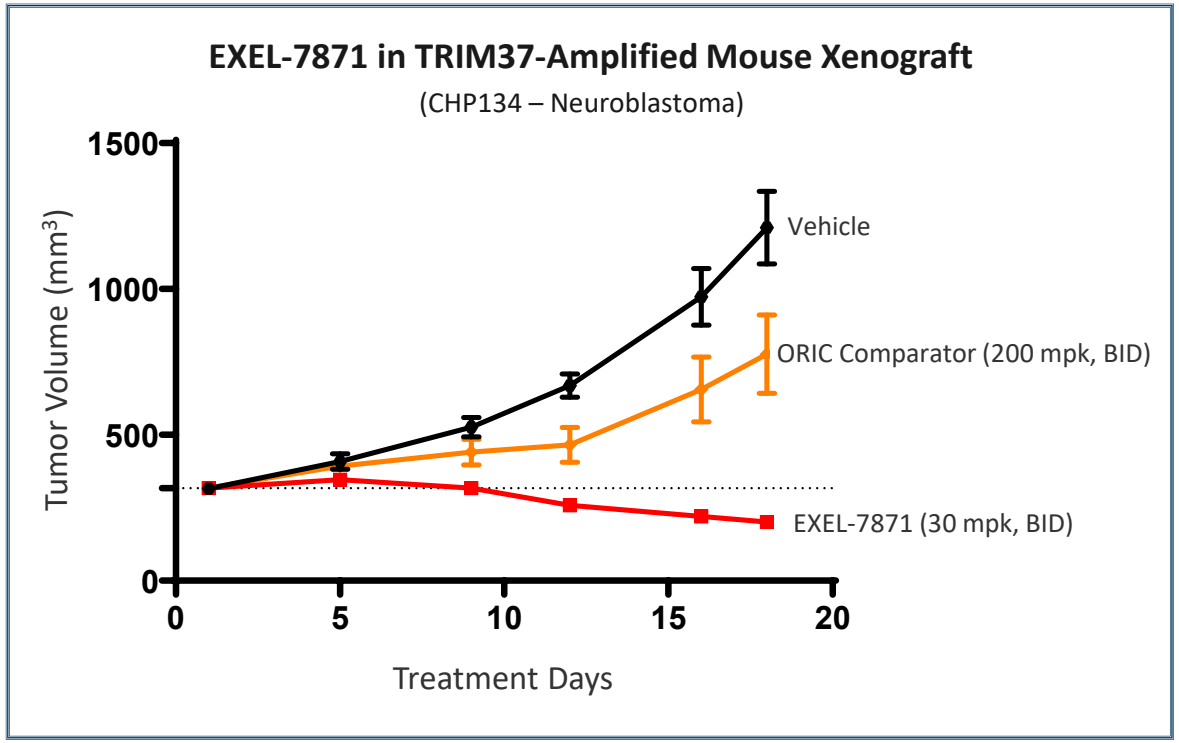
High impact of structure-enabled design and rapid library construction

PLK4 = polo-like kinase 4
EC50 = half maximal effective concentration

EXEL Lead Compounds Demonstrate Favorable Properties for Advancement

Potency / Parameter	EXEL-7871	EXEL-0067	ORIC Comparator
PLK4 IC_{50}[1], nM	8.3	3.8	2.0
Aurora B IC_{50}[1], nM	620	> 16,000	380
Cellular TE EC_{50}[2], nM	55	66	380
TRIM37 amplified viability EC_{50}[3], nM	93	100	360
Ratio: Viability EC_{50} Non-TRIM37 amplified[4]/ EC_{50} TRIM37 amplified	> 54	38	5.5

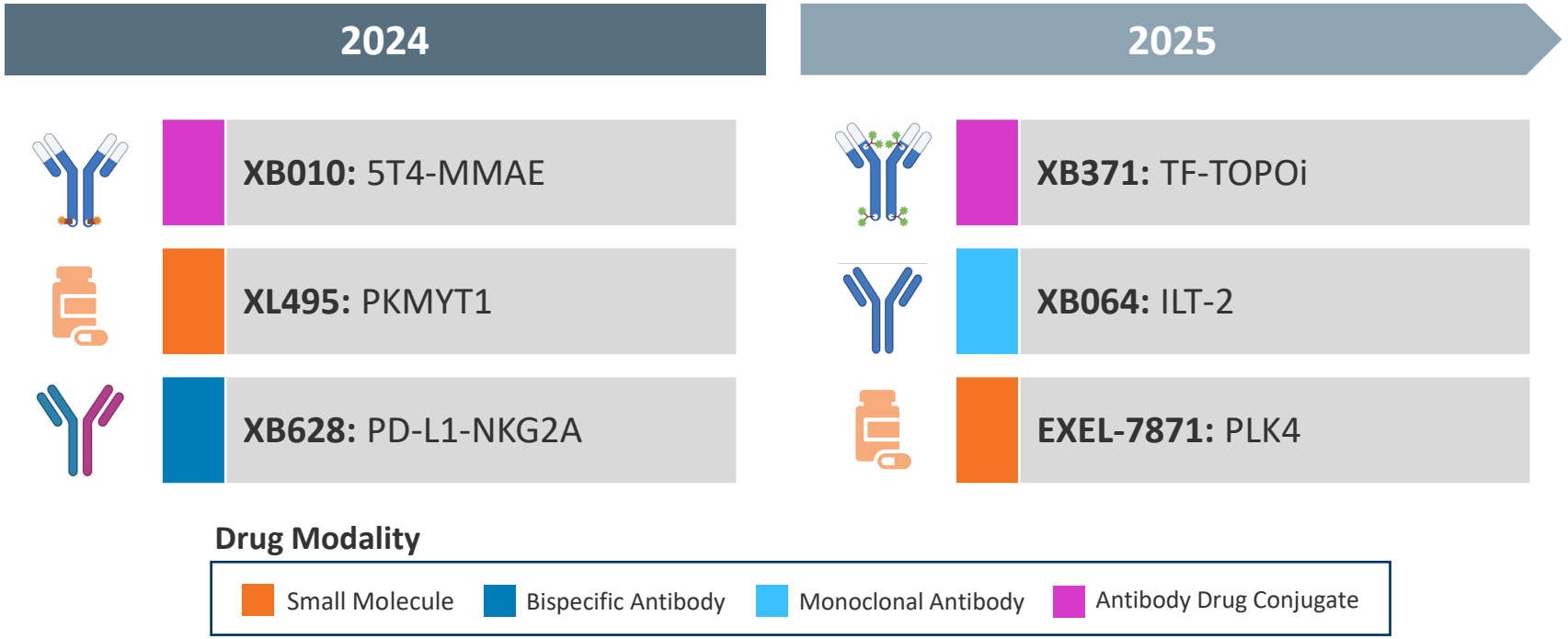
[1] Biochemical assay measuring ATP to ADP conversion, [2] Cellular NanoBRET™ target engagement, [3] Viability in CHP-134 cells, [4] Viability in MDA-MB-231 cells



PLK4 = polo-like kinase 4
EC50 = half maximal effective concentration
TRIM37 = Tripartite Motif Containing 37 gene
IC50 = half maximal inhibitory concentration

EXELIXIS®

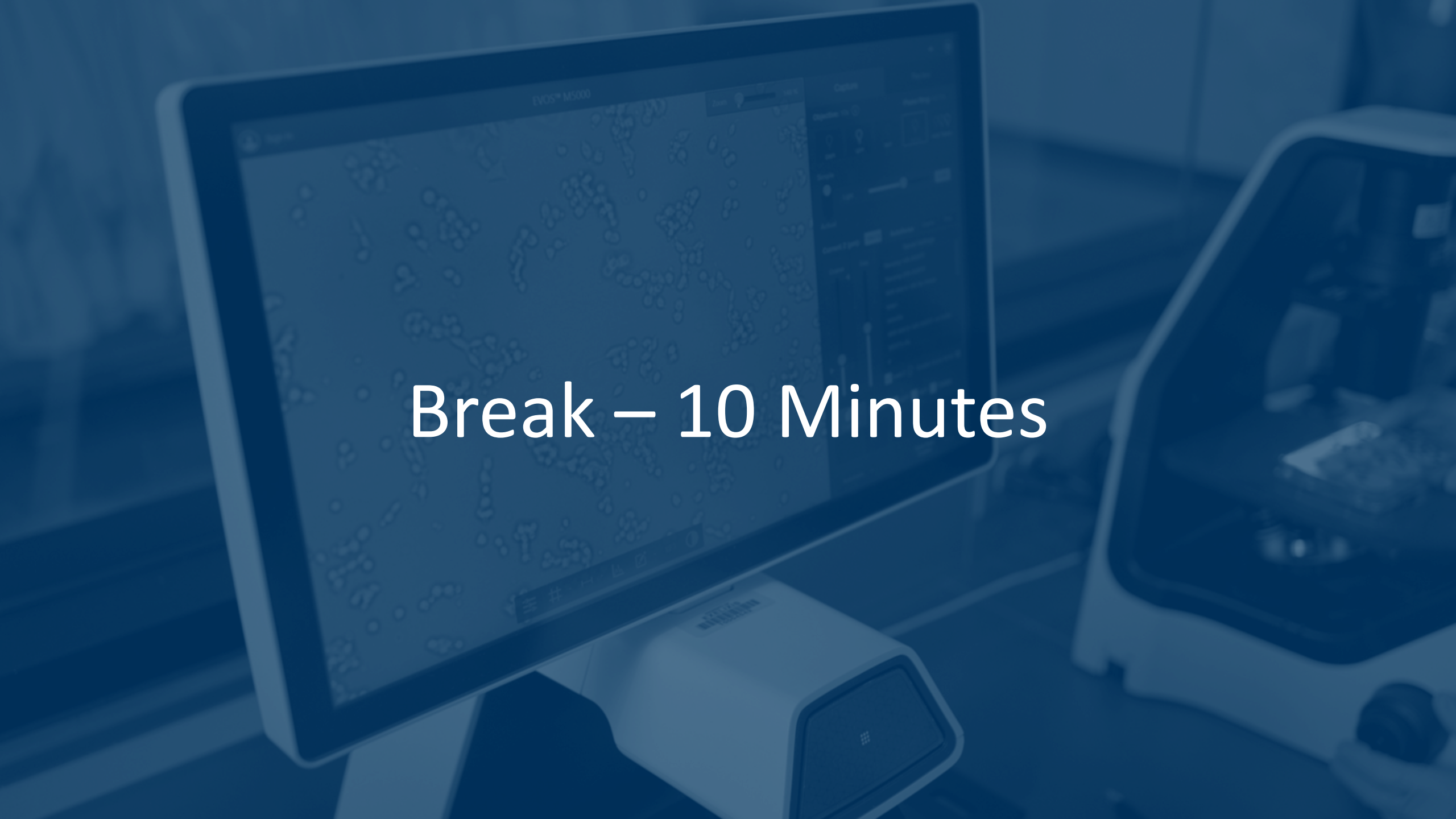
Productive Discovery Engine Has Created a Deep IND Pipeline



Consistent flow of development candidates targeting 2 INDs/year

Generating portfolio of molecules, all with potential for clinical differentiation

MMAE = monomethyl auristatin E
TF = tissue factor
ILT-2 = Ig-like transcript 2
IND = Investigational New Drug application
PKMYT1 = protein kinase membrane associated tyrosine/threonine 1
PD-L1 = programmed death-ligand 1
NKG2A = natural killer cell receptor group 2A
PLK4 = polo-like kinase 4
TOPOi = topoisomerase inhibitor



Break – 10 Minutes

Zanzalintinib

Single Agent Activity, with a Favorable Tox Profile

Zanzalintinib is a Next Generation TKI that Builds on CABO's Key Strengths, Aiming to Deliver an Improved Benefit/Risk Profile for Patients

CABOMETYX® (cabozantinib) tablets

Zanzalintinib builds on and enhances cabozantinib's key drivers of commercial success, aiming to deliver an improved benefit/risk profile for patients

- **Cabozantinib knowledge and experience** has guided zanzalintinib development
- Retains the target kinases of cabozantinib, paired with an optimized pharmacokinetic profile, aiming to deliver **differentiated tolerability and QOL for patients, without sacrificing on strong efficacy**
- Improved benefit/risk profile has potential to position zanzalintinib as the **TKI combination partner of choice**

TKI = tyrosine kinase inhibitor
QOL = quality of life
IO = immunotherapy
1L = first-line
aRCC = advanced renal cell carcinoma
OS = overall survival

Source: IQVIA BrandImpact April 2023

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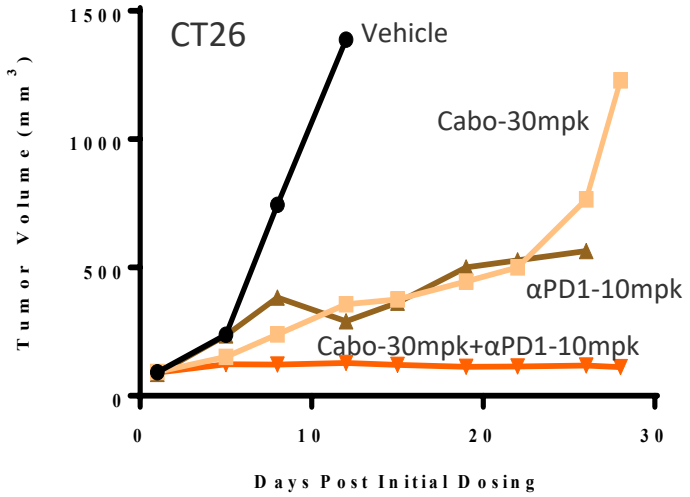
Target Profile Comparison: Zanzalintinib vs Cabozantinib

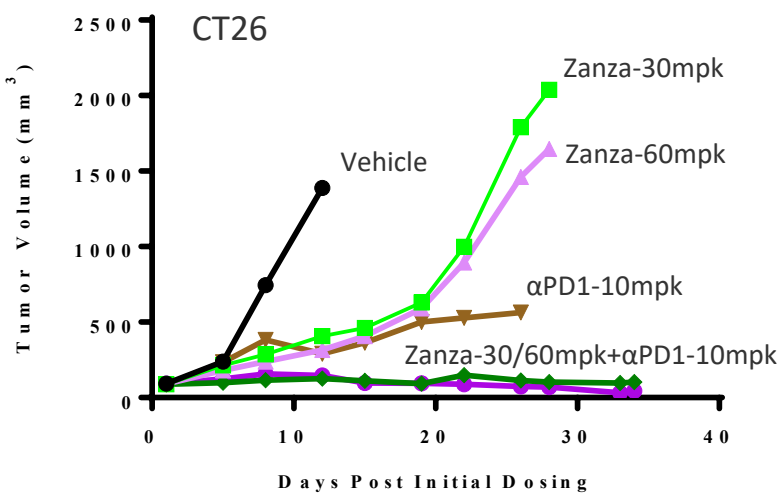
Zanza and cabo are potent ATP-competitive inhibitors of MET, VEGFR2, AXL and MER

Comparative testing on 430 kinases shows very similar broad profile

Cabozantinib +/- PD-1



Zanzalintinib +/- PD-1



- Preclinical tumor models: PK/PD and efficacy profiles reflect **faster clearance** of zanza
- **Altered ADME profile** of zanza may translate to further differentiation of PK/PD in tumors vs normal tissue, potentially leading to **improved benefit/risk profile** for zanza

ATP = adenosine triphosphate
PD-1 = programmed cell death protein 1
PK = pharmacokinetics
PD = pharmacodynamics
ADME = absorption, distribution, metabolism and excretion

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IKCS: NORTH AMERICA
INTERNATIONAL KIDNEY CANCER SYMPOSIUM

Zanzalintinib (XL092) in Clear Cell Renal Cell Carcinoma: Results From STELLAR-001

Sumanta Pal, MD, FASCO
Professor, Department of Medical Oncology & Therapeutics Research
City of Hope Comprehensive Cancer Center, Duarte, CA, USA

On behalf of Jacques Medioni,[1] Guillermo De Velasco,[2] Jaime Merchan,[3] Andrea B. Apolo,[4] Yohann Loriot,[5] Zhong Wang,[6] Mamata Singh,[6] Yijia Wang,[6] Chung-Han Lee[7]

*[1]APHP Hôpital Européen Georges Pompidou, Paris, France; Université Paris Cité, Paris, France; [2]Hospital Universitario 12 de Octubre, Madrid, Spain; [3]University of Miami Miller School of Medicine, Miami, FL, USA; [4]National Cancer Institute, Bethesda, MD, USA; [5]Institut de Cancérologie Gustave Roussy, Villejuif, France; [6]Exelixis, Inc., Alameda, CA, USA; [7]Memorial Sloan Kettering Cancer Center, New York, NY, USA**
**Affiliation where the work was conducted; current affiliation: Exelixis, Inc., Alameda, CA, USA*

Zanzalintinib and Renal Cell Carcinoma

IKCS: NORTH AMERICA
INTERNATIONAL KIDNEY CANCER SYMPOSIUM

- Vascular endothelial growth factor receptor (VEGFR)-targeted tyrosine kinase inhibitors (TKIs) such as cabozantinib are a standard of care for advanced renal cell carcinoma (RCC)[1,2]
- Zanzalintinib (XL092) is a novel, multi-targeted TKI that inhibits kinases including VEGFR, MET, and the TAM kinases (TYRO3, AXL, MER) with a short half-life, which may result in improved tolerability[3]
  - VEGFR, MET, and the TAM kinases are involved in tumor growth, angiogenesis, and immunosuppression within the tumor microenvironment[4,5]
  - Targeting MET and the TAM kinases in addition to VEGFR may prevent resistance to VEGFR inhibition[4,5]
- Here, we present preliminary efficacy and safety results of single-agent zanzalintinib from the STELLAR-001 clear cell RCC expansion cohort

1. Rathmell KW, et al. *J Clin Oncol*. 2022;40(25):2957–95. 2. Powles T, et al. *Ann Oncol*. 2021;32(12):1511–19. 3. Hsu J, et al. *Mol Cancer Ther*. 2023;22(2):179–91. 4. Choueiri TK, et al. *Lancet Oncol*. 2016;17(7):917–27. 5. Bergerot P, et al. *Mol Cancer Ther*. 2019;18(12):2185-93.

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STELLAR-001: Key Eligibility and Endpoints in ccRCC Expansion Cohort

Single-Agent Dose Escalation Cohorts (n=49)

- Inoperable, locally advanced, metastatic, or recurrent solid tumor treated with zanzalintinib 10–140 mg QD

Recommended Dose: Zanzalintinib 100 mg QD[1,a]

ccRCC Expansion Cohort (N=32)

- Advanced, metastatic, or recurrent RCC with a clear cell histology (sarcomatoid features permitted)
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1
- Received 1–3 prior systemic anticancer therapies

Safety Population N=81

- **Primary Endpoints:** ORR and PFS rate at 6 months per RECIST v1.1 by investigator
- **Secondary Endpoint:** Safety
- **Exploratory Endpoints:** PFS and DOR per RECIST v1.1 by investigator; OS

1. Sharma M, et al. *Ann Oncol.* 2022;33(7_suppl):Abstract 481P. [a]Treatment until lack of clinical benefit or unacceptable toxicity; treatment post-progression allowed if there was clinical benefit per the investigator.

ccRCC = clear cell renal cell carcinoma
QD = once-daily dosing
ORR = objective response rate
PFS = progression-free survival
DOR = duration of response
OS = overall survival
RECIST = Response Evaluation Criteria In Solid Tumors

Baseline Characteristics for Patients in ccRCC Cohort

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Characteristics, n (%)	ccRCC Cohort (N=32)
Age, median (range), years	64 (39–79)
Male	23 (72)
ECOG PS	
0	16 (50)
1	16 (50)
IMDC risk	
Favorable	4 (13)
Intermediate	26 (81)
Poor	2 (6)
Sarcomatoid component	5 (16)
Sites of metastasis	
Liver	12 (38)
Lung	20 (63)
Lymph node	19 (59)
Bone	11 (34)
Number of metastatic sites[a]	
1	3 (9)
2	8 (25)
≥3	21 (66)

Characteristics, n (%)	ccRCC Cohort (N=32)
Number of prior therapy lines, median (range)	2 (1–3)
1	5 (16)
2	14 (44)
≥3	13 (41)
Prior ICI	31 (97)
Prior VEGFR-TKI	26 (81)
Cabozantinib	17 (53)
Axitinib	8 (25)
Sunitinib	8 (25)
Pazopanib	6 (19)
Best response to last systemic anti-cancer therapy	
PR	3 (9)
SD	16 (50)
PD	11 (34)
Prior nephrectomy	22 (69)

Data cutoff: June 10, 2023. [a]Total number of distinct target and nontarget sites at baseline.

ccRCC = clear cell renal cell carcinoma
ICI = immune checkpoint inhibitor
TKI = tyrosine kinase inhibitor
PR = partial response
SD = stable disease
PD = progressive disease
IMDC = International Metastatic RCC Database Consortium

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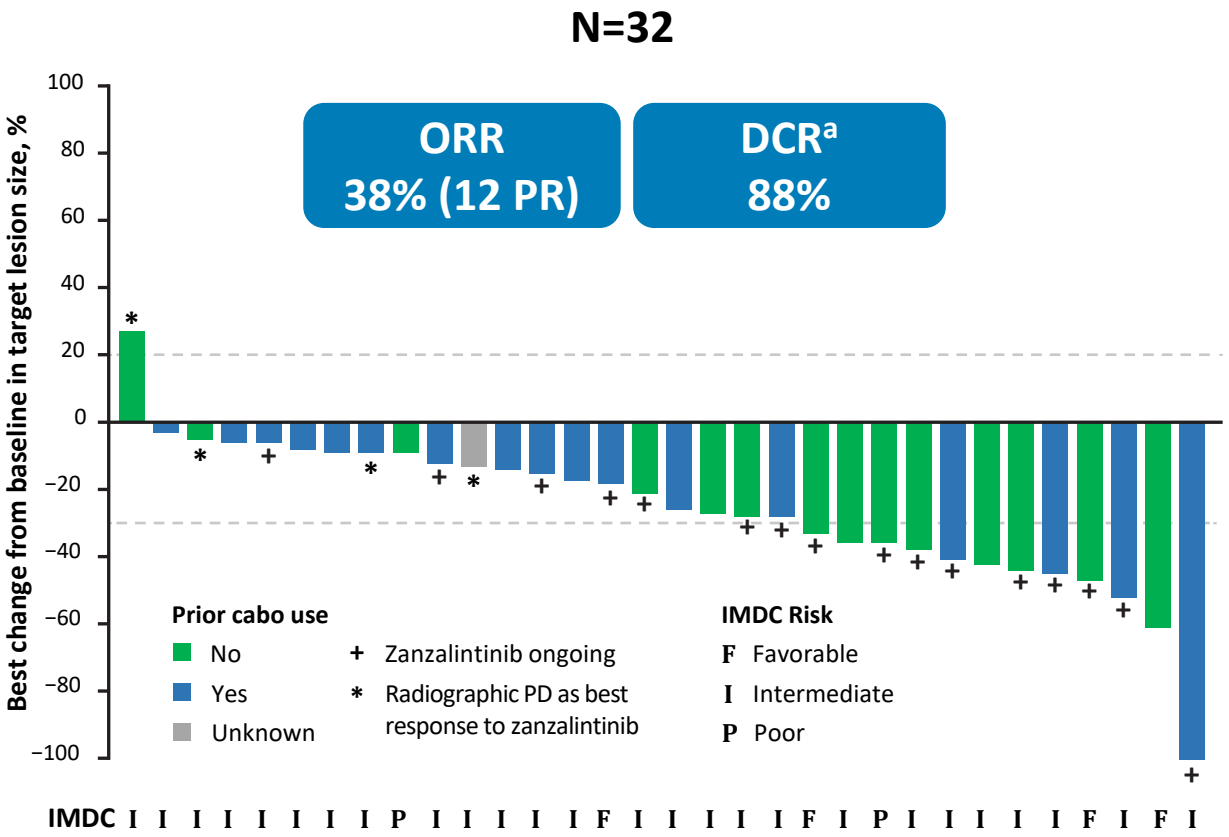
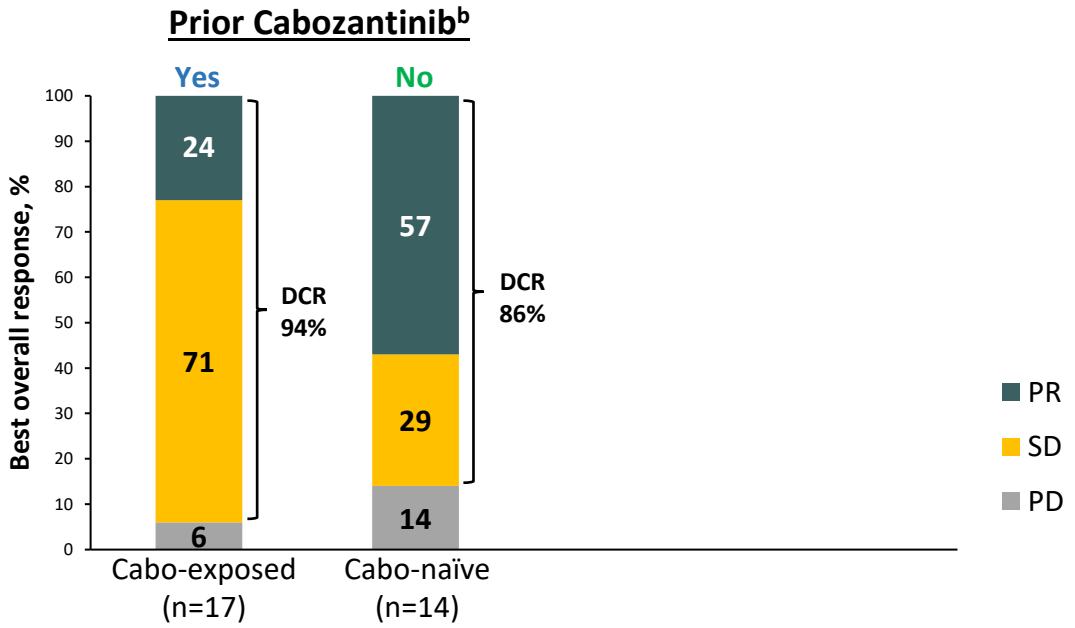
Best Response in ccRCC Cohort to Zanzalintinib





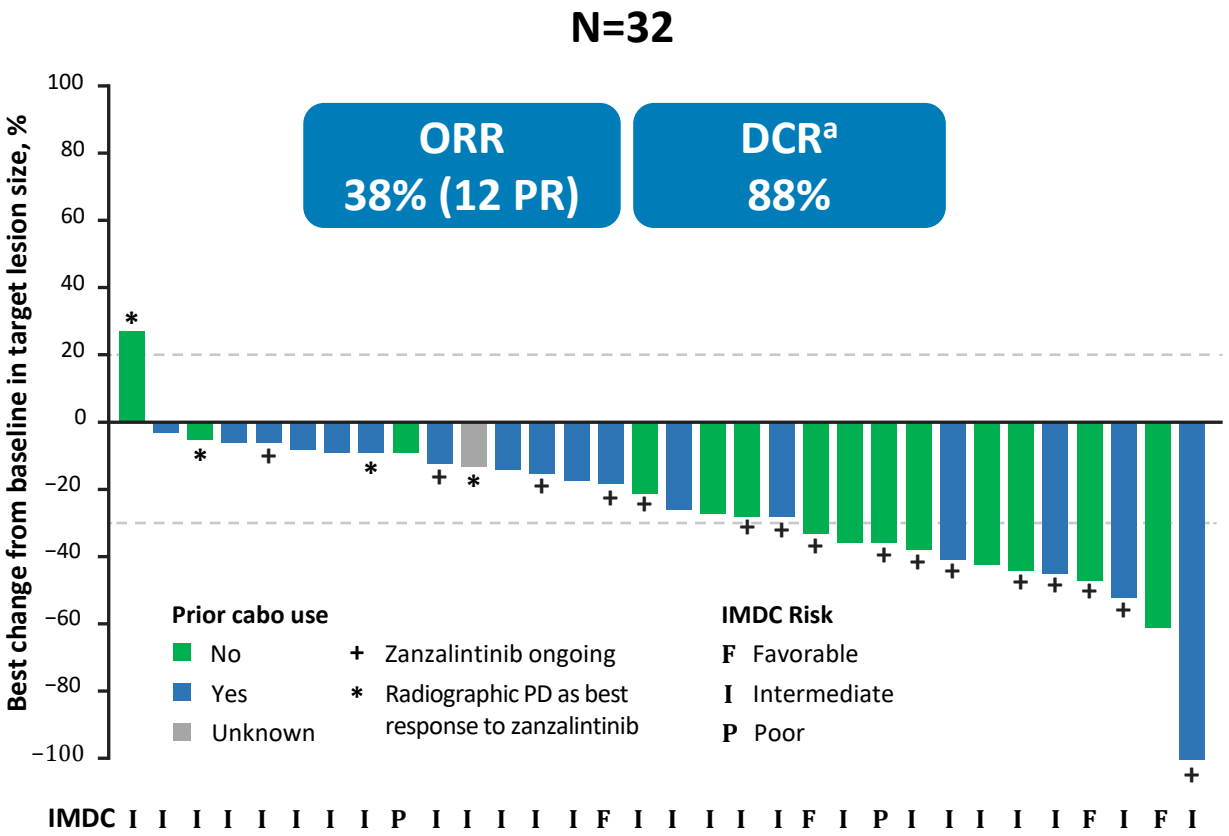
- Of the 6 patients with no prior TKI exposure, 3 were responders (50%).
- Three of the four cabo-exposed patients who responded to zanzalintinib had discontinued prior cabozantinib due to disease progression

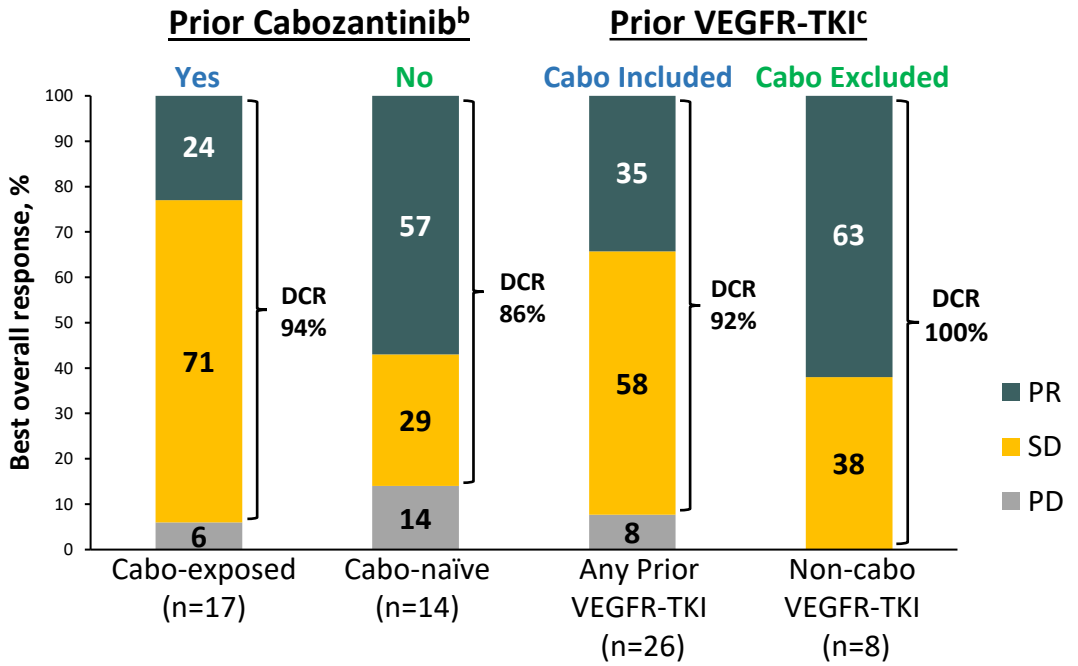
Data cutoff: June 10, 2023.

[a]DCR is defined as proportion of patients with a best overall response of confirmed CR/PR or any single best response of SD. [b]Cabo exposure was unknown for 1 patient.

ccRCC = clear cell renal cell carcinoma
ORR = objective response rate
DCR = disease control rate
TKI = tyrosine kinase inhibitor
SD = stable disease
PD = progressive disease
PR = partial response
CR = complete response
IMDC = International Metastatic RCC Database Consortium

Best Response in ccRCC Cohort to Zanzalintinib





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- Three of the four cabo-exposed patients who responded to zanzalintinib had discontinued prior cabozantinib due to disease progression

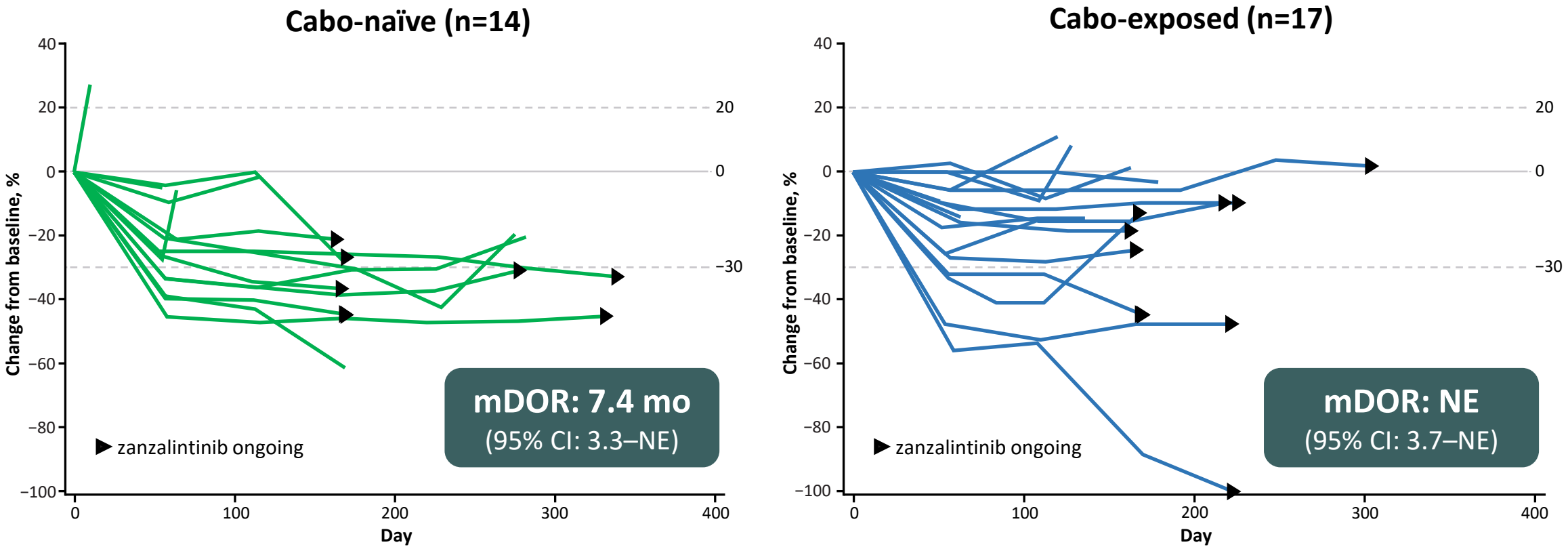
Data cutoff: June 10, 2023.

[a]DCR is defined as proportion of patients with a best overall response of confirmed CR/PR or any single best response of SD.

[b]Cabo exposure was unknown for 1 patient. [c]These subgroups are not mutually exclusive.

ccRCC = clear cell renal cell carcinoma
ORR = objective response rate
DCR = disease control rate
TKI = tyrosine kinase inhibitor
SD = stable disease
PD = progressive disease
PR = partial response
CR = complete response
IMDC = International Metastatic RCC Database Consortium

Durable Responses to Zanzalintinib in ccRCC



- At a median follow-up of 8.3 months (range: 5.7–13.7), 50% of patients were continuing treatment
- 75% of responses occurred at the first post-baseline tumor assessment, including all responders who had prior cabozantinib
- As of Sept 6, 2023, 6 of the on-going patients have been on zanzalintinib longer than their most recent prior therapy

Data cutoff: June 10, 2023.

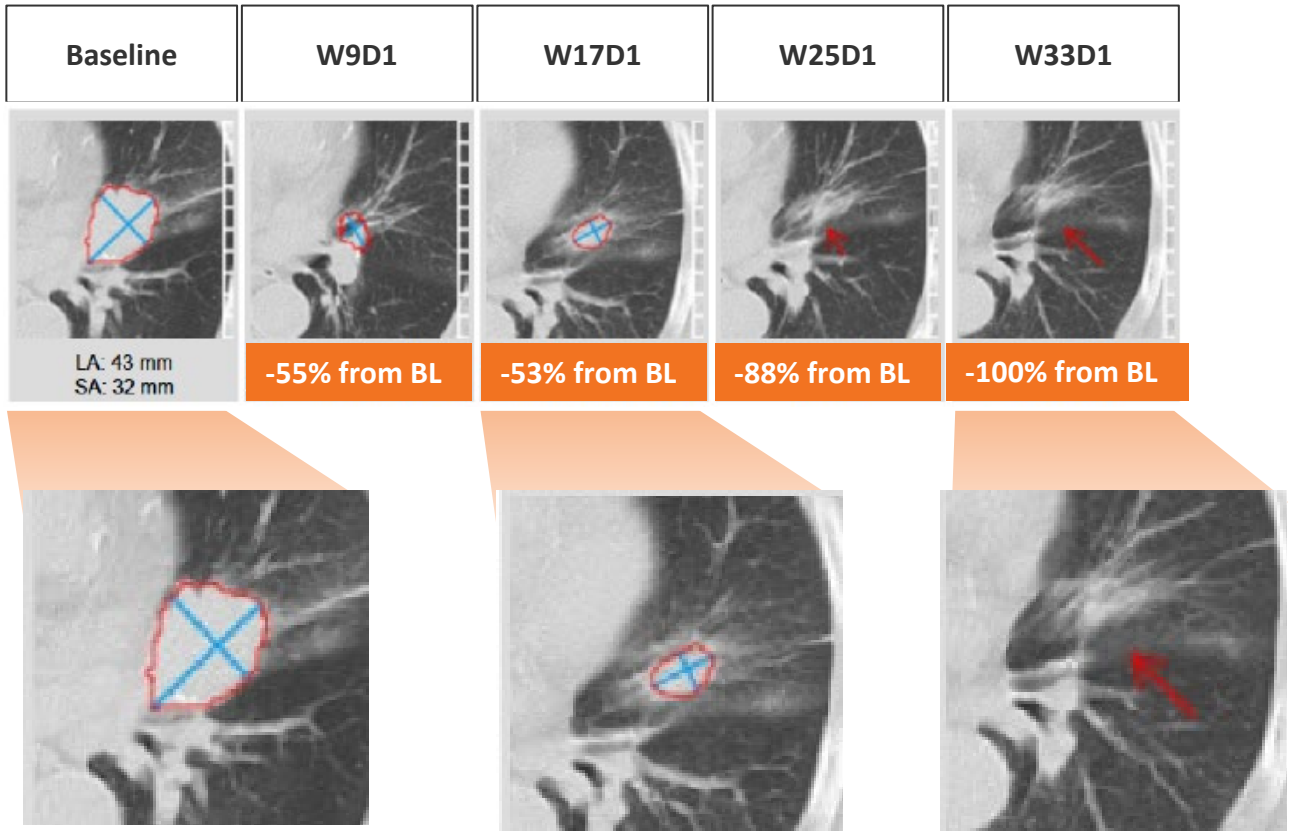
ccRCC = clear cell renal cell carcinoma
mDOR = median duration of response

Zanzalintinib Single-agent Activity in ccRCC: Case 1

- 65 year-old male, metastatic ccRCC to lung and bone 8 years following total nephrectomy
- Treatment history
  - Cabo-MK6482 (belzutifan): best response of PR; discontinued ~1 year due to toxicity
  - Nivolumab: progressed at 3 months

Started zanzalintinib 100 mg monotherapy

- Confirmed PR at 2nd post-baseline scan, bone lesions completely resolved week 25, lung lesion completely resolved week 33
- New brain lesion week 33
- No dose reductions required



Resolution of a lung target lesion from baseline to week 33

ccRCC = clear cell renal cell carcinoma
PR = partial response
BL = baseline

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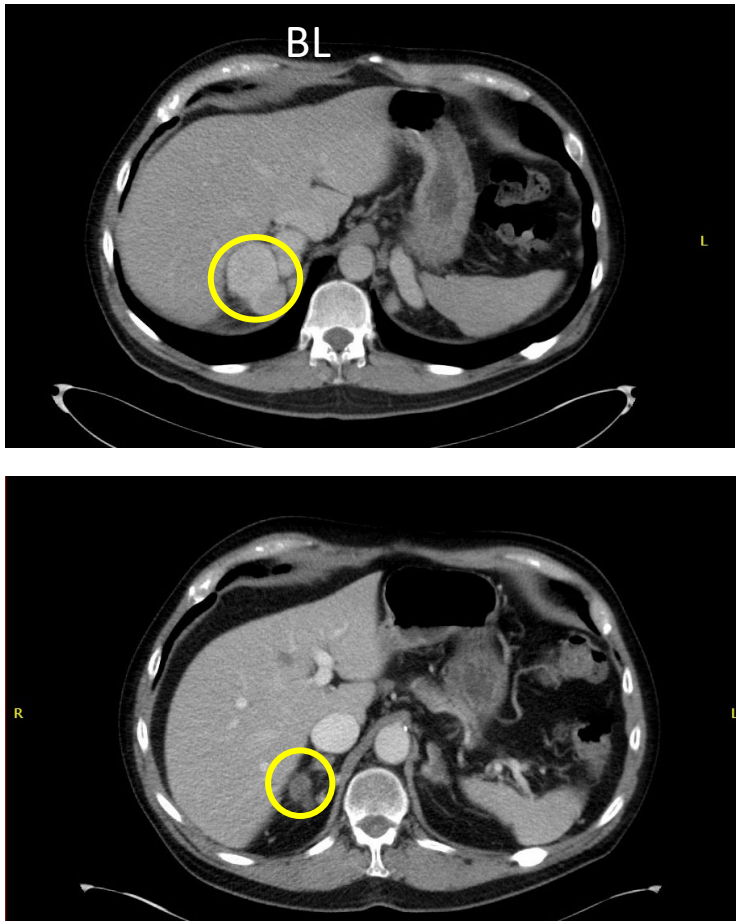
Zanzalintinib Single-agent Activity in ccRCC: Case 2

- 67-year-old male with metastatic ccRCC to right adrenal gland
- Treatment history
  - 1 year of cabo-nivo: best response SD
  - 10 months of pembro + investigational agent: best response PD

Started zanzalintinib 100 mg monotherapy

- Confirmed PR at 2nd post baseline scan
- Subsequently progressed but remains on treatment beyond PD for 77 weeks
- Dose reduction to 60 mg, then 40 mg



Reduction in size of adrenal mass from baseline to week 17

ccRCC = clear cell renal cell carcinoma
SD = stable disease
PD = progressive disease
PR = partial response
BL = baseline

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Safety Summary in 32 Patients with ccRCC

	ccRCC Cohort (N=32)
Exposure, median (range), mos	6.4 (1.0–13.2)
Grade 4 TEAE/TRAE, n (%)	1 (3) / 0
Grade 5 TEAE/TRAE, n (%)	3 (9) / 0
Dose modifications due to related AE, n (%)	
Dose reduction	16 (50)
Dose hold	22 (69)
Discontinuation due to related AE, n (%)	3 (9)

Data cutoff: June 10, 2023.

ccRCC = clear cell renal cell carcinoma
TEAE = treatment-emergent adverse event
TRAE = treatment-related adverse event
AE = adverse event

Zanzalintinib Single Agent Safety Compares Favorably to Cabo

	Zanzalintinib[1] single-agent (N=32)		Cabozantinib[2] single-agent (N=3695)	
	All Grades	≥Grade 3	All Grades	≥Grade 3
Any	**100%**	**56%**	**99.7 %**	**82.7 %**
Diarrhea	69%	3%	60.6 %	10.9 %
Hypertension	41%	16%	29.7 %	13.9 %
Decreased appetite	31%	3%	49.7%	5.4%
Proteinuria	31%	0	9.4%	1.5%
Lipase increased	25%	9%	>10%	NR
Nausea	25%	6%	45.5 %	3.9 %
Weight decreased	22%	0	32.7%	4.4%
Vomiting	19%	3%	31.7%	3.0%
Fatigue	19%	0	53.0 %	13.0 %
AST increased	16%	0	21.7%	4.3%
ALT increased	16%	0	19.2%	3.6%
Palmar Plantar erythrodysesthesia (PPE)	**9%**	**0**	**38.5 %**	**9.1 %**

Low incidence of Grade 3 events and no treatment related Grade 5 adverse events for single-agent zanza

1. *STELLAR-001 (XL092-001), 100mg ccRCC cohort mg (n=32);*
2. *Cabozantinib IBv19; all-grade AEs > 15%, plus PPE as AE of interest across all indications*

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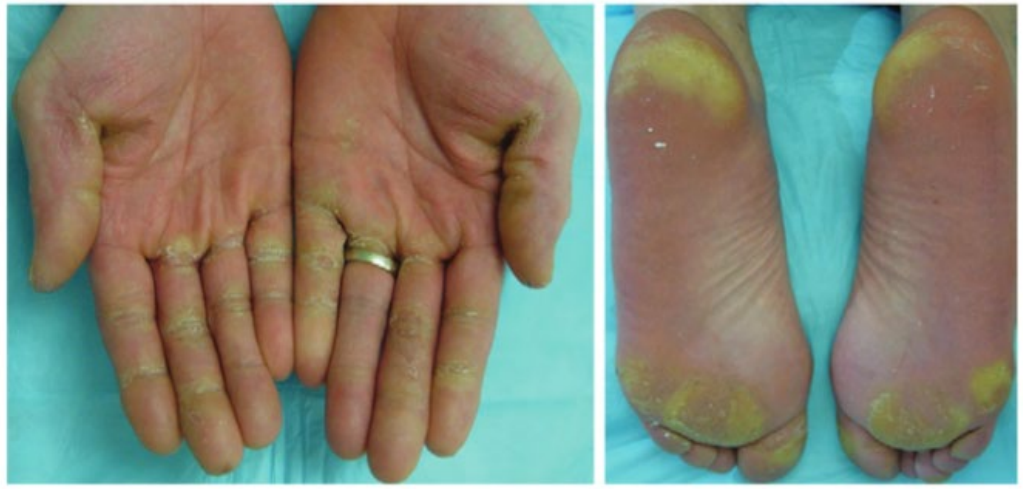
PPE (Hand-Foot Syndrome) is a Significant Burden for Patients

- Adverse event seen commonly with early generation multi-target TKIs and chemotherapy
- Painful, debilitating swelling in palms of hands and soles of feet that is painful to touch and prone to blisters and peeling
- High-grade (interferes with activities of daily living like walking, driving, dressing) occurs in up to 17% of patients, depending on the TKI
- Mechanism is poorly understood, mainstay of treatment is dose hold



TKI = tyrosine kinase inhibitor

Lacouture, M. E., *Annals of Oncology:* 19 (11): 1955–61 (sunitinib, sorafenib) – photo
Ding, F,.Journal of the American Academy of Dermatology 83 (3): 788–96..

Zanzalintinib is Well-tolerated at Full Dose in Combination with ICI

	STELLAR-001[1] zanza + atezo/ave n=121	CheckMate 9ER[2,7] cabo + nivo n=323	KEYNOTE-426[3-5] axi + pembro n=432	CLEAR[6,3] len + pembro n=355
% Any Grade ≥ 3	60	75.3	75.8	82.4
TKI-associated AEs Grade 3-4 %				
Diarrhea	3	7	11	10
Fatigue	5	8	5	9
Hypertension	10	13	24	29
PPE	0	8	5	4
AST increase	1.7	3	7	3
ALT increase	2.5	5	13	4

ICI = immune checkpoint inhibitor
TKI = tyrosine kinase inhibitor
AE = adverse event

1. Zanzalintinib IB v5. Data Cutoff Feb 8, 2023. Table 26. N=121 (n=118 treated at zanza dose 80mg daily and higher)
2. CABOMETYX (cabozantinib) [prescribing information]. Alameda, CA: Exelixis, Inc; January 2021; 3. KEYTRUDA (pembrolizumab) [prescribing information]. Merck; Aug 2021;
4. Rini BI, et al. N Engl J Med. 2019 Mar 21;380(12):1116-1127; 5. Rini B, et al. ASCO 2023, Abs LBA 4501. 6. Motzer RJ, et al. N Engl J Med 2021 Feb 13;384:1289-1300.
7. Choueiri TK, et al. ENJM 2021; 384: 829-41.

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Conclusions from ccRCC Cohort in STELLAR-001

IKCS: NORTH AMERICA
INTERNATIONAL KIDNEY CANCER SYMPOSIUM

- Single-agent zanzalintinib demonstrated promising antitumor activity in patients with heavily pretreated advanced ccRCC, with an ORR of 38% in the overall ccRCC cohort
- Antitumor activity was observed in patients who had progressed on prior VEGFR-TKIs, including cabozantinib, suggesting that zanzalintinib is able to overcome resistance to prior VEGFR inhibition
  - The ORR was 57% in cabo-naïve patients and 24% in those who received prior cabo
- Zanzalintinib appears to be generally well tolerated even in VEGFR-TKI pretreated patients
  - Patients who discontinue prior VEGFR-TKI therapy for toxicity were able to tolerate zanzalintinib
  - Rates of PPE, fatigue, diarrhea and AST/ALT elevations were relatively low compared with those reported for other VEGFR TKIs[1–3]
  - Full dose zanzalintinib can be combined with immune-checkpoint inhibitors, including atezolizumab, nivolumab and pembrolizumab

1. Choueiri TK, et al. *Lancet Oncol*. 2016;17(7):917–27. 2. Motzer, RJ, et al. *N Engl J Med*. 2007;356(2):115–24. 3. Escudier B, et al. *N Engl J Med*. 356(2):125–34.

ccRCC = clear cell renal cell carcinoma
ORR = objective response rate
TKI = tyrosine kinase inhibitor
PPE = hand-foot syndrome
AST = aspartate aminotransferase
ALT = alanine aminotransferase

EXELIXIS®

Focused Execution Drives Long-term Value Creation

Amy Peterson, M.D.
EVP, Product Development & Medical Affairs and CMO

What Disciplined Clinical Development Looks Like at Exelixis

Leverage Cabozantinib Lens for Zanzalintinib

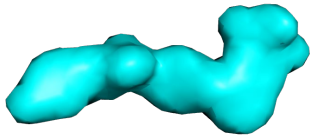
- Build on **cabozantinib clinical experience** to design efficient signal verifying studies and **accelerate into pivotal development**
- Leverage **development collaborations** to **derisk clinical investments**

Pipeline Strategy

- Develop **clinically differentiated** assets that significantly **improving standard of care for cancer patients**
- Focus on the **right strategy** for the **right asset**: probability of success, speed to market, and value creation
- Drive **right-sized growth** and **long-term value creation** by making quick to kill decisions, taking smart risks and maximizing the life cycle of each of our assets

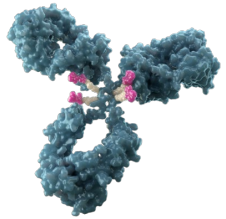
Differentiated Clinical Stage Programs Drive Long Term Value

Zanzalintinib



- Next-generation, multi-targeted TKI
- Similar kinase inhibition profile to cabozantinib, with shorter clinical half-life
- Broad applicability across multiple tumor types and novel combinations
- Encouraging data supporting broad development @ ESMO 2022, IKCS 2023

XB002



- Next-generation, TF-targeting ADC
- Potential differentiation across all aspects of the ADC
- Compelling early data presented at ENA 2022
- Plan to develop as monotherapy and in combinations across wide range of tumor types

XL309

- Highly selective, orally bioavailable small molecule inhibitor of USP1
- Best-in-class potential with broad applicability in BRCA-mutated tumors
- Strong rationale to combine with PARP inhibition
- In-licensed from Insilico Medicine in Sept. 2023

TKI = tyrosine kinase inhibitor
TF = tissue factor
ADC = antibody-drug conjugate
CDK7 = cyclin-dependent kinase 7
ENA = EORTC-NCI-AACR Symposium
IKCS = International Kidney Cancer Symposium
ESMO = European Society for Medical Oncology
USP1 = ubiquitin specific protein 1
PARP = poly ADP ribose polymerase

Zanzalintinib

3rd-generation VEGFR Targeting TKI

Zanzalintinib: a 3rd-generation TKI Created to Improve Risk/Benefit

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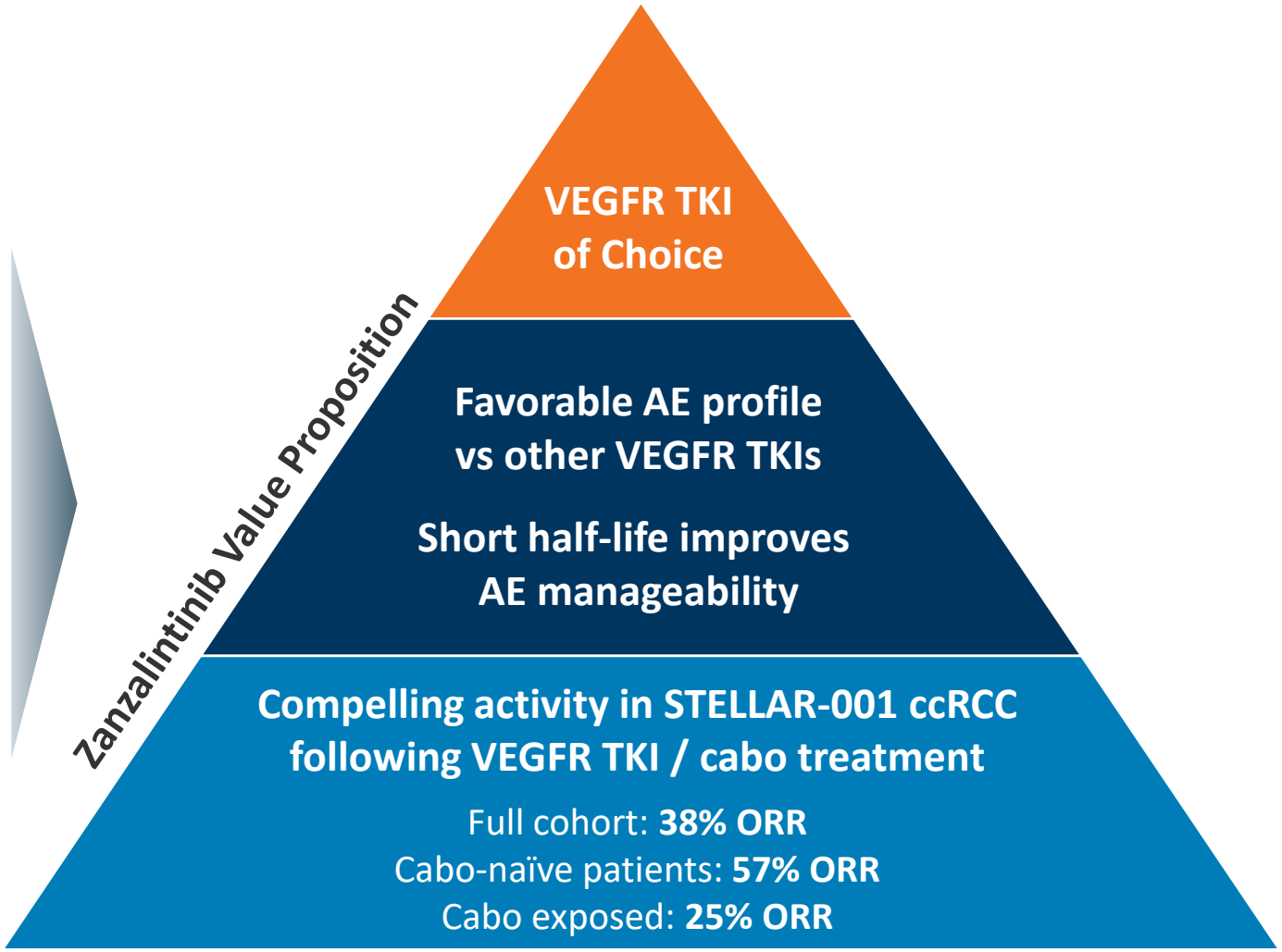
Zanzalintinib Characteristics

- Potent inhibition of multiple kinases including MET, VEGFR, AXL and MER
- Optimized pharmacokinetic profile (half-life ~1 day)
- Steady state achieved more rapidly than with cabozantinib (half-life ~4days)
- Encouraging preclinical monotherapy and combination efficacy with ICI



TKI = tyrosine kinase inhibitor
ICI = immune checkpoint inhibitor
AE = adverse event
ccRCC = clear cell renal cell carcinoma
ORR = objective response rate

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Zanzalintinib Development Vision: The VEGFR TKI of Choice for Monotherapy and Combinations

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Expand beyond ICI-TKI success to set new standards of care with triplet / novel combinations based on disease biology and therapeutic setting

+ IO

PD-(L)1

Seek opportunistic indications where TKI + ICI is not SoC and differentiate on benefit/risk profile

+ IO + PD(L)-1

LAG3 | CTLA4 | TIGIT

Seek to differentiate TKI combos with novel IO combinations supported by zanza's immunomodulatory activity

ZANZA

+ New MOAs

HIF2α ± PD-(L)1 | XB002

Strengthen RCC leadership; develop and rapidly advance best-in-class TKI + novel MOA combinations

+ CTX

Chemotherapy

Explore chemo combination potential to unlock additional opportunities

TKI = tyrosine kinase inhibitor
ICI = immune checkpoint inhibitor
IO = immunotherapy
PD-(L)1 = programmed death ligand 1 or programmed cell death protein 1
SoC = standard of care
LAG3 = lymphocyte-activation gene 3
CTLA4 = Cytotoxic T-lymphocyte associated protein 4
TIGIT = T cell immunoglobulin and ITIM domain
MOA = mechanism of action
HIF2α = hypoxia-inducible factor 2 alpha
RCC = renal cell carcinoma
CTX = chemotherapy

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Zanzalintinib Phase 1/2 Studies Inform Pivotal Studies and Design

ZANZA

Leverage Phase 1 and 2 Studies to Support Best-in-Class Combinations, Dose Optimization, Contribution of Components, Indication Selection and Line of Entry for Pivotal Studies

STELLAR 001

Regimens Evaluated

zanzalintinib
zanza + PD-L1

Tumor Types Explored

RCC, UC, CRPC
Breast

STELLAR 002

Regimens Evaluated

zanza + PD-1 +/- LAG3
zanza + PD-1 +/- CTLA4

Tumor Types Explored

RCC, UC, CRPC
CRC, HCC
NSCLC, SCCHN

STELLAR 009

Regimens Evaluated

zanza + HIF2α
zanza + PD-1 + HIF2α

Tumor Types Explored

RCC

MORPHEUS LUNG

Regimens Evaluated

zanza + PD-L1 + TIGIT

Tumor Types Explored

NSCLC

PD-L1 = programmed death ligand 1
PD-1 = programmed cell death protein 1
LAG3 = lymphocyte-activation gene 3
CTLA4 = Cytotoxic T-lymphocyte associated protein 4
HIF2α = hypoxia-inducible factor 2 alpha
TIGIT = T cell immunoglobulin and ITIM domain
RCC = renal cell carcinoma
UC = urothelial carcinoma
CRC = colorectal cancer
CRPC = castration-resistant prostate cancer
NSCLC = non-small cell lung cancer
SCCHN = squamous cell carcinoma of head & neck
HCC = hepatocellular carcinoma

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Zanzalintinib Indication Selection Strategy Leverages Cabo Data to Inform Initial Opportunities

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- What data can be leveraged to support investigating zanzalintinib in an indication?
- What patient populations have high unmet needs for better treatment options?
- What is the window of opportunity for development in the patient population?

	Tumor	Cabozantinib Clinical Data	
		Cabo SA	Cabo + ICI
GU	RCC	✓	✓
	Prostate	✓	✓
	Bladder	✓	✓
GI	HCC	✓	✓
	CRC	✓	✓
	Gastric	✓	✓
	Neuroendocrine	✓	✓
Thoracic	Thyroid	✓	✓
	SCCHN	X	✓
	NSCLC	✓	✓
	SCLC	✓	✓
GYN/Breast	Endometrial	✓	✓
	Ovarian	✓	✓
	HR+ BC	✓	X
	TNBC	✓	✓

Zanzalintinib is uniquely positioned to leverage the breadth of experience with cabozantinib, while further advancing the standard of care with novel combinations

RCC = renal cell carcinoma
HCC = hepatocellular carcinoma
CRC = colorectal cancer
SCCHN = squamous cell carcinoma of head & neck
NSCLC = non-small cell lung cancer
SCLC = small cell lung cancer
HR+ BC = hormone receptor positive breast cancer
TNBC = triple negative breast cancer
SA = single agent
ICI = immune checkpoint inhibitor
GU = genitourinary cancers
GI = gastrointestinal cancers
GYN = gynecological cancers

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Initial Pivotal Studies with Zanzalintinib Are Guided by Cabo Data and Reinforced by Emerging Data from STELLAR 001/002

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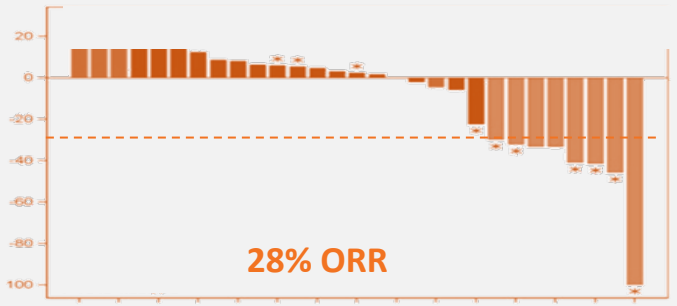
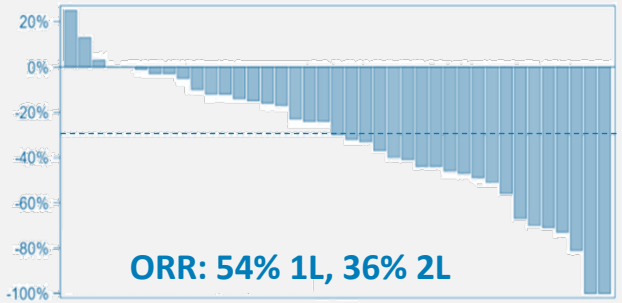
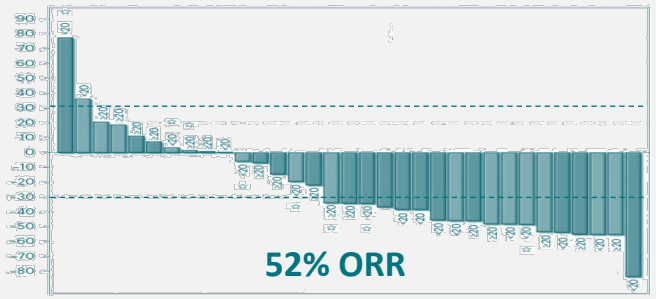
	Colorectal cancer (Phase 3)	Kidney cancer (Phase 3)	Head and Neck cancer (Ph2/3)
Pivotal Study Design	**STELLAR 303** 3L+, non-MSI high, non-dMMR mCRC → 1:1 → zanza + atezo / regorafenib 1° Endpoint: OS in NLM population, OS in ITT	**STELLAR 304** 1L, nccRCC: pap, unclass, translocation → 2:1 → zanza + nivo / sunitinib 1° Endpoint: PFS, ORR per RECIST v1.1	**STELLAR 305** PD-L1+ 1L metastatic SCCHN → 1:1 → zanza + pembro / pembrolizumab 1° Endpoint: PFS, OS
Supportive STELLAR Data	• STELLAR-001: zanza vs zanza + atezo in 2/3L mCRC • STELLAR-002: zanza + nivo in ≥2L mCRC	• STELLAR-001: zanza, zanza + atezo in ≥2L in nccRCC • STELLAR-002: zanza, zanza + nivo in 1L nccRCC	• STELLAR-002: zanza + nivo in 1L, PD-L1+ SCCHN
Initial Cabo Guiding Data	Cabo + ICI[1] 3L+ mCRC, N=29 	Cabo + ICI[2] 1L/2L nccRCC, N=40 	Cabo + ICI[3] 1L SCCHN, N=36 

1L = first-line
2L = second-line
3L = third-line
pap = papillary
NLM = non-liver metastasis
OS = overall survival
ITT = intent to treat population
MSI = microsatellite instability
mCRC = metastatic colorectal cancer
dMMR = deficient mismatch repair
ICI = immune checkpoint inhibitor
ORR = objective response rate
nccRCC = non-clear cell renal cell carcinoma
SCCHN = squamous cell carcinoma of head & neck
PD-L1 = programmed death ligand 1
RECIST = Response Evaluation Criteria in Solid Tumors
unclass = unclassified
PFS = progression-free survival
OS = overall survival

1. Saeed A et al. ASCO GI 2022 Abs 135,
2. Lee CH, et al. ASCO 2023 Poster Abs 4537
3. Saba N et al. Nat Med Apr; 29(4): 880-887.

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Zanzalintinib Current Clinical Development Program is Robust

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Study	Indication	Combination(s)	Phase 1	Phase 2	Phase 3
STELLAR 303	**Advanced/ Metastatic Microsatellite Stable (MSS) Colorectal Cancer (CRC)**[1]	zanzalintinib + atezolizumab (vs. regorafenib)			
STELLAR 304	**Advanced Non-clear Cell Renal Cell Carcinoma (nccRCC)**[2]	zanzalintinib + nivolumab (vs. sunitinib)			
STELLAR 305	**Squamous Cell Carcinoma of the Head & Neck (SCCHN)**[3]	zanzalintinib + pembrolizumab (vs. pembrolizumab)			
STELLAR 001	**Multiple Solid Tumors**[4]	zanzalintinib + atezolizumab			
STELLAR 002	**Multiple Solid Tumors**[5]	zanzalintinib + nivolumab +/- ipilimumab (CTLA-4) or relatlimab (LAG-3)			
STELLAR 009	**Advanced Clear Cell Renal Cell Carcinoma (ccRCC)**[6]	zanzalintinib + AB521 (HIF2α) +/- PD-1		EXELIXIS ARCUS BIOSCIENCES	
MORPHEUS LUNG	**PD-L1+ Non Small Cell Lung Cancer (NSCLC)**[7]	zanzalintinib + atezolizumab + tiragolumab (TIGIT)		Roche	

1. https://classic.clinicaltrials.gov/ct2/show/NCT05425940; 2. https://clinicaltrials.gov/study/NCT05678673; 3. https://clinicaltrials.gov/study/NCT06082167; 4. https://clinicaltrials.gov/study/NCT03845166; 5. https://clinicaltrials.gov/study/NCT05176483; 6. https://www.businesswire.com/news/home/20231203437225/en/; 7. https://clinicaltrials.gov/study/NCT03337698

PD-L1 = programmed death ligand 1
PD-1 = programmed cell death protein 1
LAG3 = lymphocyte-activation gene 3
CTLA4 = Cytotoxic T-lymphocyte associated protein 4
HIF2α = hypoxia-inducible factor 2 alpha
TIGIT = T cell immunoglobulin and ITIM domain

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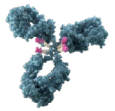
XB002

Next-generation TF-targeting ADC

XB002 (Next-generation TF-targeting ADC) Indication Selection Strategy Leverages Non-Clinical and Clinical Data

XB002



What tumor types express TF?

Which of those are responsive to tubulin inhibitors?

What Tivdak data can be leveraged to assess best-in-class potential of XB002?

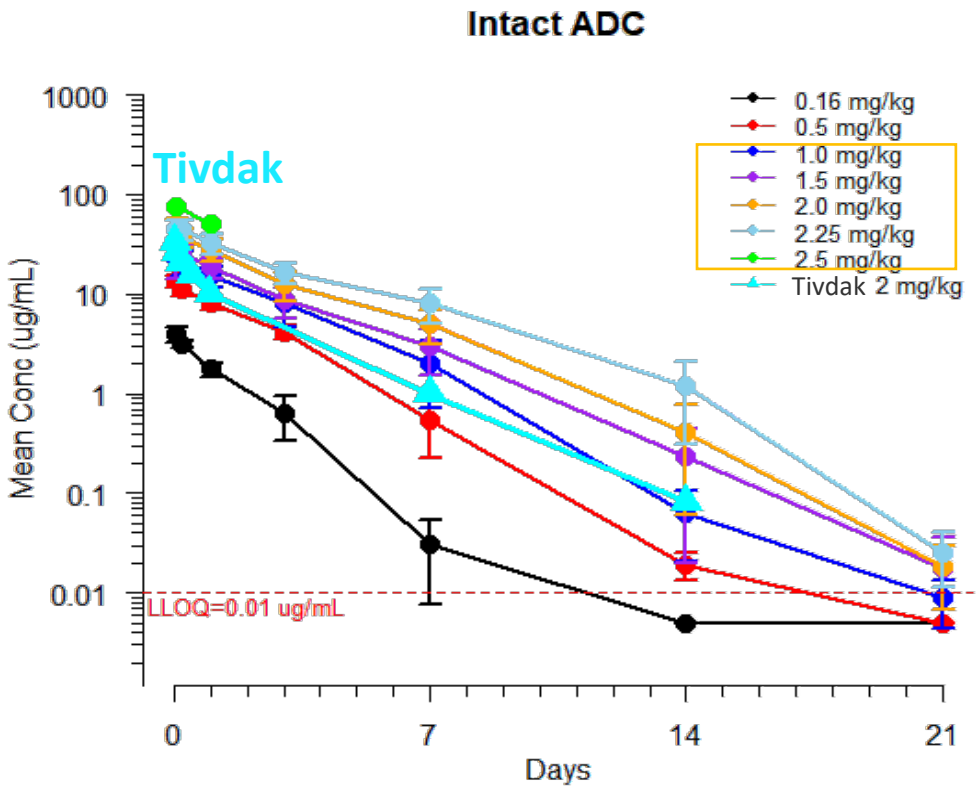
	Tumor	TF Expression Per Literature	Anti-Tubulin Sensitivity	Tivdak Clinical POC
GU	RCC			
	Bladder			
	Testicular			
	Prostate			
GI	Esophageal			
	Pancreatic			
	CRC			
	Gastric			
Thoracic	Thyroid			
	SCCHN			
	NSCLC			
GYN/Breast	Endometrial			
	Cervical			
	Ovarian			
	Breast			
Other	Osteosarcoma			
	Glioma			

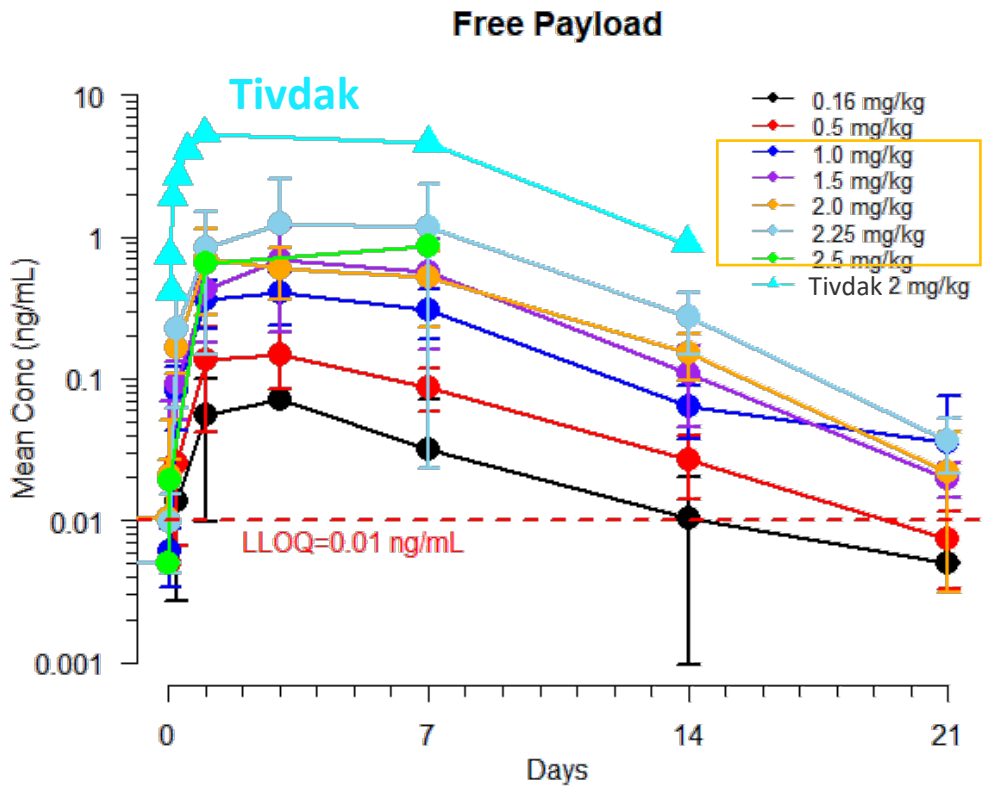
Low **Attractiveness** High

Rational selection of potential indications further profiled on unmet need, probability of success, speed to market and value proposition

TF = tissue factor
ADC = antibody-drug conjugate
GU = genitourinary tumors
RCC = renal cell carcinoma
GI = gastrointestinal tumors
CRC = colorectal cancer
SCCHN = squamous cell carcinoma of head & neck
NSCLC = non-small cell lung cancer
GYN = gynecologic tumors
POC = proof of concept

High Intact ADC Exposure and Low Free Payload with XB002





2 mg/kg of XB002 compared to 2 mg/kg Tivdak:

2x higher **Intact XB002 ADC exposure** compared to Tivdak ADC

10x lower **Circulating MTI payload exposure** compared to Tivdak MMAE payload

ADC = antibody-drug conjugate
LLOQ = lowest limit of quantitation
Conc = concentration
MTI = auristatin-based microtubulin inhibitor
MMAE = monomethyl auristatin E

Data cut date: 4/5/23

Substantial Development Potential for XB002 as Monotherapy or in Combination

Combine with IO to Improve Patient Outcomes

Maximize XB002 Development Opportunities

Internal Combinations Increase Portfolio Value

XB002 + PD-(L)1

- Non-Small Cell Lung
  Head & Neck
- Esophageal
- Cervical
  Breast

XB002 Monotherapy

- mCRPC
- Esophageal, Pancreatic
- Non-Small Cell Lung
  Head & Neck
- Endometrial, Cervical,
  Ovarian, Breast
- TF+ Solid Tumors

XB002 + Zanzalintinib

- Non-Small Cell Lung
  Head & Neck
- Endometrial
  Ovarian

IO = immunotherapy
PD-L1 = programmed death-ligand 1
mCRPC = metastatic castration-resistant prostate cancer
TF = tissue factor

GU = genitourinary tumors
GI = gastrointestinal tumors
GYN= gynecologic tumors

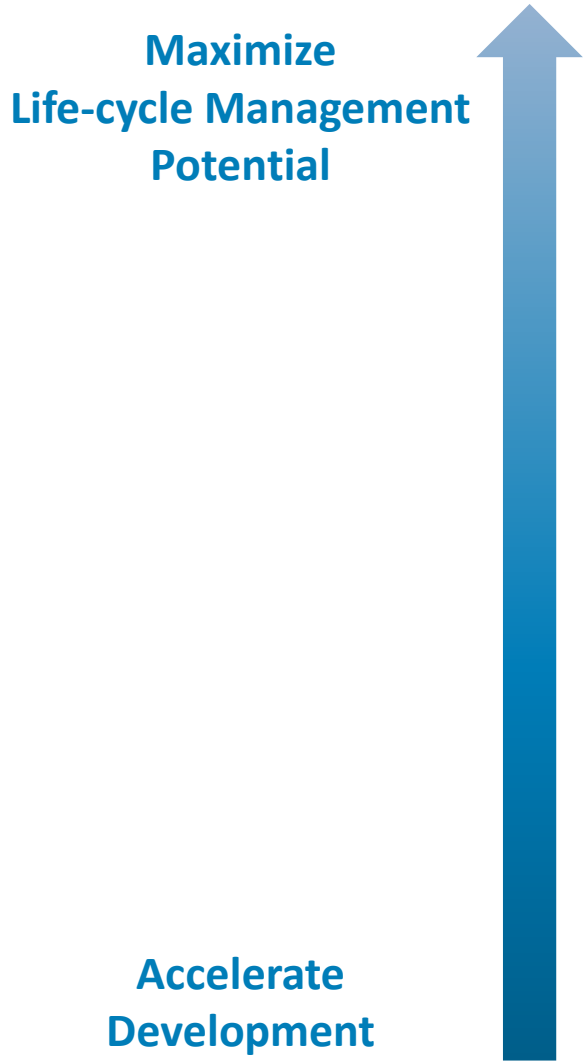
GU GI Lung/ H&N GYN / Breast

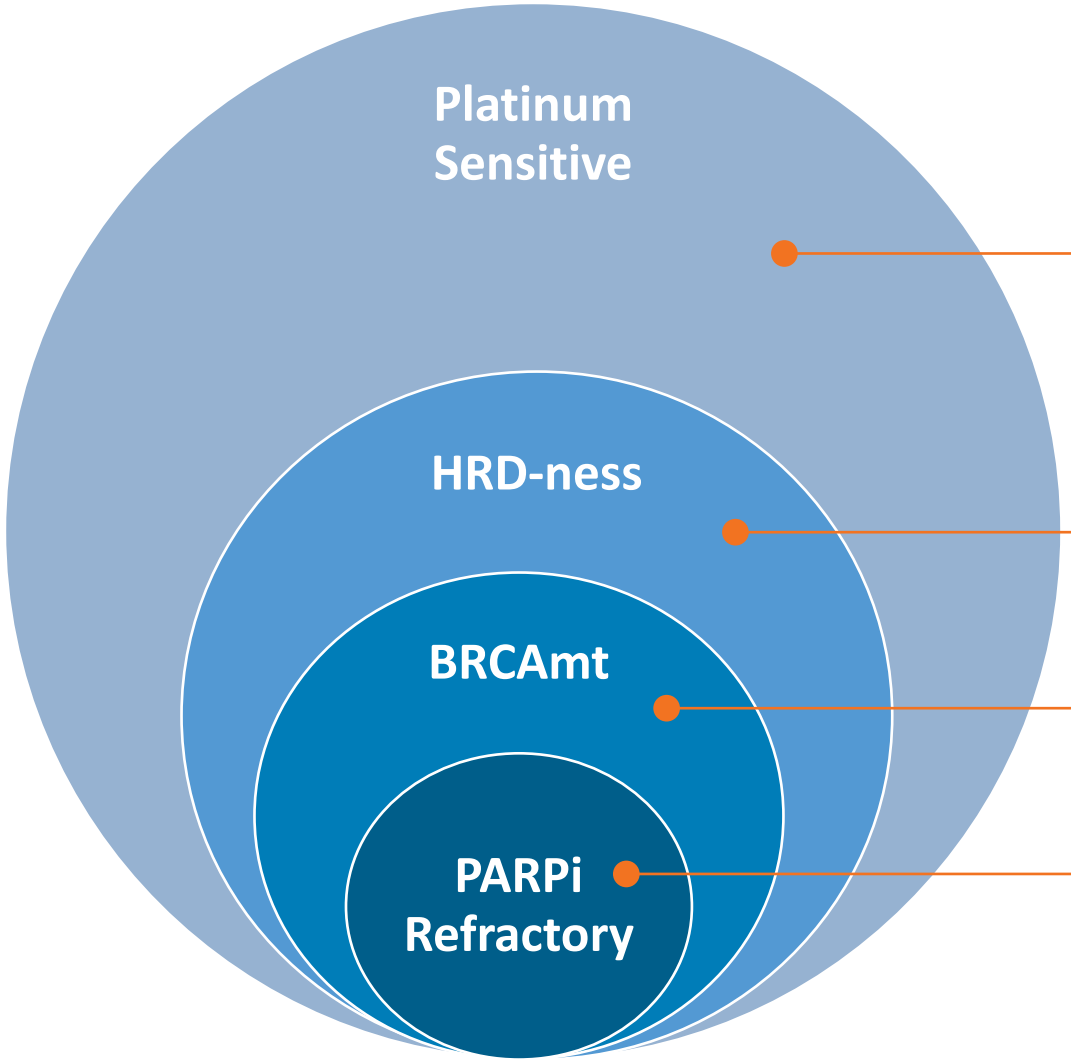
XL309

A small molecule inhibitor of USP1

XL309 Has Potential to Deepen and Prolong Responses to PARPi and May Provide Benefit to a Broader Population

XL309





XL309 + *TBD* (platinum-based chemo, maintenance post platinum)

XL309 + PARPi

XL309 + XL495/*TBD*

XL309 Monotherapy

XL309 + PARPi ± XL495

XL309 Monotherapy

XL309 + XL495

PARPi = poly ADP ribose polymerase inhibitor
HRD = homologous recombination deficiency
BRCAmt = BRCA mutation positive

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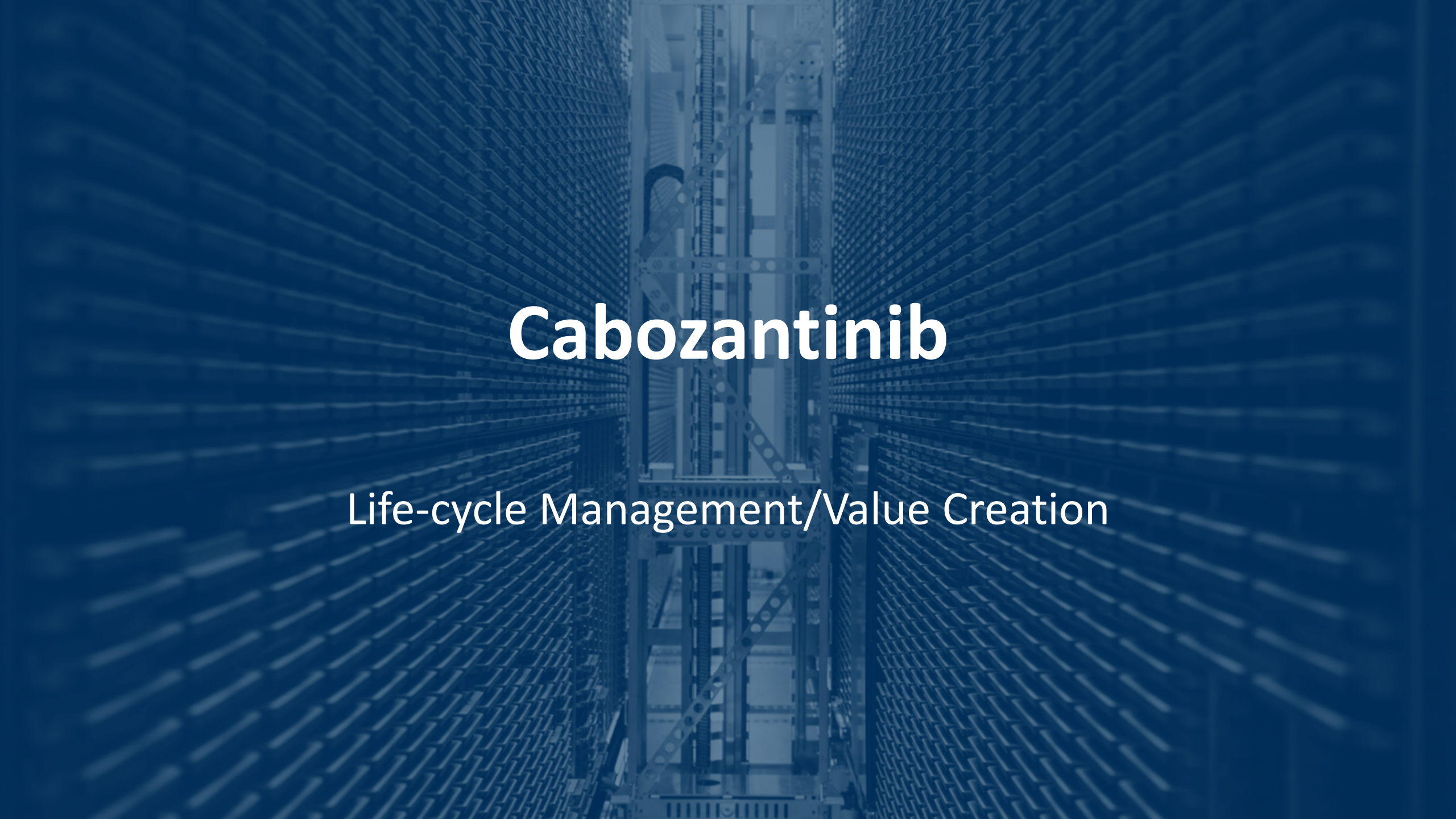


Cabozantinib

Life-cycle Management/Value Creation

Three Positive Phase 3 Data Readouts for Cabozantinib in Third Quarter 2023

CONTACT-02

1L/2L mCRPC

Key Endpoints
- **Primary:** BICR-PFS, OS
- **Secondary:** BIRC-ORR, DOR, PSA

CONTACT-02: Pivotal phase 3 study of cabozantinib + atezolizumab vs. 2nd NHT in patients with previously treated mCRPC

- Top-line press release announcing positive PFS results on August 21st
- Data presentation targeted for early 2024

CABINET

2L pNET and epNET

Key Endpoints
- **Primary:** BICR-PFS
- **Secondary:** OS, ORR, Safety

CABINET: Two pivotal phase 3 studies conducted by The Alliance for Clinical Trials in Oncology evaluating cabozantinib vs. placebo in patients with either advanced pancreatic (p) or extra-pancreatic (ep) neuroendocrine tumors (NET)

- Top-line press release announcing positive results on August 24th
- Data presented by Dr. Jennifer Chan at 2023 ESMO Congress on October 22nd

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

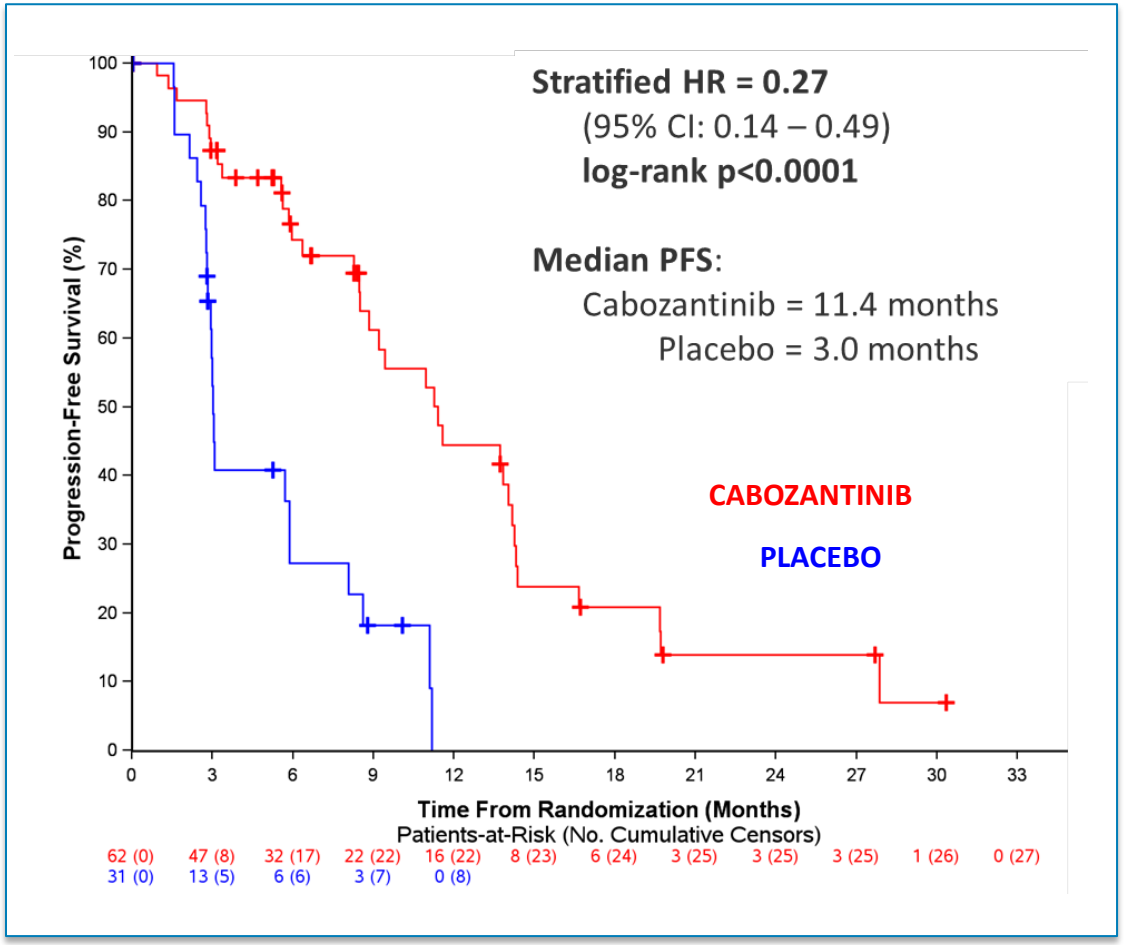
NCI National Clinical Trials Network
a National Cancer Institute program

1L = first-line
2L = second-line
PFS = progression-free survival
OS = overall survival
ORR = objective response rate
DOR = duration of response
PSA = prostate-specific antigen
NHT = novel hormonal therapy
pNET = pancreatic neuroendocrine tumors
epNET = extra-pancreatic neuroendocrine tumors
mCRPC = metastatic castration-resistant prostate cancer
BICR = blinded independent central radiology review
ESMO = European Society for Medical Oncology

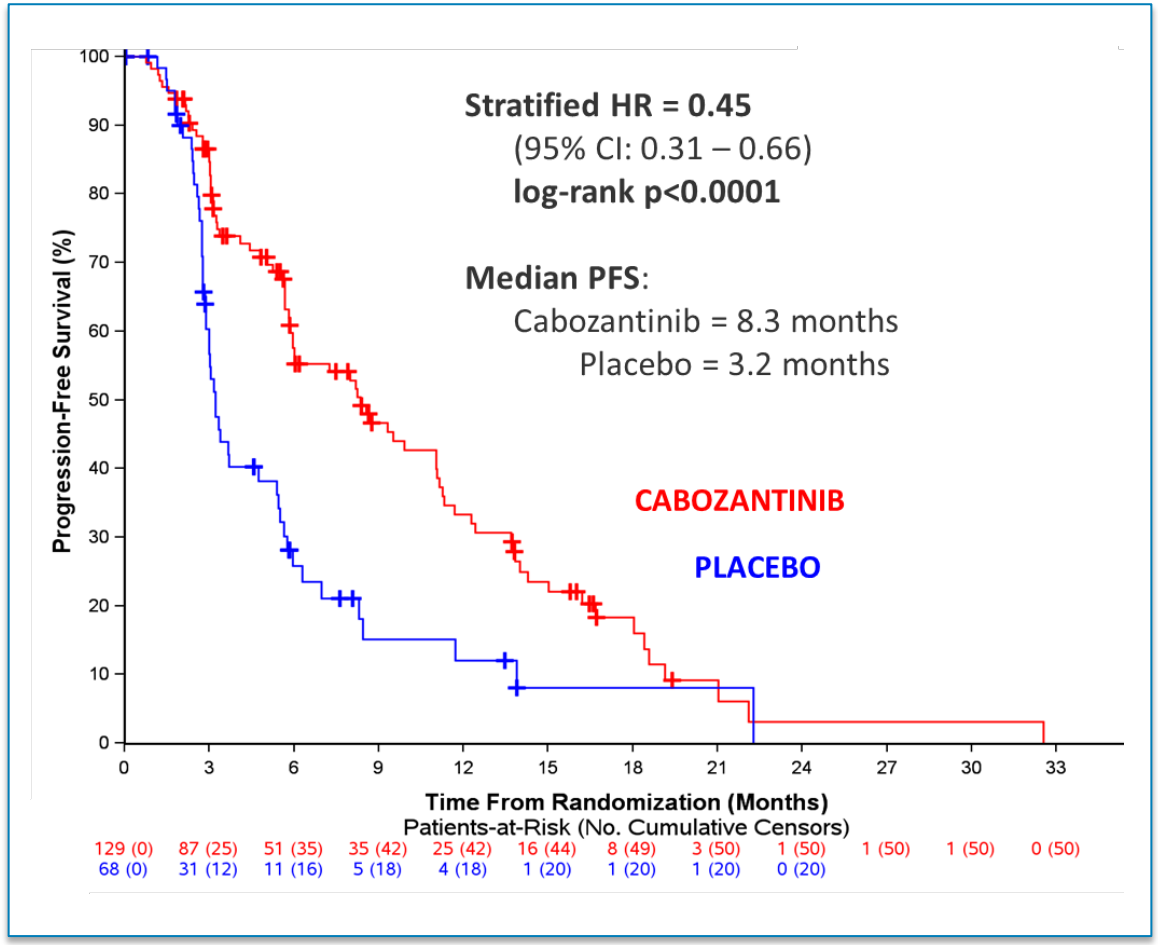
Cabozantinib Extends Progression Free Survival by >3x in pNET and by >2x in epNET vs Placebo

MADRID 2023 ESMO congress

Pancreatic (p) NET



Extra-pancreatic (ep) NET



pNET = pancreatic neuroendocrine tumors
epNET = extra-pancreatic neuroendocrine tumors
PFS = progression-free survival
HR = hazard ratio
CI = confidence interval

EXELIXIS®

Vision for Development Will Bring Value to Patients

Biology-centric

- Validated/known targets
- Characterize differentiation for best-in-class opportunity
- Rational combinations/indications

Combinations/ Approaches

- Leverage internal pipeline and external collaborations
- High probability of success programs
- Best-in-class/first-in-class potential

Efficient

- Leverage existing data
- Speed to monotherapy and combination dose
- Rapidly accelerate to pivotal trials

Industry-Leading Cycle Times

- Data-driven decision-making
- Streamline operations to enhance speed of clinical execution
- Quick to kill and quick to go decisions

Experienced

- Scale appropriately
- Decide with discipline
- Build upon strong relationships

Partner of choice

- Patient and investigator focused
- Partner with companies that are aligned with our strategic interests
- Collaborate for optimal outcomes

Closing Remarks

Michael M. Morrissey, Ph.D.
President and CEO

Exelixis R&D: Uniquely Positioned to Drive Value Creation

CABO **Experience**

Disciplined **Strategy**

Deep **Portfolio**

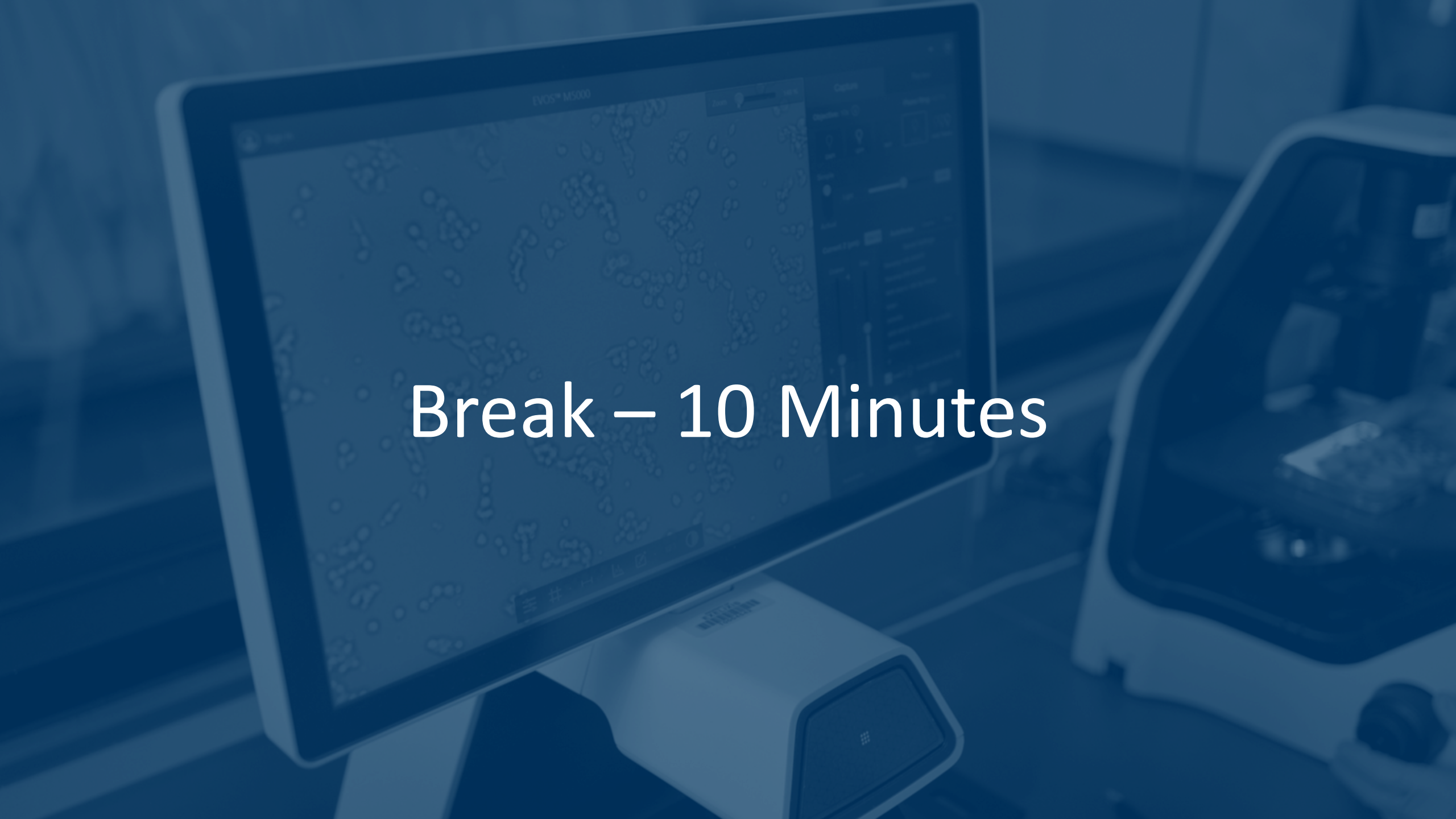
Pharma **Scale**

Biotech **Speed**

Value Creation

2023	2024-2027	2028+
Maximize cabo LCM to fuel clinical pipeline expansion	**Expand beyond cabo with zanza, XB002, XL309**	**Multiple product launches with broad patient impact across solid tumors**
Focus on mCRPC/NET and continued commercial execution in RCC/HCC/DTC	**Potential for first pivotal read-outs from zanza and XB002 in core commercial indications**	**Balanced portfolio of clinically differentiated assets across small molecules and biotherapeutics**

LCM = life-cycle management
mCRPC = metastatic castration-resistant prostate cancer
NET = neuroendocrine tumors
RCC = renal cell carcinoma
HCC = hepatocellular carcinoma
DTC = differentiated thyroid cancer



Break – 10 Minutes

DECEMBER 12, 2023

Q&A Session

Exelixis R&D Day: Science & Strategy

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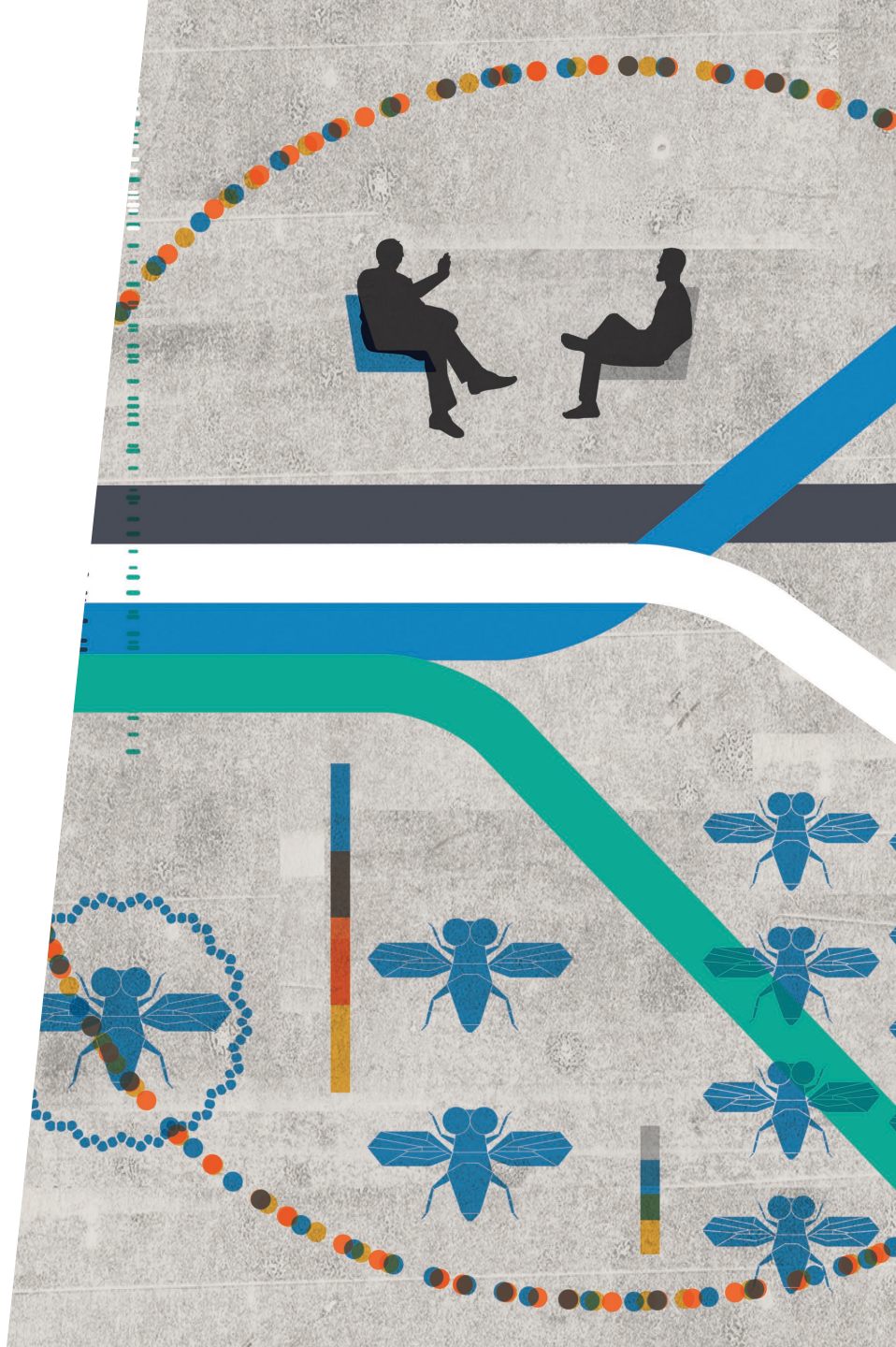

DECEMBER 12, 2023

Thank You

Exelixis R&D Day: Science & Strategy

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