Building a Differentiated Next-Generation Pipeline in Oncology

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Safe Harbor Statement

This presentation, including any oral presentation accompanying it, contains forward-looking statements, including, without limitation, statements related to: potential discovery, clinical and regulatory milestones for Exelixis in 2021, including potential regulatory pathways for cabozantinib based on COSMIC-312 and COSMIC-021 clinical data, potential pivotal trials for XL092 and moving small molecule and biologics discovery programs towards development candidate status; Exelixis' strategy to build a robust and diverse oncology pipeline through discovery and collaboration efforts, and targeting patient populations with significant unmet needs; Exelixis' potential future financial and other obligations under its various collaboration agreements; Exelixis' plans to utilize its various partnered programs to expand its small molecule capabilities and develop next-generation ADCs, including the opportunity to improve the therapeutic index of mAb-based therapeutics and broaden the list of potential mAb cell surface targets; Exelixis' development plans for XL102 and XB002; Exelixis' belief that XL102 has the potential to be a best-in-class therapeutic agent; Exelixis' belief that its pipeline may yield one additional IND in 2021, as well as multiple INDs and DCs in the coming years; and Exelixis' plans to augment its pipeline through BD efforts. 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 continuing COVID-19 pandemic and its impact on Exelixis' clinical trial and drug discovery activities; the level of costs associated with Exelixis' commercialization, research and development, in-licensing or acquisition of product candidates, and other activities; the potential failure of 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' dependence on its relationships with its collaboration partners, including their adherence to their obligations under relevant collaboration agreements and the level of their assistance to Exelixis in completing clinical trials, pursuing regulatory approvals or successfully commercializing partnered compounds in the territories where they may be approved; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' and its partners' continuing compliance with applicable legal and regulatory requirements; Exelixis' dependence on third-party vendors for the development, manufacture and supply of its product candidates; Exelixis' and its partners' ability to protect their respective intellectual property rights; market competition; changes in economic and business conditions; and other factors affecting Exelixis and its product pipeline discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 6, 2021, and in Exelixis' future filings with the 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.

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Executing Towards Our Goal of Becoming a Multi-Product Oncology Company

Commercial success with CABOMETYX® franchise

- Currently the #1 TKI in both RCC and 2L HCC; only single agent with OS benefit in both indications
- >$1B in cabozantinib global net revenue (2019, 2020)*; approved in more than 50 countries
- Successful launch of CABOMETYX and OPDIVO® combination in 1L RCC in Jan. 2021

Robust clinical and regulatory activity

- COSMIC-311/DTC data presented at ASCO'21; sNDA submitted to the FDA
- Clinical data readouts from COSMIC-312/1L HCC and COSMIC-021 Cohort 6/CRPC; plan to discuss next steps toward potential regulatory path with the FDA
- Rapid development of XL092 as a single agent and in combination regimens, with potential to initiate pivotal trials this year
- Phase 1 trials for XL102 (CDK7 inhibitor) and XB002 (TF-targeting ADC) underway

Broad and deep early pipeline across small molecules and biologics

- Proven history of drug discovery and expansive ~4.6M in-house compound library
- Small molecule collaborations with Aurigene and StemSynergy to in-license novel targets
- Seven biologics collaborations to complement small molecule discovery efforts

1L = first-line
2L = second-line
TKI = tyrosine kinase inhibitor
RCC = renal cell carcinoma
HCC = hepatocellular carcinoma

OS = overall survival
DTC = differentiated thyroid cancer
sNDA = supplemental New Drug Application
FDA = U.S. Food and Drug Administration

CDK7 = cyclin-dependent kinase 7
TF = tissue factor
ADC = antibody-drug conjugate
CRPC = castration-resistant prostate cancer

**Includes ex-U.S. revenues from partners Ipsen and Takeda*

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A Strong Network of Clinical and Pipeline Collaborations to Advance the Next Wave of Our Small Molecule and Biologic Therapeutics

Commercial Partnerships

IPSEN
Innovation for patient care

Takeda

Genentech
A Member of the Roche Group

Daiichi-Sankyo

Clinical Collaborations

Roche

Bristol Myers Squibb™

MERCK

NIH NATIONAL CANCER INSTITUTE | Cooperative Group ISTs

Pipeline Expansion

AURIGENE
Accelerating Discovery

SSTI
StemSynergy Therapeutics, Inc.

invenra

ICONIC THERAPEUTICS

Catalent

NBE therapeutics
Innovating medicines

WuXi Biologics
Global Solution Provider

ADAGENE

GAMAMABS PHARMA

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Building a Robust and Diverse Oncology Pipeline Through Discovery and Collaboration Efforts

Strategy	Key Activities
Investment to expand CABOMETYX indications	Ongoing pivotal trials
Target novel / promising MOAs with next generation approaches	XL092, XL102, XB002 and others
Broaden discovery capabilities beyond small molecules	In-licensing biologics capabilities to build next-generation ADC platform

MOAs

- Tyrosine kinases
- Tissue factor
- CDK7
- Others

Modalities

- Small Molecules
- Bispecifics
- ADCs

MOA = mechanisms of action
CDK7 = cyclin-dependent kinase 7
ADC = antibody-drug conjugate

Exelixis Partnering Strategy

Building an innovative oncology pipeline that targets patient populations with significant unmet needs

MOA

- First-in-Class
- Best-in-Class
- Highly differentiated
- Broad indications, combinability, or clear biomarker strategy

Stage

- Clinical stage (Phase 1 or Phase 2) programs
- Near-IND preclinical programs
- Innovative technology platforms

Modality

- Small molecules
- Biologics
  - mAbs
  - bi-/multi-specifics
  - fusion proteins
  - ADCs

MOA = mechanisms of action
IND = Investigational New Drug application

mAbs = monoclonal antibodies
ADC = antibody-drug conjugate

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Small Molecule Pipeline

A Proven History of Drug Discovery and Development

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Expanding Our Drug Discovery Efforts

Fully-enabled small molecule discovery capabilities built on foundation of previous discovery expertise

- High throughput screening, biology, pharmacology, medicinal chemistry

Significant expansion of footprint and capabilities over the next year

- New labs completed
- New head of Discovery in place

Two lead optimization programs ongoing

- XL092 previously advanced to the clinic
- Multiple high throughput screenings in progress

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Supplementing Small Molecule Discovery Efforts with Strategic Collaborations

	Program Name	Origin / Partner	Mechanism / Target
SMALL MOLECULE PIPELINE	XL092	EXELIXIS®	TKI; MET/VEGFR/AXL/MER-targeting
	XL102/Other programs	AURIGENE Accelerating Discovery	CDK7-inhibitor/Other targets undisclosed
	EXEL-4329	SSTI®	Casein Kinase 1 Alpha activator

Collaborations provide complementary small molecule expertise or approaches

- Additional bandwidth and expertise
- Broaden access to chemical matter and technologies

TKI = tyrosine kinase inhibitor
CDK7 = cyclin-dependent kinase 7

Broad Discovery Collaboration with Aurigene Focused on Oncology

Exclusive option and licensing agreement to discover and develop novel therapies for cancer

AURIGENE
Accelerating Discovery

Capabilities range from lead finding through to IND

- Medicinal chemistry, modeling, structural biology, cell biology, ADME/PK, efficacy
- Non-GLP and GLP toxicology, process chemistry, formulation and scale up

Brings complementary small molecule approach to internal discovery efforts and expands preclinical pipeline

- Expertise in optimization of covalent inhibitors
- Novel approaches to induced protein degradation
- Expands small molecule capabilities from both biology and chemistry perspective

IND = Investigational New Drug application
ADME = absorption, distribution, metabolism and excretion
PK = pharmacokinetics
GLP = Good Laboratory Practice

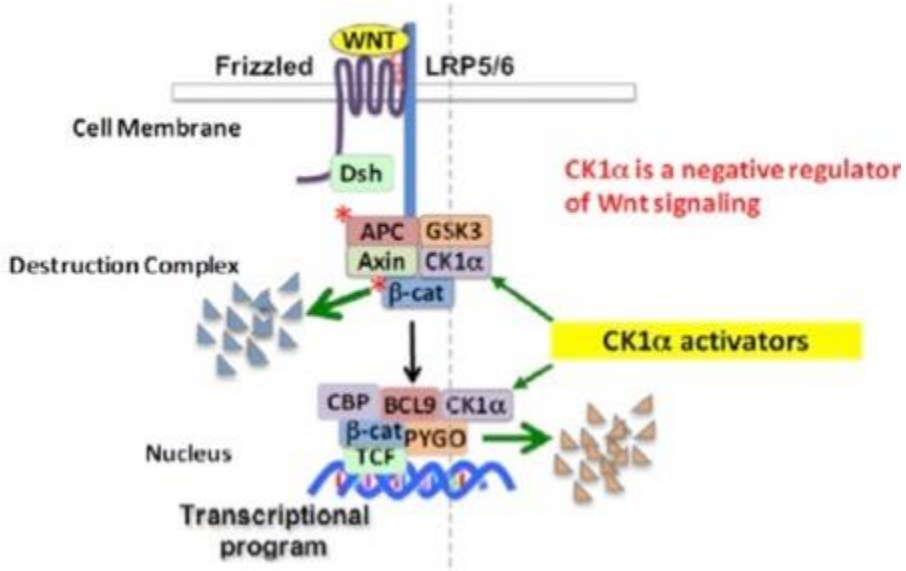
Collaboration with StemSynergy for CK1α Activator Program

Exclusive agreement for the discovery/development of compounds targeting Casein Kinase 1α

- Component of the Wnt signaling pathway implicated in key oncogenesis processes
- Activation of β-catenin, downstream of Wnt, upregulated in multiple tumors, including 90% of CRC
- Preclinical data in CRC models show degradation of β-catenin, inhibition of tumor growth

Partners conducting preclinical and clinical studies with CK1α program compounds

- Exelixis solely responsible for the commercialization of products that arise from the collaboration



CK1α = casein kinase 1 alpha
CRC = colorectal cancer

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Biologics Pipeline

In-licensing Building Blocks for Next-Generation Biologics

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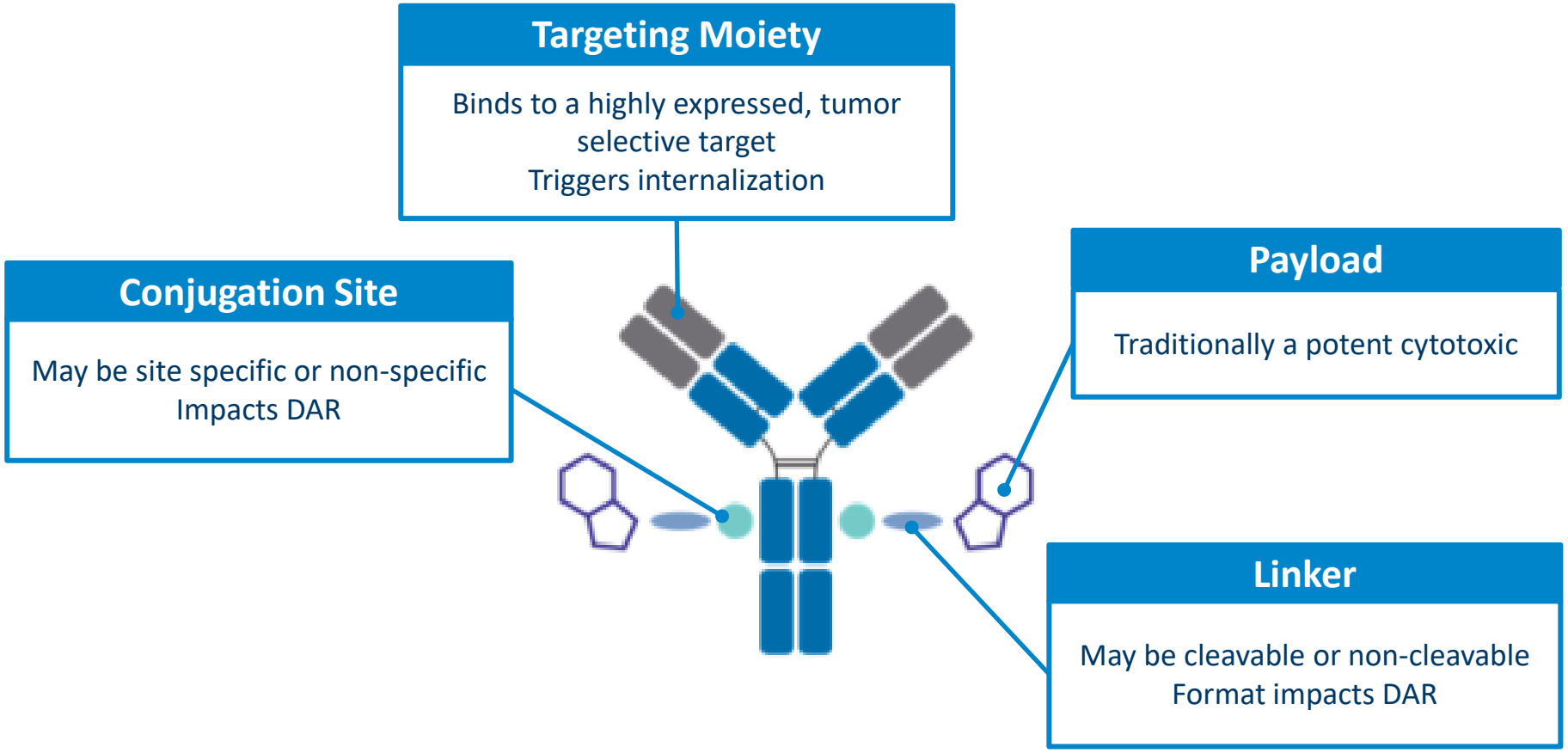
Rapidly Establishing an Oncology-focused Biologics Pipeline

BIOLOGICS		
Platform / Program	**Collaborator**	**Mechanism / Target**
XB002	ICONIC THERAPEUTICS	ADC targeting tissue factor in solid tumors
B-Body™ Biologics Platform	invenra	Biologics and multi-specific antibodies; targets undisclosed
SMARTag® ADC Platform	Catalent	ADCs; targets undisclosed
SMAC-Technology™ Platform	NBE therapeutics	ADCs; targets undisclosed
SAFEbody™ Platform	ADAGENE	Masked mAbs for ADCs / biologics
Panel of Monoclonal Antibodies	WuXi Biologics Global Solution Provider	mAbs for ADCs or bispecifics; targets undisclosed
AMHR2 Antibody Technology / GM-102	GAMAMABS PHARMA	Anti-AMHR2 antibodies for ADCs

ADC = antibody-drug conjugate
mAb = monoclonal antibody
AMHR2 = anti-Müllerian hormone receptor 2

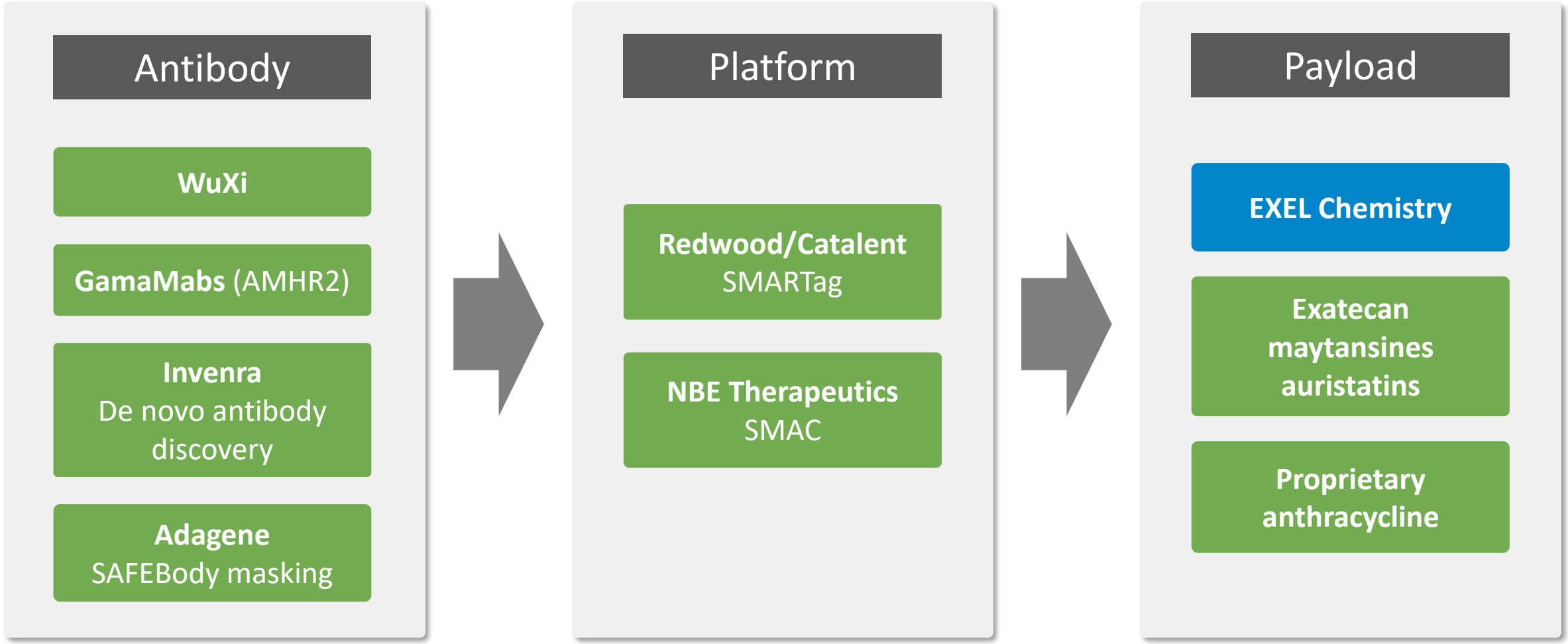
Features of Antibody-Drug Conjugates

ADC optimization ideally involves exploration of all these factors to obtain an agent with optimal efficacy and therapeutic index



ADC = antibody-drug conjugate
DAR = Drug Antibody Ratio

Exelixis' ADC Platform



ADC = antibody-drug conjugate
AMHR2 = anti-Müllerian hormone receptor 2

Exelixis ADC Platform Approach Maximizes Optionality, Enables Innovation and Facilitates Building an ADC Pipeline

The combined technologies provide flexibility at all points in ADC discovery

- Antibody format, DAR, payload
- Addresses the “one size does not fit all” issue for ADCs
- Manufacturing suitable to support clinical trials demonstrated

Opportunity to follow the Iconic Therapeutics model of making next-generation ADCs against targets with clinical POC

The various platforms also provide a foundation on which we can innovate

- Biparatopic/bispecific ADCs, masked antibodies, novel targets
- Proprietary conjugation technologies
- Proprietary payloads / custom EXEL generated payloads

ADC = antibody-drug conjugate
DAR = Drug Antibody Ratio
AMHR2 = anti-Müllerian hormone receptor 2
POC = proof-of-concept

Leveraging Invenra's Biologics Platform to Discovery Antibodies and Bispecifics

Invenra has significant expertise in antibody and bispecific discovery

- Multiple antibody generation approaches
- B-body bispecific platform

Invenra responsible for antibody lead discovery/generation

Exelixis to lead IND-enabling studies, manufacturing, clinical development, regulatory and commercialization activities

Multiple oncology-focused antibody and bispecific programs underway

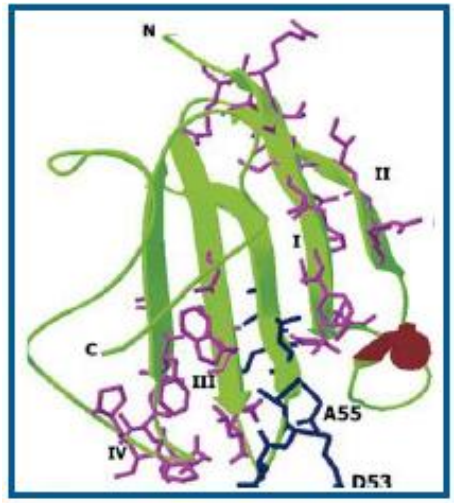
- Initial antibody panels delivered and provided to ADC partners

IND = investigational new drug application
ADC = antibody-drug conjugate

Recent GamaMabs AMHR2 Antibody Platform Acquisition

Anti-Mullerian Hormone Receptor 2 is an ALK family member and the receptor for anti-mullerian hormone

- Responsible for male sexual differentiation
- Highly restricted adult tissue expression (testes, ovarian granulosa cells)



AMHR2 is overexpressed in several solid tumors

- Ovarian, colorectal, NSCLC, hepatocellular and renal cell carcinomas
- Under certain circumstances may impact tumor phenotype

Cancer type	N samples	% samples > 1.5 global score and ≥ 1 membrane
Renal Cell	35	71
Hepatocarcinoma	40	68
Colon	30	64
Lung	19	48

AMHR2 = anti-Müllerian hormone receptor 2
NSCLC = non-small cell lung cancer

Recent GamaMabs AMHR2 Antibody Platform Acquisition

GAMAMABS PHARMA

Antibodies
- GMP GM102 antibody
- Panel of additional AMHR2 antibodies, differing affinities, epitopes and species

Cell lines
- GM102 master cell bank
- AMHR2 high and low expressing cell lines

Data / protocols
- Tumor expression data, associated IHC / FACs protocols
- Extensive tumor model AMHR2 expression data

Antibodies and binders from GamaMabs and WuXi flow either into Invenra's bispecific B-Body platform or move into ADC-focused collaborations with Catalent and NBE

ADC = antibody-drug conjugate
AMHR2 = anti-Müllerian hormone receptor 2
IHC = immunohistochemistry
FACs = Fluorescence-activated cell sorter

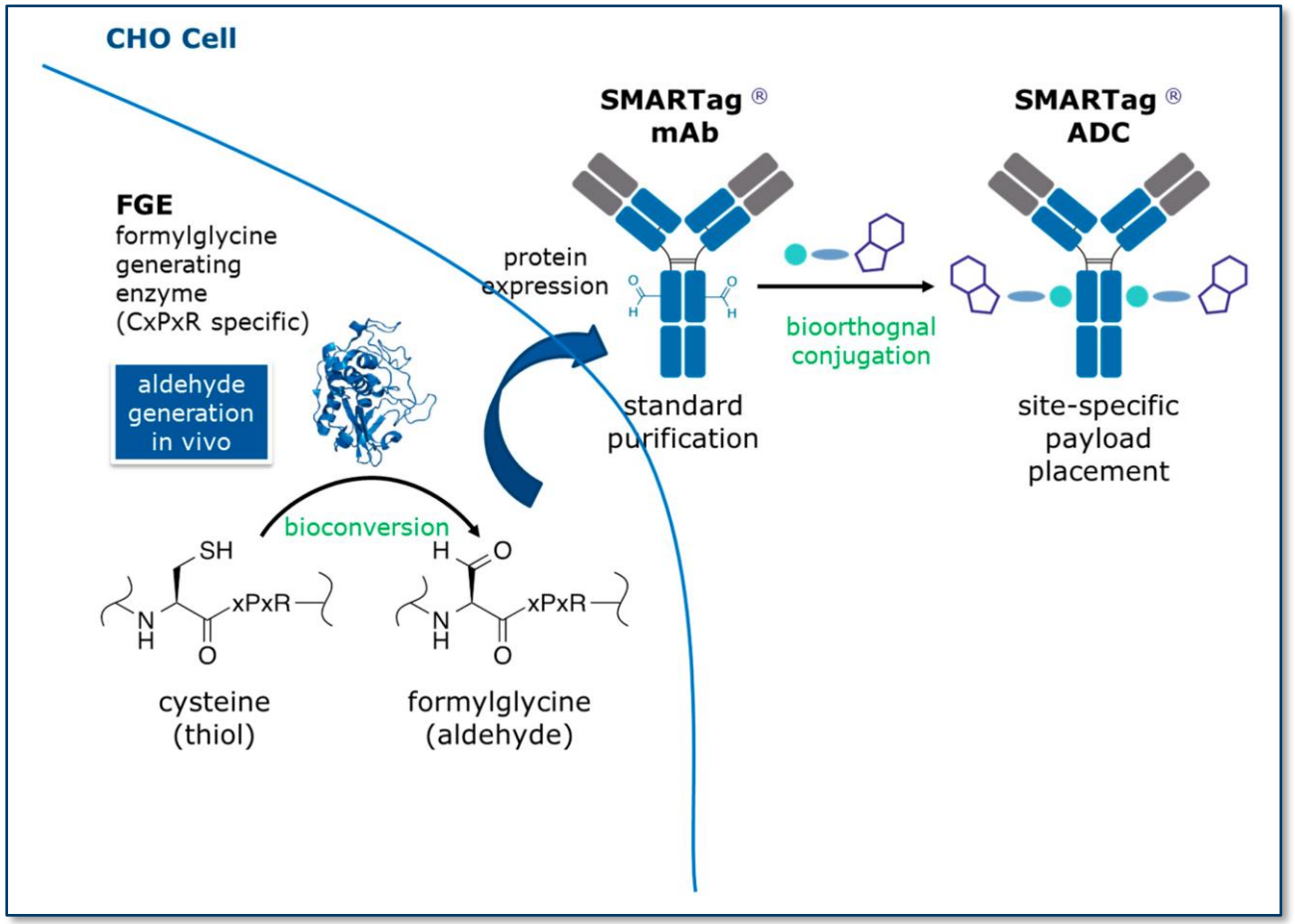
Redwood/Catalent Platform Overview

SMARTag conjugation technology

- Control of conjugation site and DAR (typically 2-4)
- Stable linker

Access to a range of payloads

- Maytansines, auristatins
- Exatecans
- Ducaromycins
- Custom / EXEL-generated



Liu et al 2019 Methods Mol. Biol. v2033 131
Agarwal et al 2013 PNAS v110 46

DAR = Drug Antibody Ratio
mAb = monoclonal antibody
ADC = antibody-drug conjugate

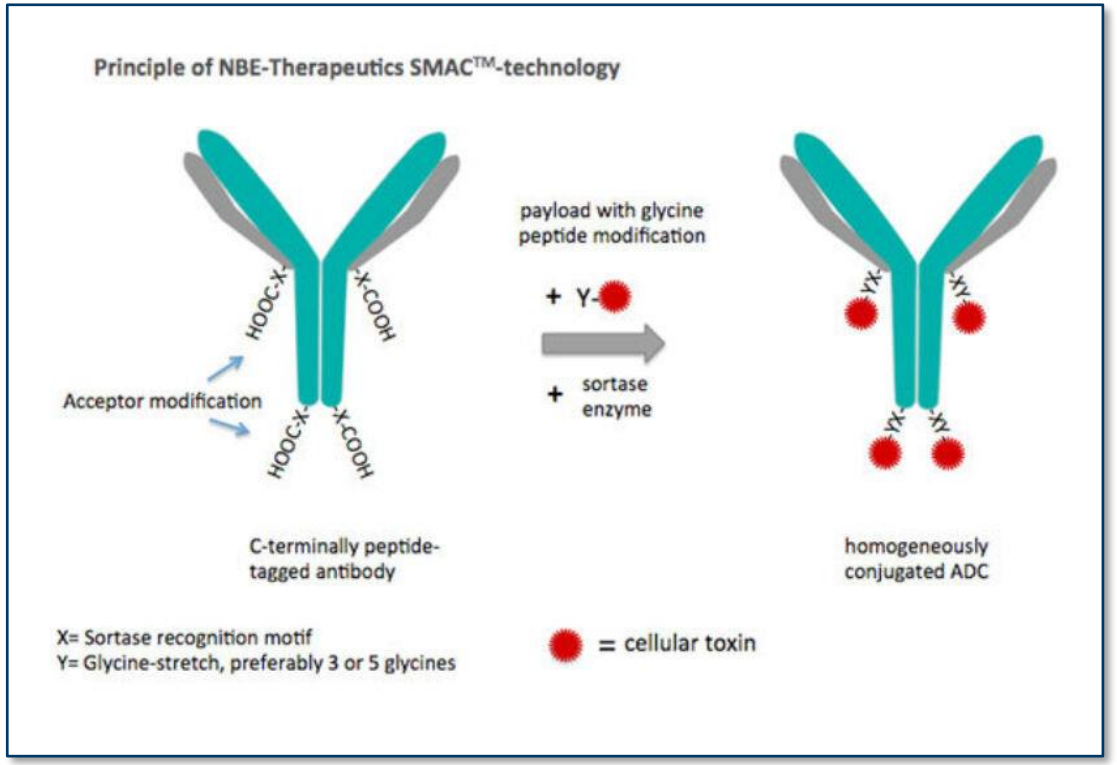
NBE Platform Overview

Sortase-mediated antibody conjugation (SMAC) technology

- Precise control of DAR (2 or 4)
- Conjugation efficiencies >98%, homogeneous product
- Highly stable linker

Proprietary anthracycline-based payload

- DNA intercalator
- Non cardiotoxic
- Not a Pgp substrate



Beerli et al 2015 PLOS ONE 10 e131177

DAR = Drug Antibody Ratio
ADC = antibody-drug conjugate
Pgp = P-glycoprotein

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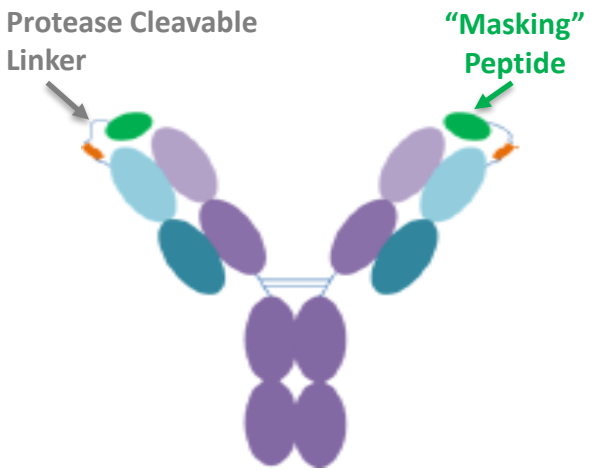
Adagene's SAFEbody Platform

A "masking" technology platform may afford Exelixis the opportunity to improve the therapeutic index of mAb-based therapeutics and broaden the list of potential mAb cell surface targets

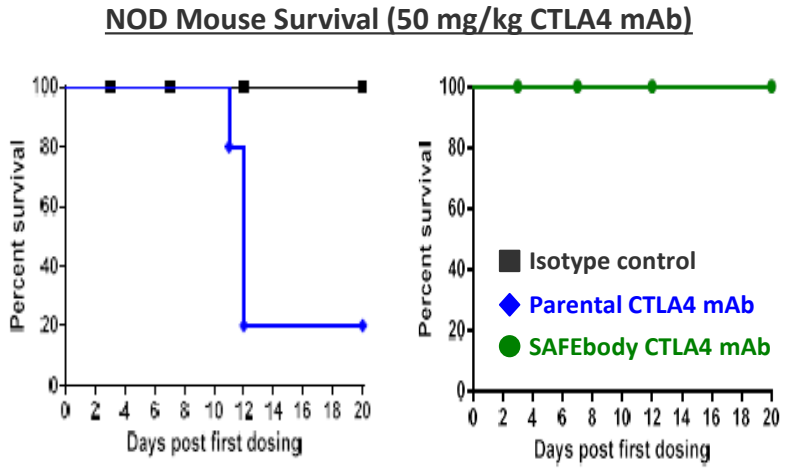
SAFEbody: **S**pecific shield **A**ctivation **F**or **E**nhanced therapeutic window

- Fab domains conjugated to a "masking" peptide via a protease-cleavable linker

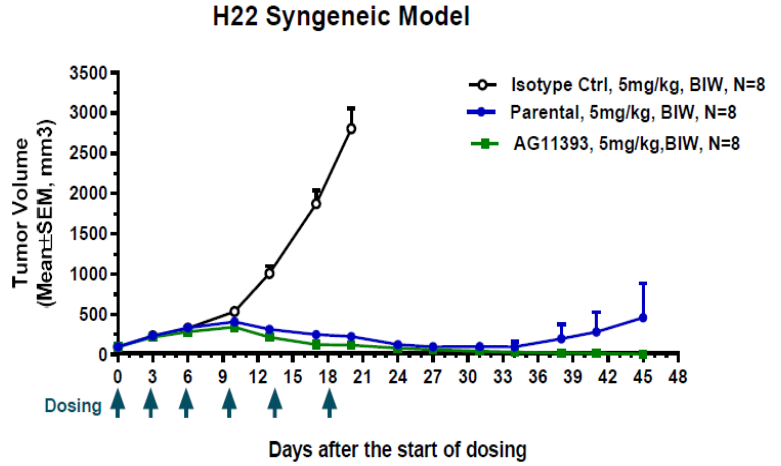
SAFEbody Platform



A SAFEbody CTLA4 mAb Demonstrates Improved Tolerability in Mice



A SAFEbody CTLA4 mAb Demonstrates Similar Antitumor Efficacy *In Vivo*



*** 200 mg/kg SAFEbody CTLA4 mAb was also tolerated in NHPs ***

mAb = monoclonal antibody
CTLA4 = cytotoxic T-lymphocyte-associated antigen 4
NHP = non-human primate

Pipeline Progress

Advancing Next-Generation Exelixis Medicines in the Clinic

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Development Progress with Early-stage Pipeline Assets

XL102

- Potent, selective and orally bioavailable inhibitor of CDK7
- In-licensed from Aurigene in 2020

Phase 1 trial underway; cohort dose escalation ongoing

XB002

- Rationally designed, next-generation ADC targeting tissue factor
- In-licensed from Iconic Therapeutics in 2020

Phase 1 trial underway

CDK7 = Cyclin-dependent Kinase 7
ADC = antibody-drug conjugate
IND = Investigational New Drug application

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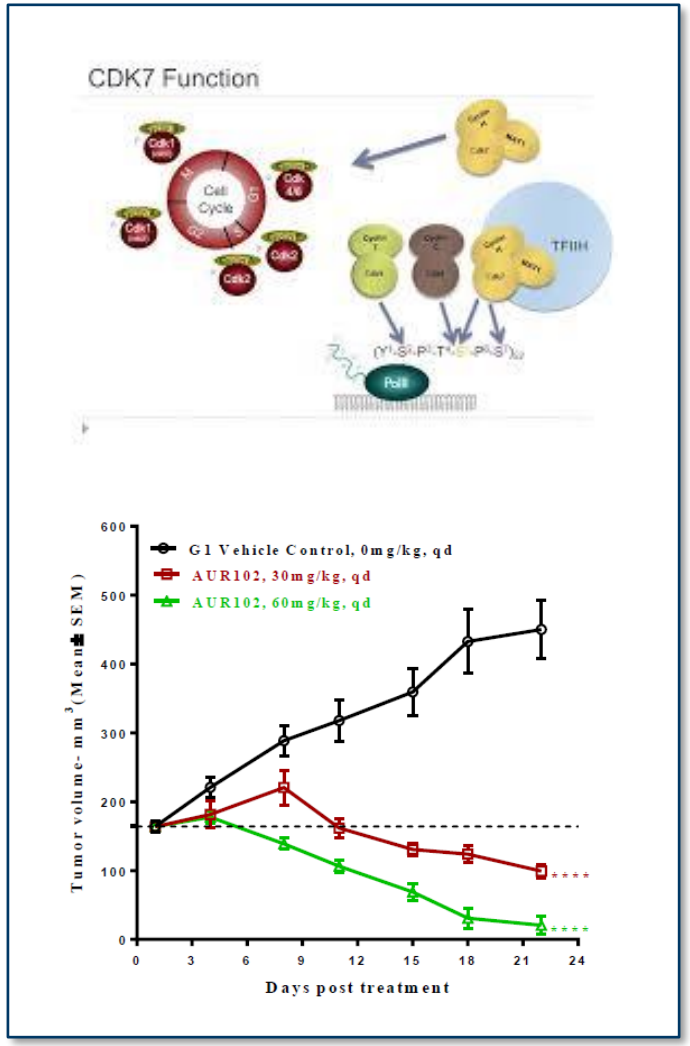
XL102: Covalent Orally Available CDK7 Inhibitor

CDK7 regulates cell cycle progression and transcription; CDK7-inhibitors have broad potential in oncology

- Combination with aromatase inhibitor or SERM in ER+ breast cancer
- Potential for activity in CDK4/6 inhibitor resistant tumors
- Monotherapy or combination with SOC in TNBC, HGOC, AML, DLBCL, MM
- Combination with targeted therapies

XL102 has the potential to be best-in-class due to the combination of selectivity, potency and oral bio-availability

- Active in multiple xenograft models including DLBCL and TNBC



CDK7 = Cyclin-dependent Kinase 7
SERM = selective estrogen receptor modulators
ER+ = estrogen receptor positive

SOC = standard of care
TNBC = triple-negative breast cancer
HGOC = high-grade ovarian cancer

AML = acute myeloid leukemia
DLBCL = diffuse large b-cell lymphoma
MM = multiple myeloma

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XB002: Tissue Factor-Targeting ADC

Tissue factor is normally involved in mediating coagulation

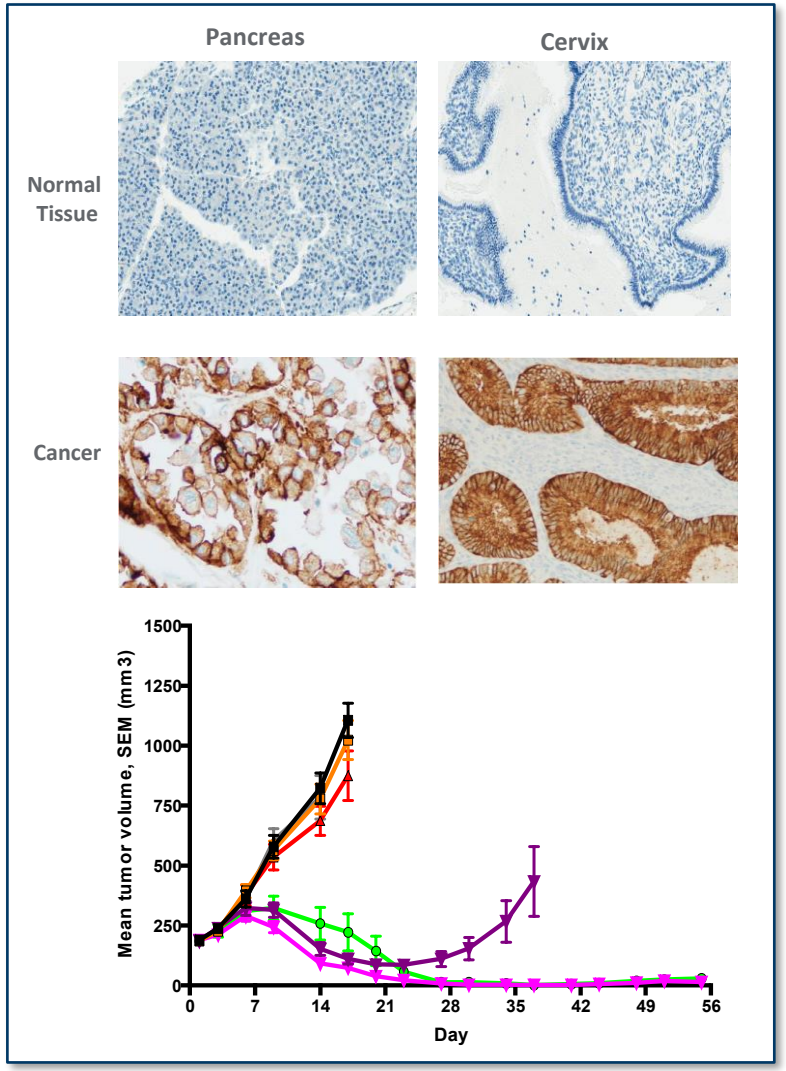
- Overexpressed in many solid tumors

TF-ADC approach clinically validated activity in cervical cancer

- Bleeding AEs due to Ab interference with TF function
- First generation linker/payload

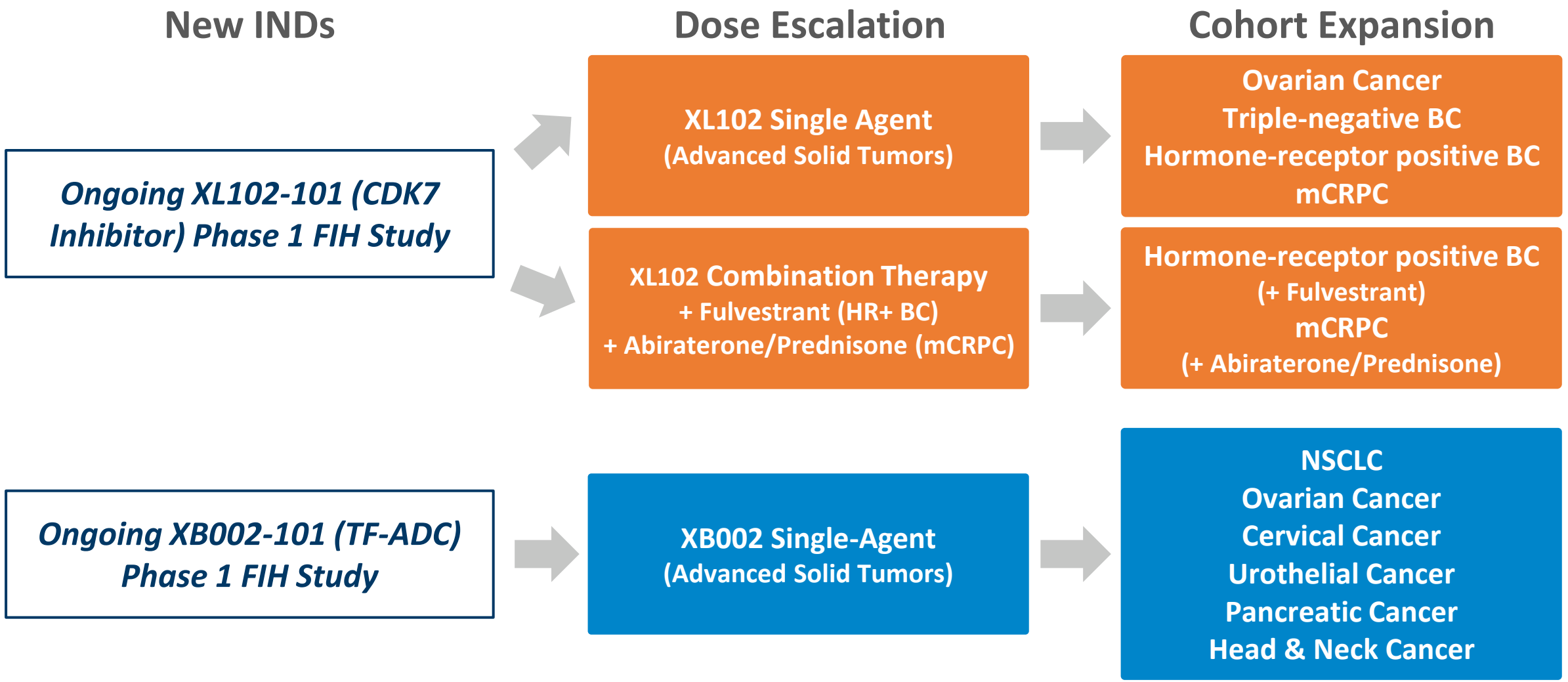
XB002 TF antibody has significant advantages

- Next-generation linker payload, improved TI in preclinical studies
- No inhibition of coagulation



TF = tissue factor
ADC = antibody-drug conjugate
AE = adverse event
Ab = antibody
TI = therapeutic index

XL102 and XB002 Phase 1a/b Development Plans



IND = Investigational New Drug application
CDK7 = cyclin-dependent kinase 7
FIH = first-in-human

TF = Tissue Factor
ADC = antibody-drug conjugate
HR+ = hormone-receptor positive

BC = breast cancer
mCRPC = metastatic castration-resistant prostate cancer
NSCLC = non-small cell lung cancer

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Conclusion

We are advancing a robust portfolio of preclinical and early clinical programs

- XL092, XL102 and XB002 in Phase 1
- Potential for one additional IND this year
- Small molecules and biologics

We have significant momentum that could yield multiple INDs and DCs in the coming years

- A total of ~25 preclinical programs
- More than 200 dedicated FTEs across Exelixis and its partners

Pipeline will be augmented through BD efforts as appropriate assets are identified

IND = Investigational New Drug application
DC = development candidate
BD = business development

Building a Differentiated Next-Generation Pipeline in Oncology

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