Transforming into a Global, Multi-Product Oncology Company

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Forward-Looking Statements

This presentation, including any oral presentation accompanying it, contains forward-looking statements, including, without limitation, statements related to: Exelixis' belief that in 2022, the company is on the path to becoming a global multi-product oncology company with a diverse and expanding pipeline of therapeutic candidates; the potential for up to three pivotal trial top-line readouts for cabozantinib in 2022 to create opportunities for CABOMETYX label-expansion; Exelixis' anticipated clinical pipeline milestones for 2022, including the planned launch of an XL092 pivotal trial program during the first half of 2022 and expansion of the XL092, XL102, XB002 clinical programs across new indications and combinations, with initial phase 1 data readouts expected during 2022; Exelixis' discovery plans for 2022, including advancing up to five development candidates across both small molecules and biotherapeutics into preclinical development and leveraging the company's collaboration network to generate novel ADCs and other biotherapeutics; Exelixis' expansion initiatives, including the expected completion of new facilities to support our expanding pipeline and organization in the first half of 2022 and plans for EXEL East to build toward a global footprint; Exelixis' 2022 financial guidance; Exelixis' belief that recent accomplishments set foundation for transformational 2022; anticipated cabozantinib clinical program milestones in 2022, including multiple data readouts from COSMIC and CONTACT trials and completion of enrollment for CONTACT-02; Exelixis' expectations regarding the clinical and therapeutic potential of XL092, including its potentially improved safety profile, to set new standards of care with novel treatment regimens; Exelixis' expectations regarding the clinical and therapeutic potential of XB002 and belief that the recently amended collaboration agreement with Iconic creates an opportunity for a potential TF-targeting franchise; Exelixis' expectations regarding the clinical and therapeutic potential of XL102 and belief that XL102 has the potential to be best-in-class due to the combination of selectivity, potency and oral bio-availability; Exelixis' development plans for XL114, including the initiation of a phase 1 trial in patients with NHL during the first half of 2022; Exelixis' belief that recent progress enables Exelixis' return to a discovery powerhouse in 2022; Exelixis' belief that XB010 has the potential for a good therapeutic index and expectation that XB010 will enter preclinical development shortly; and Exelixis' anticipated milestones for 2022 and summary of key corporate objectives to maximize benefit for patients and drive shareholder value in 2022 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 continuing COVID-19 pandemic and its impact on Exelixis' clinical trial, drug discovery and commercial activities; 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 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' 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 products; 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 discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 2, 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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Note Regarding Preliminary Financial Results

This presentation includes Exelixis' preliminary financial results for the quarter and fiscal year ended December 31, 2021. Exelixis is currently in the process of finalizing its full financial results for the quarter and fiscal year ended December 31, 2021, and the preliminary financial results presented in this presentation are based only upon preliminary information available to Exelixis as of January 9, 2021. Exelixis' preliminary financial results should not be viewed as a substitute for full audited financial statements prepared in accordance with U.S. GAAP, and undue reliance should not be placed on Exelixis' preliminary financial results. Exelixis' independent registered public accounting firm has not audited or reviewed the preliminary financial results included in this presentation or expressed any opinion or other form of assurance on such preliminary financial results. In addition, items or events may be identified or occur after the date of this presentation due to the completion of operational and financial closing procedures, final audit adjustments and other developments may arise that would require Exelixis to make material adjustments to the preliminary financial results included in this presentation. Therefore, the preliminary financial results included in this presentation may differ, perhaps materially, from the financial results that will be reflected in Exelixis' audited consolidated financial statements for the fiscal year ended December 31, 2021.

2022: On the Path to Becoming a Global Multi-Product Oncology Company with a Diverse and Expanding Pipeline of Therapeutic Candidates

CABOMETYX® commercial success provides the fuel for growth

- ~$1.08B in preliminary FY2021 net product revenues
- Up to three pivotal top-line readouts create opportunities for label expansion

Multiple clinical pipeline milestones anticipated this year

- Launch pivotal trial program for XL092, next-generation oral TKI, in 1H 2022
- Expand XL092, XL102 and XB002 clinical programs, with initial phase 1 data this year
- Advance all three compounds across new indications and combinations

Robust EXEL Discovery network making significant progress

- 10+ programs advancing through internal and collaborative efforts
- Up to five development candidates anticipated across small molecules and biotherapeutics
- Leverage collaboration network to generate novel ADCs and other biotherapeutics

Ambitious expansion initiatives underway

- Completion in 1H 2022 of new facilities to support our expanding pipeline and organization
- Plans for EXEL East: Access to biopharma talent and build toward global footprint

TKI = tyrosine kinase inhibitor
ADC = antibody-drug conjugate

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A Broad Network of Partnerships and Collaborations to Drive Rapid Growth

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 Collaborations

AURIGENE
Accelerating Discovery

SSTI®
StemSynergy Therapeutics, Inc.

invenra

ICONIC THERAPEUTICS

Catalent

NBE therapeutics
Innovating medicines

WuXi Biologics
Global Solution Provider

ADAGENE

GAMAMABS PHARMA

STORM THERAPEUTICS

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Significant Growth for CABOMETYX in 2021, Strong Momentum into 2022

2021 Performance Summary

- CABOMETYX maintained strong demand growth driven by CheckMate -9ER 1L RCC launch in January 2021
  - +50% TRx / +40% NRx growth Q4'21 vs. Q4'20
- CABOMETYX continues to have the leading market share among TKIs
  - TRx and NRx share continued to increase Q1'21 to Q4'21 (TRx: 30% → 35% / NRx: 29% → 33%)

Commercial Milestones

☑ CheckMate -9ER (1L RCC) launch was the key driver of growth in 2021
- Longer DOT of the CABOMETYX + nivolumab combination expected to provide continued future growth
- No significant impact from competition on CABOMETYX market share

☑ COSMIC-311 (DTC) launched on Sept. 20, 2021
- Exceeded expectations and provided incremental growth to larger RCC business

5 Consecutive Quarters of TRx / NRx Market Share Growth

1L = first-line
TKI = tyrosine kinase inhibitor
RCC = renal cell carcinoma
DTC = differentiated thyroid cancer

TRx = total prescriptions
NRx = new prescriptions
DOT = duration of therapy

Source: IQVIA data ending 12/31/2021
Includes Cabometyx, Inlyta, Sunitinib, Votrient, Lenvima; Includes scripts across indications
**Sunitinib includes TRx and NRx from generic Sutent*

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Preliminary Unaudited FY/Q4 2021 Financial Results

	Fourth Quarter 2021	Full Year 2021
Net Product Revenues	~ $300M	~ $1.08B
COGS*	~ 4.3%	~ 4.9%
R&D Expenses	~ $220M	~ $690M
SG&A Expenses	~ $100M	~ $400M

The table above does not include Fourth Quarter or Full Year 2021 Total Revenues preliminary results as Exelixis is waiting for its partners to provide final confirmation of their 2021 cabozantinib net sales performance. Exelixis will provide these metrics when the company reports its fourth quarter and full year 2021 financial results on February 17, 2022.

** COGS = Cost of goods sold*

Note: The preliminary 2021 financial information presented in these slides has not been audited and is subject to change. The complete Exelixis Fourth Quarter and Full Year 2021 Financial Results are planned for release after market on Thursday, February 17, 2022. See Slide 1 – Forward-looking Statements and Good Faith Revenue Estimate. See Slide 2 – Note Regarding Preliminary Financial Results.

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2022 Financial Guidance*

	Financial Guidance (Provided January 9, 2022)
Net Product Revenues	$1.325B - $1.425B
COGS**	5% - 6% of net product revenues
R&D Expenses	$725M - $775M Includes **$45M** of non-cash stock-based compensation expense
SG&A Expenses	$400M - $450M Includes **$50M** of non-cash stock-based compensation expense
Effective Tax Rate	20% - 22%

The table above does not include Total Revenues 2022 Guidance for the same reason as stated on the previous slide. Exelixis will provide this guidance when the company reports its fourth quarter and full year 2021 financial results on February 17, 2022.

The above amounts are intended to represent GAAP guidance.
**The financial guidance above reflects U.S. GAAP amounts.*
***COGS = Cost of goods sold*

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Recent Accomplishments Set Foundation for Transformational 2022

Regulatory Success

- ☑ **U.S. FDA Approvals of sNDAs** for CheckMate -9ER (1L RCC) and COSMIC-311 (2L+ DTC)
- ☑ **CABOMETYX approvals across partner networks** Ipsen and Takeda (CheckMate -9ER)

Commercial Execution

- ☑ **Generated >$1B in 2021 total and net product revenues** in the U.S. for the first time
- ☑ **~45% YoY net product revenue growth** driven by CABOMETYX RCC business

Significant Pipeline Progress

- ☑ **Phase 3 enrollment completions** COSMIC-313 (1L RCC), CONTACT-01 (NSCLC), -03 (RCC)
- ☑ **Phase 1 initiations** XL102 (CDK7 inhibitor) and XB002 (TF-targeting ADC)
- ☑ **New clinical collaboration agreements for XL092** Merck KGaA, Bristol Myers Squibb
- ☑ **Expansions and execution across ongoing collaborations**
  Invenra (additional 20 targets), Aurigene (XL114), Iconic (broad rights to XB002)
- ☑ **Robust business development activity** Adagene, WuXi, GamaMabs, STORM, Iconic

1L = first-line
2L = second-line
RCC = renal cell carcinoma
sNDA = supplemental New Drug Application
DTC = differentiated thyroid cancer
NSCLC = non-small cell lung cancer
CDK7 = cyclin-dependent kinase 7
TF = tissue factor
ADC = antibody-drug conjugate

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Continued Success of the CABOMETYX Franchise

Potential Label Expansion Opportunities in 2022

CABOMETYX Poised for Continued Growth Through Lifecycle Expansion

Successful Execution of Existing Label

METEOR
Ph3: 2L RCC

CABOSUN
Ph2: 1L RCC

CELESTIAL
Ph3: 2L aHCC

CheckMate -9ER
Ph3: 1L RCC

COSMIC 311
Ph3: 2L DTC

Potential Additional Expansion Opportunities

COSMIC 312
Ph3: 1L aHCC

COSMIC 313
Ph3: 1L RCC

CONTACT-01
Ph3: NSCLC

CONTACT-02
Ph3: mCRPC

CONTACT-03
Ph3: RCC

1L = first-line
2L = second-line
RCC = renal cell carcinoma
DTC = differentiated thyroid cancer
aHCC = advanced hepatocellular carcinoma
mCRPC = metastatic castration-resistant prostate cancer
NSCLC = non-small cell lung cancer

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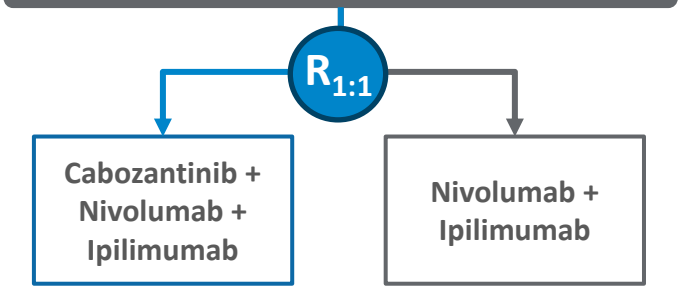
COSMIC Clinical Program: Multiple Data Readouts Anticipated in 2022

Exelixis-sponsored Studies Evaluating Cabozantinib in Combination with ICI's Across Broad Range of Tumor Types

COSMIC 313

Phase 3 Trial *(Collaboration with BMS)*

1L Advanced or Metastatic RCC
- Intermediate- or poor-risk RCC as defined by IMDC criteria
- Measurable disease per RECIST 1.1



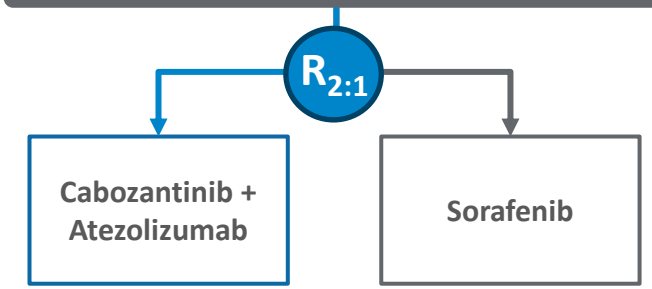
Key Endpoints
- **Primary:** PFS
- **Secondary:** OS and ORR

Top-line results expected in the first half of 2022

COSMIC 312

Phase 3 Trial *(Collaboration with Roche)*

1L Advanced HCC
- Not amenable to curative treatment (ablation, transplant, surgery, etc.)
- Measurable disease per RECIST 1.1



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

Final OS analysis expected in early 2022

COSMIC 021

Phase 1b Basket Trial *(Collaboration with Roche)*

Multiple Tumor Types Across 24 Cohorts, including:

ccRCC* (n=30) Clear cell, treatment naïve	**CRPC* (n=30 → expanded to 80)** Prior enzalutamide or abiraterone
nccRCC* (n=30) Non-clear cell, treatment naïve	**NSCLC* (n=30 → expanded to 80)** Prior ICI therapy
UC* (n=30) Prior platinum-chemotherapy	**Colorectal adenocarcinoma (n=30)** Prior fluoropyrimidine chemo

Cabozantinib + Atezolizumab

Key Endpoint

Preliminary Efficacy based on ORR per RECIST 1.1

Data from CRC cohort to be presented at ASCO GI; informed first XL092 pivotal trial

1L = first-line
RCC = renal cell carcinoma
ccRCC = clear cell RCC
nccRCC = non-clear cell RCC
HCC = hepatocellular carcinoma
CRPC = castration-resistant prostate cancer
NSCLC = non-small cell lung cancer
UC = urothelial carcinoma
CRC = colorectal cancer
PFS = progression-free survival
OS = overall survival
ORR = objective response rate
IMDC = International Metastatic RCC Database Consortium
BIRC = blinded independent review committee
ICI = immune checkpoint inhibitor

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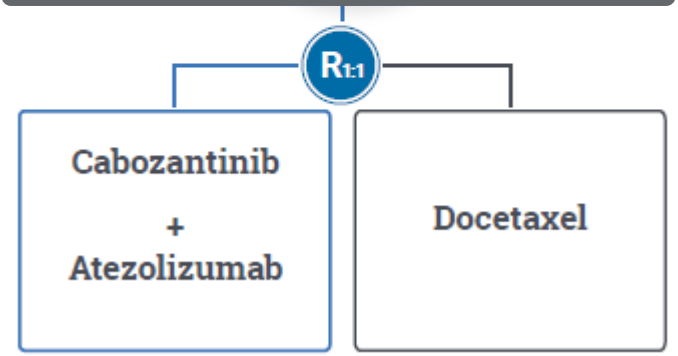
CONTACT Phase 3 Pivotal Trials: Potential for Two Data Readouts in 2022

Clinical Collaboration Between Exelixis and Roche

CONTACT-01

Metastatic NSCLC
- Squamous & non-squamous
- No EGFR or ALK mutations
- Prior PD-1/L1 and platinum-CTX

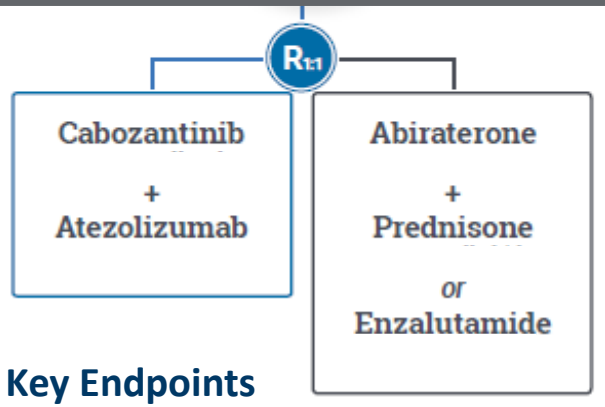


Key Endpoints
- **Primary:** OS
- **Secondary:** PFS, ORR, INV-DOR

Enrollment complete
Initial data expected in 2H 2022

CONTACT-02

Metastatic CRPC
- Measurable visceral disease or extrapelvic adenopathy
- 1 prior NHT

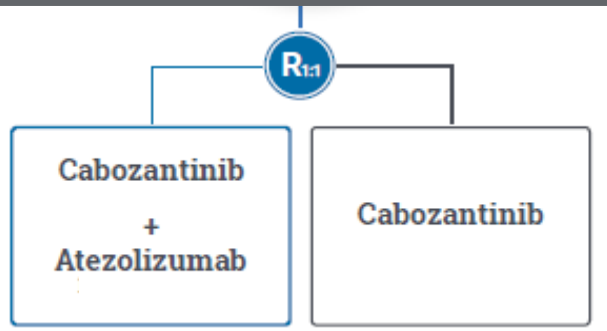


Key Endpoints
- **Primary:** BIRC-PFS, OS
- **Secondary:** BIRC-ORR, DOR, PSA

Anticipate completing enrollment by YE 2022

CONTACT-03

Advanced or Metastatic RCC
- ccRCC or nccRCC; sarcomatoid features allowed
- Progression on or after 1 prior ICI



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

Enrollment complete
Initial data expected in 2H 2022

NSCLC = non-small cell lung cancer
CRPC = castration-resistant prostate cancer
RCC = renal cell carcinoma
OS = overall survival
PFS = progression-free survival
ORR = objective response rate
DOR = duration of response
INV = investigator-assessed
BIRC = blinded independent review committee
PSA = prostate-specific antigen
NHT = novel hormonal therapy
ICI = immune checkpoint inhibitor

Building a Differentiated Oncology Pipeline

Advancing a Diverse and Expanding Portfolio of Small Molecule and Biotherapeutic Candidates

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Diverse and Rapidly Evolving Pipeline Beyond Cabozantinib

Encompassing Multiple Modalities & Mechanisms across Small Molecules and Biologics

Program Name	Mechanism	Discovery / Preclinical	IND	Phase 1a	Phase 1b	Phase 2 / 3
XL092	Next-generation TKI targeting MET/VEGFR/AXL/MER					
XB002	Next-generation TF-targeting ADC					
XL102	Potent, selective, orally bioavailable CDK7 inhibitor					
XL114	CARD11-Bcl10-MALT1 pathway inhibitor					
XB010	Next-generation 5T4 targeting ADC					
Aurigene Collaboration Programs	CDK12 and MALT1 inhibitors					
Invenra Collaboration Programs	PD-L1 + CD47 and PD-L1 + NKG2A					
StemSynergy Collaboration Programs	CK1α activators and selective Notch inhibitors					
STORM Therapeutics Collaboration Program	ADAR1					
Exelixis Discovery Programs	G9a inhibitors					
Biologics Programs *Invenra, NBE Therapeutics, Catalent, GamaMabs WuXi & Adagene Collaborations*	AMHR2, ROR1/2, TF, DLL3					

Additional undisclosed programs ongoing with Aurigene, Invenra, STORM Therapeutics and through internal Exelixis Discovery

TKI = tyrosine kinase inhibitor
CDK7 = cyclin-dependent kinase 7
CK1α = casein kinase 1 alpha
TF = tissue factor
ADC = antibody-drug conjugate
IND = Investigational New Drug application
CDK12 = cyclin-dependent kinase 12
NKG2A = natural killer cell receptor group 2A
ADAR1 = adenosine deaminase 1

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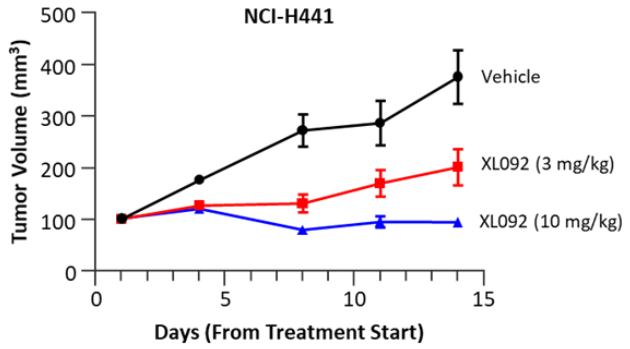
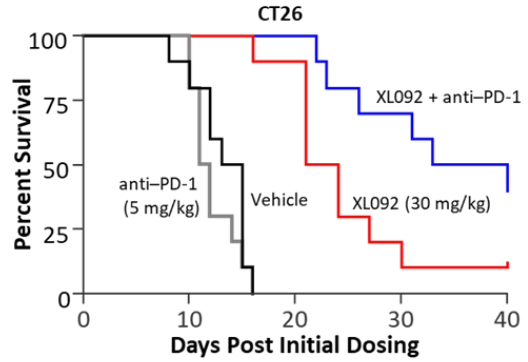
XL092: Next-generation Multi-targeted TKI with Broad Therapeutic Potential

Similar target profile to cabozantinib with shorter clinical half-life (~24 hrs vs ~99 hrs)

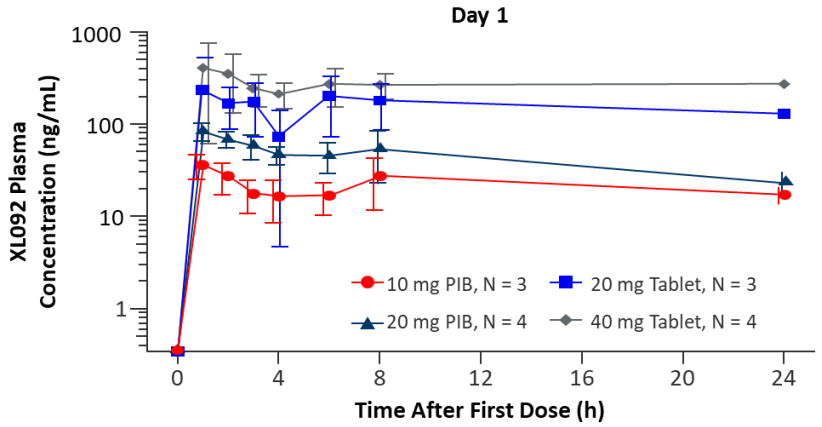
- Potent inhibitor of MET, VEGFR2, AXL and MER in biochemical / cellular assays
- Structure intended to modulate half-life

Strong *in vivo* activity at well tolerated doses in xenograft models as single agent and in combination with PD-1 antibody





Phase 1 Clinical Pharmacokinetics



- Exposure increased with increasing doses for PIB and tablet formulation at steady state
- Mean terminal $T_{1/2}$ of 20-28 hours

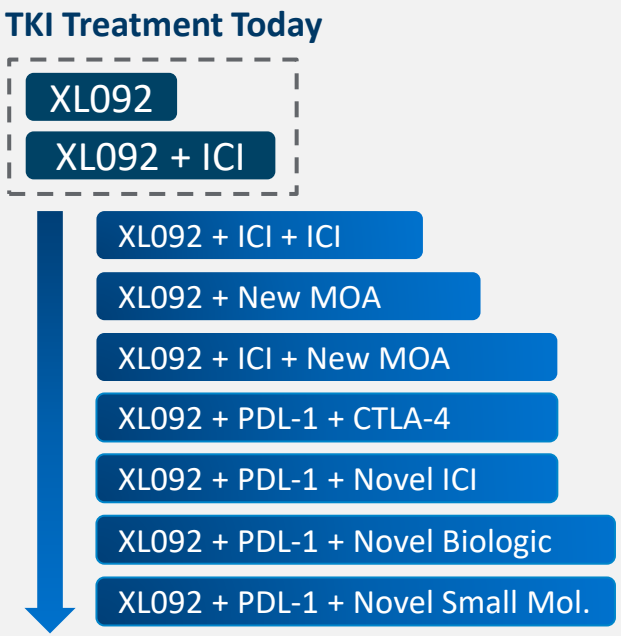
TKI = tyrosine kinase inhibitor
PIB = powder in bottle
$T_{1/2}$ = half-life

Extensive Development Plan Supported by XL092's Differentiated Clinical Profile and Potentially Improved Safety Profile – Anticipated Pivotal Trial Initiation in 1H 2022

XL092 Development Strategy	Potential Tumors / Settings
FAST TO MARKET High unmet need indications with **potential for rapid development**	Endometrial, Sarcoma, CRC, NETs
MOVING BEYOND CABOZANTINIB Build on clinical experience in tumors where cabozantinib is approved or being developed, with the goal to develop **new standards of care** with novel and expanded combinations	RCC, HCC, mCRPC, NSCLC
EXPANDING TKI FOOTPRINT **Explore new indications with ICI presence** where XL092 can potentially improve outcomes through cooperative activity with ICI or re-establishing immuno-sensitivity	Urothelial, Gastric, Ovarian, Melanoma
NEW OPPORTUNITIES **Expand to treatment settings that may be accessible to XL092** with potentially improved tolerability due to shorter half-life	Neoadjuvant, Adjuvant, Maintenance, mCSPC

Combination Approaches

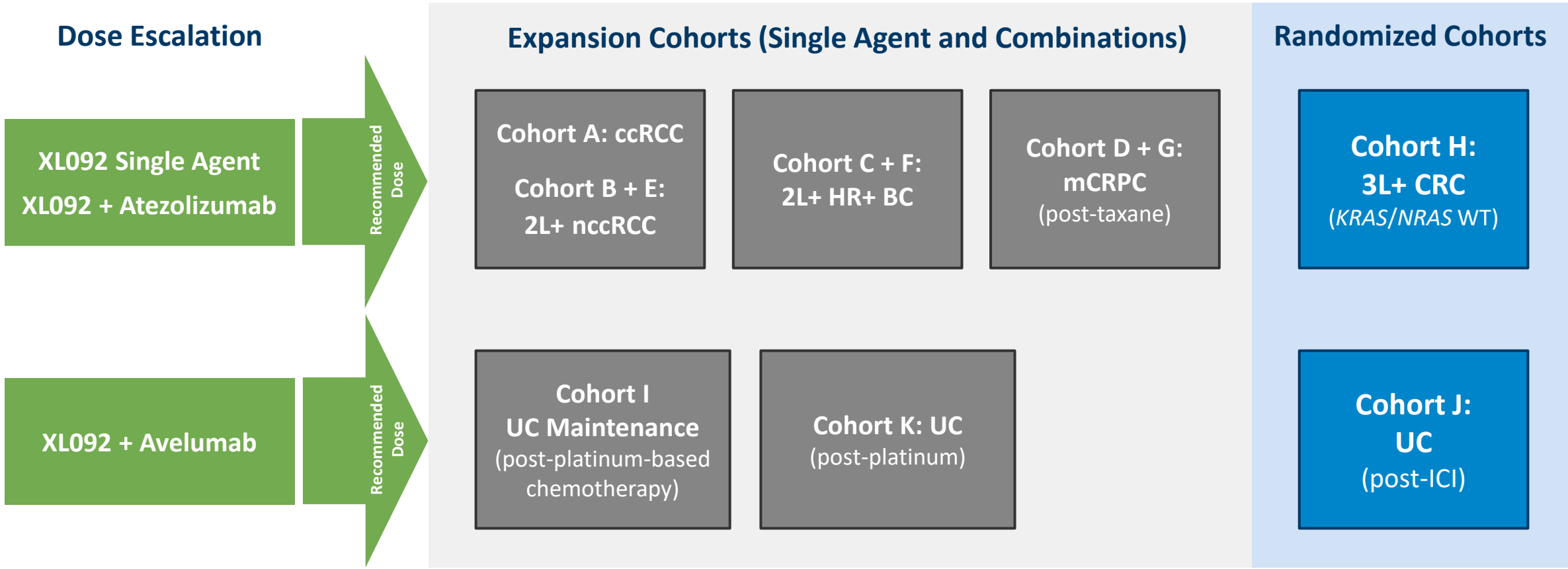
Expanding Beyond ICI-TKI Success to set new standards of care with triplet and novel combinations based on indication, therapeutic setting and line of therapy



TKI = tyrosine kinase inhibitor
CRC = colorectal cancer
NETs = neuroendocrine tumors
RCC = renal cell carcinoma
HCC = hepatocellular carcinoma
mCRPC = metastatic castration-resistant prostate cancer
NSCLC = non-small cell lung cancer
mCSPC = metastatic castration-sensitive prostate cancer
ICI = immune checkpoint inhibitor
MOA = mechanism of action
CTLA = cytotoxic T-lymphocyte-associated protein

XL092: STELLAR-001 Phase 1 Study Design

Exelixis-sponsored Study in Collaboration with Roche and Merck KGaA



First global phase 3 pivotal trial initiation in CRC expected in the first half of 2022

2L = second-line
3L = third-line
CRC = colorectal cancer
ccRCC = clear cell renal cell carcinoma
nccRCC = non-clear cell RCC
UC = urothelial carcinoma
mCRPC = metastatic castration-resistant prostate cancer
HR+ BC = hormone receptor positive breast cancer
ICI = immune checkpoint inhibitor

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XL092: STELLAR-002 Phase 1b Study Design

Exelixis-sponsored Study in Collaboration with Bristol Myers Squibb

Dose Escalation Phase

XL092 + Nivolumab

XL092 + Nivolumab + BEMPEG

XL092 + Nivolumab + Ipilimumab

Recommended Dose

Randomized Expansion Cohorts

1L and 2L ccRCC, nccRCC

UC (ICI naïve/ experienced)

mCRPC (post-NHT)

Each expansion cohort has multiple treatment arms which may also include XL092 single agent and standard of care ICI/IL-2 combination therapies

Dose escalation phase currently enrolling; plans to expand study into potential new tumor types, and IO and other targeted therapy combination regimens throughout 2022

1L = first-line
2L = second-line
UC = urothelial carcinoma
ccRCC = clear cell renal cell carcinoma
nccRCC = non-clear cell RCC
ICI = immune checkpoint inhibitor
mCRPC = metastatic castration-resistant prostate cancer
NHT = novel hormonal therapy
IO = immunotherapy

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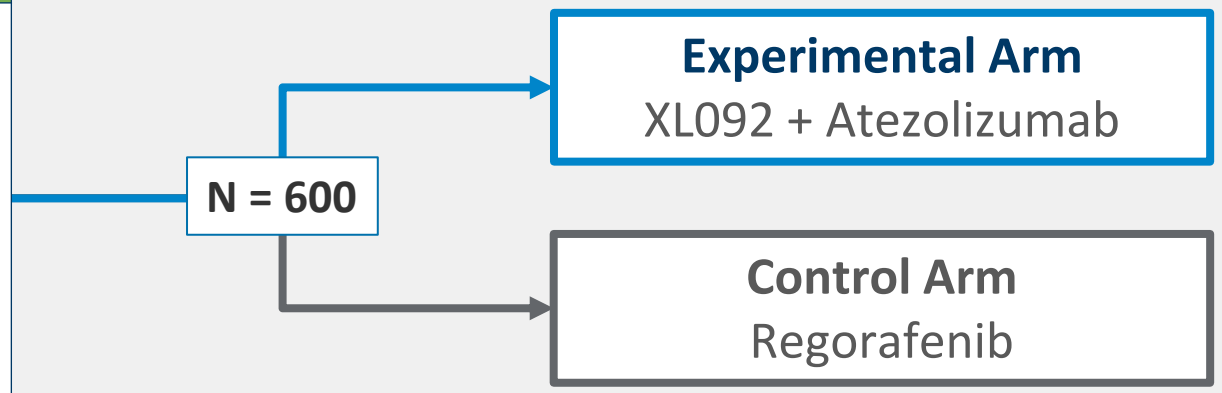
STELLAR-303: Phase 3 Trial Design for First Pivotal Study of XL092 in 3L+ CRC

Exelixis-sponsored Study with Drug Supply Agreement with Genentech/Roche

STELLAR-303 (Ph 3)

- A study of XL092 + atezolizumab in microsatellite stable metastatic colorectal cancer patients who have progressed after or intolerant to standard of care therapy
- Requires documented RAS status



Stratification Factors

- Geographical region (Asia vs. other)
- Documented RAS status (wild type vs. mutant)
- Left vs. Right-sided disease

Key Study Objectives

- **Primary:** OS (ITT RAS wild type)
- **Additional:** PFS, ORR, DOR, QOL

OS = overall survival
PFS = progression free survival
ORR = objective response rate
ITT = intent to treat
DOR = duration of response
QOL = quality of life
3L = third-line
CRC = colorectal cancer
RAS = rat sarcoma virus

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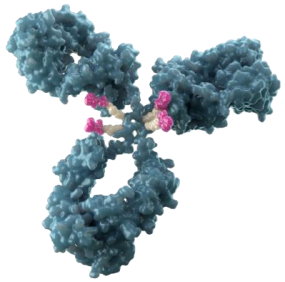
XB002: Building the Foundation for a TF-Targeting Oncology Franchise



Tissue factor is normally involved in mediating coagulation

- Overexpressed in many solid tumors: TF-ADC approach clinically validated in cervical cancer

XB002 TF antibody has significant advantages over 1st generation TF-targeted therapies

- Improved preclinical TI: binder non-competitive with Factor VII, next-generation linker-payload
- Early clinical experience: excellent stability of intact ADC and low free payload concentration; early safety data are encouraging, including no bleeding events observed to date

XB002-101: Phase 1 Clinical Study Ongoing

Dose Escalation	Cohort Expansion
XB002 Single-Agent (Advanced Solid Tumors)	**NSCLC, Ovarian, Cervical, Urothelial, Squamous Cell Head and Neck, Pancreatic, Esophogeal, mCRPC, TNBC and HR+ BC**

XB002 Development Plans

- Expand development as monotherapy and in combination with ICIs and other targeted therapies across wide range of tumor types
- Recently amended agreement with Iconic Therapeutics creates opportunity for potential TF-targeting oncology franchise
- Initial clinical data expected in 2022

TF = tissue factor
ADC = antibody-drug conjugate
TI = therapeutic index
ICI = immune checkpoint inhibitor

NSCLC = non-small cell lung cancer
mCRPC = metastatic castrate resistant prostate cancer
TNBC = triple negative breast cancer
HR+ BC = hormone receptor positive breast cancer

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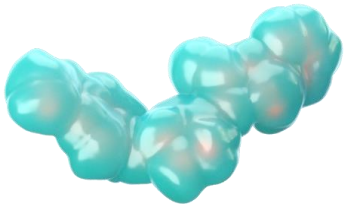
XL102: Covalent Orally Available CDK7 Inhibitor with Broad Potential in Oncology



CDK7 regulates cell cycle progression and transcription

- Potential for activity in CDK4/6 inhibitor resistant tumors - combination with targeted therapies

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

- Early clinical experience: near complete target engagement in PBMCs

XL102-101: Phase 1 Clinical Study Ongoing

Dose Escalation	Cohort Expansion
XL102 Single Agent (Advanced Solid Tumors)	**Ovarian Cancer** **Triple-negative BC** **HR+ BC** **mCRPC**
XL102 Combination Therapy + Fulvestrant (HR+ BC) + Abiraterone/Prednisone (mCRPC)	**HR+ BC** (+ Fulvestrant) **mCRPC** (+ Abiraterone / Prednisone)

XL102 Development Plans

- Dose escalation phase enrollment ongoing in single-agent and combination therapy cohorts
- Initiation of cohort expansion phase across combination regimens expected in 1H 2022, based on early clinical signals
- Clinical updates and initial data readout expected in 2022

CDK = cyclin-dependent kinase
PBMC = peripheral blood mononuclear cell
HR+ BC = hormone receptor positive breast cancer
mCRPC = metastatic castration-resistant prostate cancer

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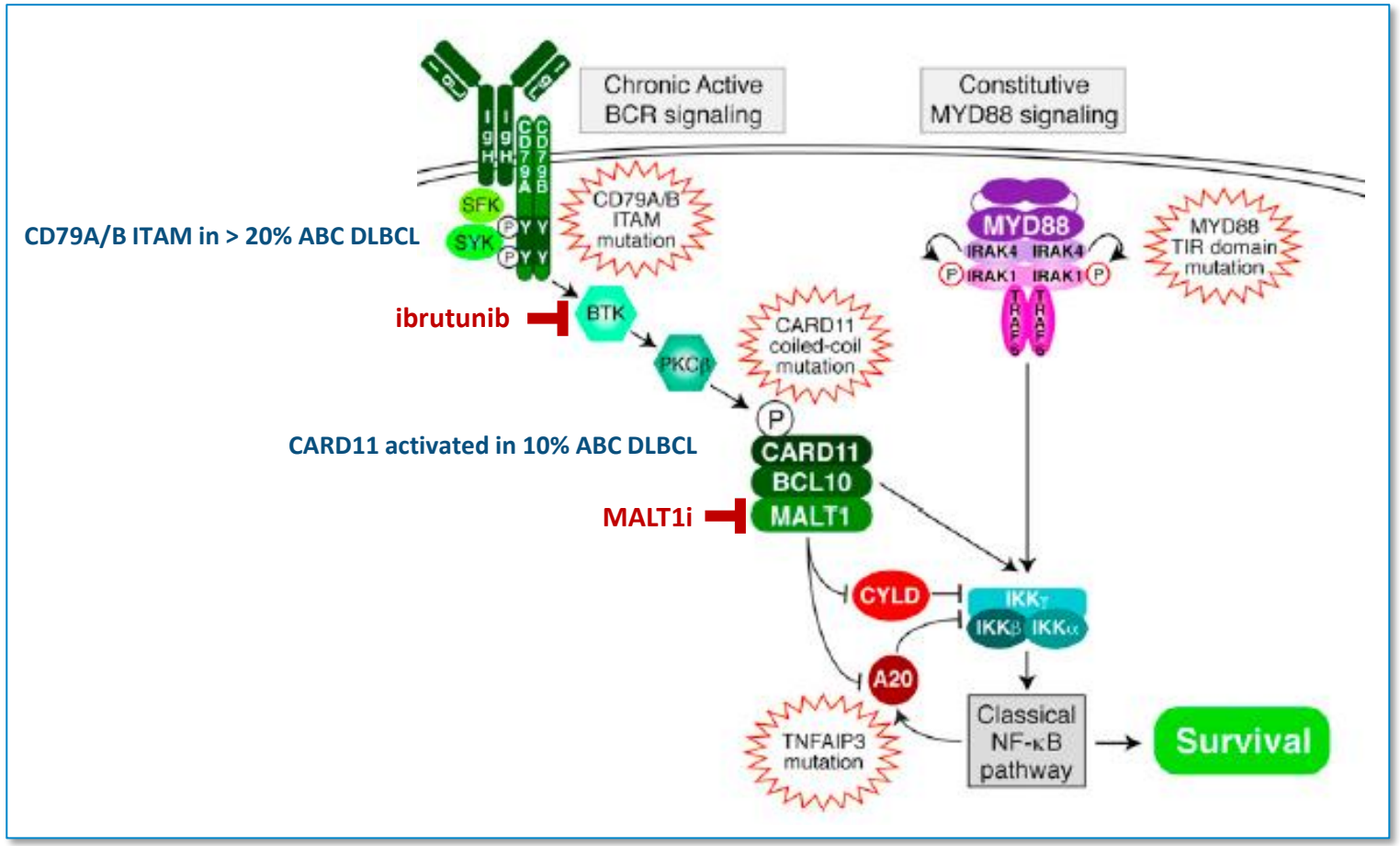
XL114: Inhibitor of MALT1 Activation and B-Cell Lymphoma Cell Growth



Source: Young and Staudt, Cancer Cell 22 (2012)

XL114 inhibits the CBM signaling pathway that promotes lymphocyte survival and proliferation

- Acts downstream of BTK
- Activity in BTK resistant lymphoma models and subsets of BCL where BTK inhibitors are not active

XL114 IND is active and phase 1 trial initiation in NHL expected in the first half of 2022

ABC = activated B-cell subtype
DLBCL = diffuse large B-cell lymphoma
BCL = B-cell lymphoma
NHL = non-Hodgkin's lymphoma
IND = Investigational New Drug application
BTK = Bruton's tyrosine kinase
CBM = CARD11-BCL10-MALT1

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A Strong Foundation of Discovery

Driving Rapid Growth Through Internal Expansion and a Robust Network of Collaborations

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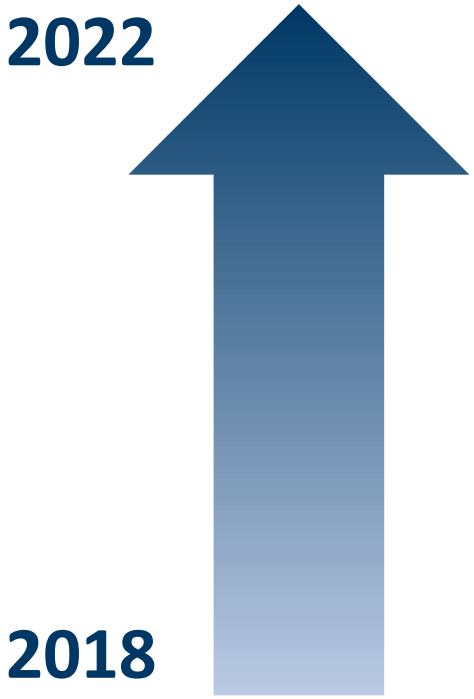
Significant Progress and Execution Over the Past Few Years Enables Exelixis' Return to a Discovery Powerhouse in 2022



10+ Discovery programs advancing through internal and collaborative efforts

Up to 5 New development candidates expected to progress into preclinical development

4 New IND candidates from 2019-2021 (XL092, XB002, XL102, XL114)

~3x Increase in available lab space at Alameda HQ enhancing small molecule discovery capabilities

10 Pipeline collaborations established between 2018-2021 across biologics and small molecules to complement internal discovery efforts

- ***Discovery programs encompass multiple modalities and mechanisms across small molecules and biotherapeutics***
- ***Established a next-generation ADC platform through an external collaboration network focused on identification and optimization of ADCs with excellent* in vitro *and* in vivo *activity***

IND = Investigational New Drug
ADC = antibody-drug conjugate

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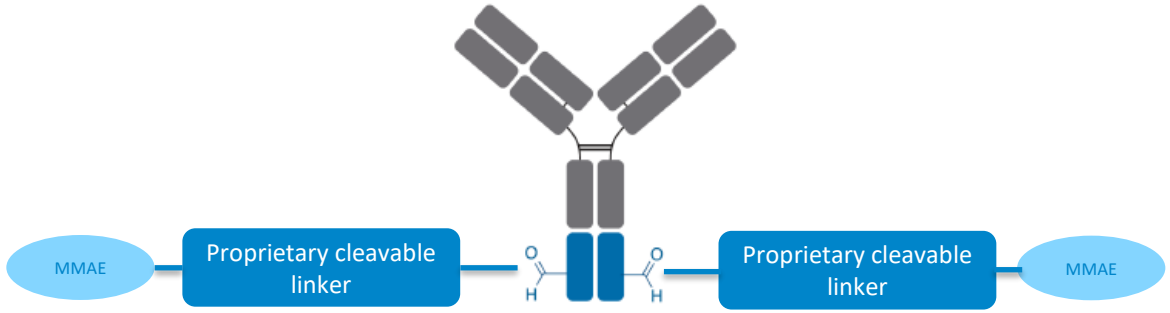
XB010: Newly Designated Development Candidate, 5T4-MMAE ADC

First custom ADC generated through Exelixis' collaboration network

- High affinity 5T4 antibodies sourced from Invenra
- Utilizes Catalent SMARTag® conjugation platform to produce homogenous ADC with defined DAR, and incorporated highly stable next-generation proprietary linker technology (requires two cleavage events to release payload)
- Highly efficacious and well tolerated *in vivo*, with potential for a good therapeutic index

Targets oncofetal antigen 5T4

- Overexpressed on broad range of solid tumors including NSCLC, HNSCCs, gastric and breast carcinomas



XB010 designated as DC in late 2021, expected to enter preclinical development shortly

ADC = antibody-drug conjugate
DAR = drug-to-antibody ratio
DC = development candidate
NSCLC = non-small cell lung cancer
HNSCC = head and neck squamous cell carcinoma
MMAE = monomethyl auristatin E

Additional Potential Development Candidates Progressing Toward Preclinical Development

ADC Development Candidates	
XB010	Target: oncofetal antigen 5T4; First custom generated Exelixis ADC
Multiple Potential DCs	Targets: AMHR2, ROR1/2, TF, DLL3; Utilize variety of partner conjugation technologies and payloads

Potential Bispecific Development Candidates	
Invenra #1	Target: PD-L1 + CD47; blocks macrophage checkpoint
Invenra #2	Target: PD-L1 + NKG2A; Promote NK cell activation

Potential Small Molecule Development Candidates	
Exelixis	Target: G9a inhibitors
Aurigene	Target: MALT1 and CDK12 inhibitors
StemSynergy	Target: Notch and CK1α activators
STORM Tx	Target: ADAR1

Additional early-stage programs are also in progress at the Exelixis discovery laboratories, as well as through our collaborations with Aurigene and STORM

ADC = antibody-drug conjugate
TF = tissue factor
CK1α = casein kinase 1 alpha
CDK12 = cyclin-dependent kinase 12
NKG2A = natural killer cell receptor group 2A
ADAR1 = adenosine deaminase 1

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Summary of Key Corporate Objectives to Maximize Benefit for Patients and Drive Shareholder Value in 2022 and Beyond

Commercial execution of CABOMETYX franchise to fuel plans for growth

- Maximize currently approved indications to continue to drive near-term revenue growth
- Complete ongoing pivotal COSMIC and CONTACT studies to extend label expansion opportunity

Build on success and clinical experience of cabozantinib to drive robust XL092 development plan

- Similar target profile to cabozantinib with potentially significantly improved safety enables blockbuster potential for XL092 across indications, tumor types and novel therapeutic combination regimens

Expansion of current clinical programs to maximize patient benefit and commercial opportunity

- Potential for broad new TF-targeting oncology franchise around XB002 and anti-TF antibody
- Expedite development of XL102 with combination regimens in new tumor types; initiate XL114 Phase 1 study

Execution across preclinical pipeline and collaborations to rapidly advance new programs into the clinic

- Continue legacy of small molecule discovery and maximize potential of next-generation ADC platform and biologics

Complete new facilities in Alameda to support growing pipeline and organization, begin buildout of EXEL East and continue targeted BD assessment to support expansion of product pipeline

TF = tissue factor
ADC = antibody-drug conjugate
BD = business development

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Anticipated Milestones for 2022

Program		Milestone
COSMIC-313	❑	Report top-line results in the first half of 2022 for phase 3 trial of triplet combination cabozantinib + nivolumab + ipilimumab vs nivolumab + ipilimumab in 1L RCC
COSMIC-312	❑	Report final OS data in early 2022 and file sNDA for cabozantinib + atezolizumab in 1L HCC, data dependent
CONTACT-01/-02/-03	❑	Report initial data in the second half of 2022 from pivotal trials of cabozantinib + atezolizumab in forms of NSCLC (CONTACT-01) and RCC (CONTACT-03). Complete enrollment in pivotal trial of cabozantinib + atezolizumab in mCRPC (CONTACT-02)
COSMIC-021	❑	Present data from CRC cohort of phase 1b trial of cabozantinib + atezolizumab at ASCO GI, on Jan. 22, 2022
XL092	❑	Initiate STELLAR-303 global phase 3 pivotal trial of XL092 + atezolizumab in 3L+ CRC in first half 2022
	❑	Initiate additional pivotal trials of XL092 global phase 3 program across various tumor types and combination regimens
	❑	Expand and report clinical updates from phase 1b STELLAR-001/-002 trials into new tumor types and combination therapies
XB002	❑	Expand development of XB002 as monotherapy and in combination with ICIs and other targeted therapies, broadly across tumor types, including NSCLC, UC, HNSCC, mCRPC, TNBC, HR+ BC, pancreatic, esophageal, ovarian and cervical cancers
	❑	Provide clinical updates and present initial data from ongoing phase 1 study
XL102	❑	Initiate cohort expansion of ongoing phase 1 study with combination regimens in HR+ BC, other tumor types in first half of 2022
	❑	Provide clinical updates and present initial data from phase 1 study
XL114	❑	Initiate dosing in phase 1 trial of XL114 in patients with NHL during the first half of 2022
Preclinical	❑	Advance up to five new development candidates across multiple modalities / mechanisms of small molecules and biologics

1L = first-line
3L = third-line
RCC = renal cell carcinoma
CRC = colorectal cancer
HCC = hepatocellular carcinoma
NSCLC = non-small cell lung cancer
UC = urothelial carcinoma
ICI = immune checkpoint inhibitor
sNDA = supplemental New Drug Application
mCRPC = metastatic castration-resistant prostate cancer
HNSCC = head and neck squamous cell carcinoma
HR+ BC = hormone receptor positive breast cancer
TNBC = triple negative breast cancer
PFS = progression-free survival
ORR = objective response rate
NHL = non-Hodgkin's lymphoma
OS = overall survival

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Q&A

Transforming into a Global, Multi-Product Oncology Company

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

40th Annual J.P. Morgan Healthcare Conference
January 10, 2022

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Appendix

Targets Overview – Small Molecules

Target	Description
CDK7	Cyclin-dependent kinase 7, activates downstream cell cycle regulatory kinases CDK4/6 and CDK1/2. Also promotes activity of ER and AR by phosphorylation of ER or AR transcription cofactor MED. Potential applicability in multiple tumors including ER+ breast, CRPC, ovarian, TNBC
G9a	Histone methyltransferase involved in regulating gene expression. Modulates MYC and b-catenin dependent gene expression. Inhibitors induce autophagy and promote immune recognition of tumors. Potential broad applicability (breast, CRC, melanoma etc)
MALT1	Paracaspase that plays a key role in b-cell receptor signaling as part of the CARD11/BCL10/MALT1 complex. Cleaves inhibitors of NFkB signaling. Activated in B-cell lymphomas, inhibitor would be active in BTKi resistant tumors. Potential emerging role in certain solid tumors and in immune suppression
CDK12	Cyclin-dependent kinase that regulates a subset of gene expression – not a cell cycle regulator. Regulates expression of DDR genes
Notch	Notch activation drives a program of gene expression through formation of a complex containing the Notch ICD. Notch signaling is upregulated in many tumors including breast, prostate, esophageal and T-ALL, and plays a role in driving cancer stem cell renewal
CK1α	Kinase that phosphorylates b-catenin and promotes its degradation. Downregulated in tumors, Activators induce b-catenin degradation. Potential broad applicability
ADAR1	Adenosine deaminase converts A to I in dsRNA, destabilizes ds thereby reducing activation of IFN/cytokine expression. Activity required for survival of up to 30% of solid tumors that have chronic stimulation of this pathway. Amplified in sqLC

Targets Overview – Biotherapeutics

Target	Description
CD47	Major macrophage checkpoint, inhibits tumor cell efferocytosis by TAMs
NKG2A	Inhibitory receptor expressed on NK cells and CD8+ T-cells. Ligand is HLA-E, overexpressed on a variety of solid tumors, not on normal tissues
AMHR2	Anti-Mullerian Hormone Receptor 2 plays role in male sexual differentiation during development, very restricted adult tissue expression. Overexpressed in multiple solid tumors including ovarian, cervical HCC, RCC, CRC, NSCLC
ROR1/2	RTK expressed during development but with restricted adult tissue expression . Overexpressed in multiple tumors e.g lymphomas, CRC, breast ovarian, gastric cancers
TF	Tissue factor, initiates coagulation cascade after tissue injury, binds factor VII. Overexpressed in multiple solid tumors e.g. cervical, pancreatic, gastric, lung, breast bladder
DLL3	Delta-like Ligand 3. Overexpressed in neuroendocrine tumors notably SCLC and NE-CRPC

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