# Building a Leading Multi-Product Oncology Company

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

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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 CABOMETYX has multi-billion-dollar revenue potential; the potential for Exelixis' 9 ongoing pivotal trials to drive revenue growth for cabozantinib in 2021 and beyond; the continued buildout of the Exelixis pipeline towards Exelixis' goal of becoming a multi-product company, including plans to progress XL092 into pivotal trials in 2021 and initiate new phase 1 trials for XL102, XB002 and potentially others in 2021; Exelixis' 2021 financial guidance; the potential for broad use of CABOMETYX in combination with Opdivo in 1L RCC, and potential label expansions for CABOMETYX following upcoming data readouts; Exelixis' anticipation of a projected annualized run-rate of approximately \$1.5 billion for U.S. RCC business by the end of 2022; market trends and sequencing dynamics in the RCC and HCC markets and the commercial potential for CABOMETYX in these markets; Exelixis' expectations for, and the related anticipated timelines for, completing enrollment in, conducting analyses of and obtaining top-line results from its ongoing potential label-enabling clinical studies evaluating cabozantinib, and if supported by the data, pursuing potential regulatory approvals; Exelixis' expectations regarding the clinical and therapeutic potential of XL092 to set new SOC with novel treatment regiments and development plans for XL092, including in combination with ICIs; and Exelixis' anticipated milestones and expectations for 2021. 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 forwardlooking 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 5, 2020, 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.



## **Note Regarding Preliminary Financial Results**

This presentation includes Exelixis' preliminary financial results for the quarter and fiscal year ended January 1, 2021. Exelixis is currently in the process of finalizing its full financial results for the quarter and fiscal year ended January 1, 2021, and the preliminary financial results presented in this presentation are based only upon preliminary information available to Exelixis as of January 10, 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 January 1, 2021.



## **Exelixis: Who We Are**



#### Successful commercial execution with CABOMETYX® in RCC and HCC

- Franchise in a product, with multi-billion-dollar potential
- 9 ongoing pivotal trials with label-enabling potential may drive revenue growth in
   2021 and beyond

#### Robust clinical development with goal of becoming a multi-product company

- XL092: next-generation TKI currently in Phase 1a/b; slated to progress into pivotal trials in 2021
- New Phase 1 trials for XL102, XB002 and potentially others in 2021

#### Proven history of drug discovery

- 4 EXEL approved drugs: CABOMETYX, COMETRIQ®, COTELLIC® and MINNEBRO®
- Advancing next-generation small molecules and biologics through internal research and collaborative efforts

Active business development to deploy cash and supplement internal efforts



## A Broad Network of Partnerships and Collaborations with Industry Leaders

# **Commercial Partnerships** Innovation for patient care Genentech A Member of the Roche Group Daiichi-Sankyo







## **Preliminary Unaudited FY/Q4 2020 Financial Results**

	Full Year 2020 Fourth Quarter 202	
Total Revenues	\$988 M	\$270 M
Net Product Revenues	\$741 M	\$200 M
COGS*	4.9%	4.5%
R&D Expenses	\$549 M \$155 M	
SG&A Expenses	\$295 M \$83 M	
Cash and Investments (at year-end 2020)	\$1.5 B	



## **2021 Financial Guidance**

	2021 Guidance (Provided January 10, 2021)
Total Revenues	\$1,150 M - \$1,250 M
Net Product Revenues	\$950 M - \$1,050 M
COGS*	5 - 6% of net product revenues
R&D Expenses	\$600 M - \$650 M Includes \$45 M in non-cash stock-based compensation
SG&A Expenses	\$375 M - \$425 M Includes \$60 M in non-cash stock-based compensation
Effective Tax Rate	20 - 22%
Cash and Investments** (at year-end 2021)	\$1.6 B - \$1.7 B



<sup>\*</sup>COGS = Cost of goods sold

<sup>\*\*</sup>This cash guidance does not include any potential new business development activity.
The financial guidance above reflects U.S. GAAP amounts.

## **Strong Execution in 2020 Sets the Stage for 2021**

# Clinical Execution

- Positive data readouts with label expansion potential CheckMate -9ER (1L RCC), COSMIC-021 (mCRPC), COSMIC-311 (DTC)
- ☑ Phase 3 trial enrollment completion COSMIC-312 (1L HCC)
- New pivotal trial initiations CONTACT-01 (NSCLC), -02 (CRPC), -03 (RCC)

## Regulatory Progress

- ☑ CheckMate -9ER sNDA filing Priority Review, February 20th PDUFA date
- ☑ CABOMETYX approvals across partner networks Ipsen and Takeda

## Pipeline Expansion

- ☑ IND accepted & near-term Phase 1 initiation XL102 (CDK7 inhibitor)
- ☑ Progressed XB002 towards IND filing and Phase 1 initiation
- **☑** Advanced XL092 and current preclinical compounds
- ✓ New business development deals Catalent and NBE-Therapeutics

CDK7 = cyclin-dependent kinase 7 PDUFA = Prescription Drug User Fee Act

IND = Investigational New Drug application

sNDA = supplemental New Drug Application



# Clinical Readouts in 2020 Highlight Cabozantinib's Strong Activity Across Various Indications, Tumor Types and Combinations

Indication	Dataset	Treatment	Key Results
2L HCC	CheckMate 040 ASCO GI	Cabo + Nivo Cabo + Nivo + Ipi	<ul> <li>mOS = 21.5 m, mPFS = 5.4 m, 19% ORR</li> <li>mOS not yet reached, mPFS = 6.8 m, 29% ORR</li> </ul>
1L/2L mCRPC	COSMIC-021 Cohort 6 ASCO GU	Cabo + Atezo	<ul><li>32% ORR and 80% DCR</li><li>mDOR = 8.3 m</li></ul>
2L/3L NSCLC	COSMIC-021 Cohort 7 ASCO	Cabo + Atezo	■ 27% ORR, DCR = 83%, and mPFS = 4.2 m
2L+ UC	COSMIC-021 Cohort 2 ASCO	Cabo + Atezo	■ 27% ORR, DCR = 63%, and mPFS = 5.4 m
1L RCC	CheckMate -9ER ESMO	Cabo + Nivo	<ul> <li>OS: HR = 0.60, p&lt; 0.001 (mOS not yet reached)</li> <li>Doubling of PFS (HR = 0.51, p&lt;0.0001) and ORR vs sunitinib</li> </ul>
1L ccRCC	COSMIC-021 Cohort 1 ESMO	Cabo + Atezo	<ul> <li>53% ORR, DCR = 94%, and mPFS = 19.5 m</li> <li>mDOR not yet reached</li> </ul>
2L DTC	COSMIC-311 Top-line Results	Cabo (60 mg)	<ul> <li>PFS: 78% reduction in risk of disease progression or death (HR = 0.22, p&lt;0.0001)</li> </ul>

#### Cabozantinib 40 mg dose with full ICI dosing regimens in combination therapies

## Multiple Catalysts for Significant CABOMETYX Growth in 2021 and Beyond





### **Next Opportunity: CheckMate -9ER in 1L RCC**

- Compelling data supports potential for broad use in 1L setting
- Market share and duration from CheckMate -9ER may create significant revenue growth

### **Potential CABOMETYX Label Expansions**

- 2/3L DTC with cabo (COSMIC-311)
- 1/2L mCRPC with cabo + atezo (COSMIC-021 & CONTACT-02)
- 1L HCC with cabo + atezo (COSMIC-312)
- Post-ICI 2L NSCLC with cabo + atezo (CONTACT-01)
- 1L RCC with cabo + nivo + ipi (COSMIC-313)
- 2/3L RCC with cabo + atezo (CONTACT-03)

Accelerate growth in 2021 and beyond



## **CABOMETYX Commercial Opportunity Provided by CheckMate -9ER Results**

sNDA Filing Currently Under Review at the U.S. FDA with February 20, 2021 PDUFA Date

CheckMate -9ER
CABOMETYX plus OPDIVO®
Phase 3: 1L RCC

Strong differentiation vs other ICI combination therapies currently available

- **✓** Doubling of median PFS and ORR
- **✓** Superior OS
- **✓** Clinical benefits regardless of IMDC risk status
- **✓** Compelling safety and tolerability
- ✓ Favorable quality of life

*ICI* = *immune checkpoint inhibitor* 

sNDA = supplemental New Drug Application

PDUFA = Prescription Drug User Fee Act

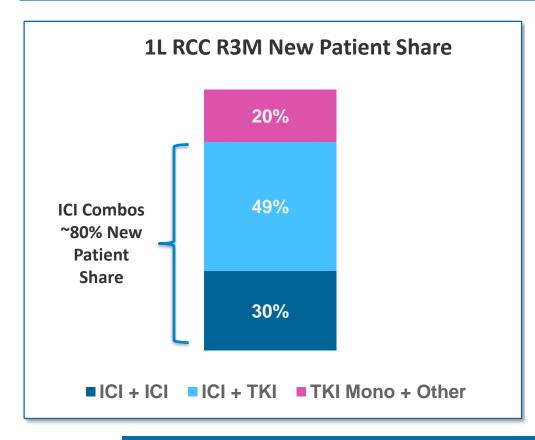
FDA = Food and Drug Administration

Projected run-rate of ~\$1.5 billion for U.S. RCC business by the end of 2022



## **CABOMETYX Commercial Opportunity Provided by CheckMate -9ER Results**

sNDA Filing Currently Under Review at the U.S. FDA with February 20, 2021 PDUFA Date



- 1L RCC market is >15,000 drug treatable patients annually\*
- ICI combos dominate 1L space at ~80% new patient share, additional capture ~20% in 2L\*\*
- ICI + TKI new patient share ~50% and widely used across all clinical risk groups
- Broad potential for CABOMETYX with OPDIVO in the
   1L setting
- Single agent CABOMETYX 38% market share in 2L setting\*\*

CheckMate -9ER results enable potential to target all three competitive segments of the current 1L market: ICI+ICI, ICI+TKIs, and TKI monotherapies



## **COSMIC-312: Growing Commercial Opportunity in HCC**



Phase 3 Pivotal Trial of Cabozantinib + Atezolizumab (1L HCC)

Primary Endpoints: PFS, OS

Secondary: ORR, Safety

**Top-line results** expected in the first half of 2021

## **2L+ CABOMETYX** commercial sales in-line with expectations

Demonstrated OS benefit with CABOMETYX (Phase 3 CELESTIAL study)

### **Future growth potential**

- Bevacizumab + atezolizumab combination therapy changing treatment landscape, driving more patients toward medical oncologists
- Cabozantinib + atezolizumab TKI-ICI combination uniquely positioned to compete in 1L market
- 2L market growth potential for cabozantinib as a TKI monotherapy post-ICI combination regimens in 1L



## **COSMIC-021: Significant Cabozantinib Label Expansion Opportunity in CRPC**



Phase 1b Basket Study of Cabozantinib + Atezolizumab (Multiple Tumors)

**Cohort 6: mCRPC** 

Preliminary Efficacy based on ORR per RECIST v1.1

sNDA filing seeking
Accelerated Approval
anticipated in 2021,
if data continue
to be supportive

#### Positive efficacy and safety data presentation at ASCO GU and ASCO 2020

#### **Summary of preliminary results from Cohort 6:**

- 32% ORR
- 80% DCR
- Median DOR 8.3 months (range 2.8 to 12.5+ months)
- Adverse event profile consistent with each drug's single agent adverse event profile
- Results suggest cooperative activity, with potential for cabozantinib to improve ICI activity

#### Study execution and progress in 2020

- Expanded Cohort 6 from 30 to 130 subjects for potential accelerated approval pathway
- Cohort 6 enrollment completion in Q3 2020
- Steady progress with enrollment of cohorts evaluating contribution of components

#### **High unmet need in 1L+ mCRPC**

- Lack of treatment options in 1/2L due to early use of NHTs for CSPC and M0 CRPC
- Non-hormonal treatment options limited to chemotherapy, radioligand therapy and sipuleucel-T



## **Additional Cabozantinib Pivotal Studies and Anticipated Milestones**

Study	Setting	Status	Next Milestone(s)
CSMIC 311 Cabozantinib	DTC Previously treated with a VEGF TKI	Analysis conducted per plan in Q4 2020: Cabo reduced the risk of death or PD by 78%, HR 0.22, p<0.0001	Present detailed data at an upcoming medical meeting; File sNDA in 2021
Cabozantinib + Nivolumab + Ipilimumab	1L Advanced RCC IMDC intermediate and poor risk	Expanded enrollment to 840 patients to provide additional power to assess secondary endpoint OS	Event-driven analysis 2022
CONTACT-01 Cabozantinib + Atezolizumab	mNSCLC after ICI and platinum chemo	Actively enrolling globally	Study enrollment ongoing; No guidance on timelines
CONTACT-02 Cabozantinib + Atezolizumab	mCRPC after one NHT	Actively enrolling globally	Study enrollment ongoing; No guidance on timelines
CONTACT-03 Cabozantinib + Atezolizumab	Advanced RCC w/progression during or following ICI	Actively enrolling globally	Study enrollment ongoing; No guidance on timelines

Other Ongoing Potential Label-Enabling Cabozantinib Trials: PDIGREE [CTEP]

CABINET [CTEP]

Ph3: 1L advanced RCC

Ph3: NET & Carcinoid



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

## Similar target profile to cabozantinib with shorter clinical half-life

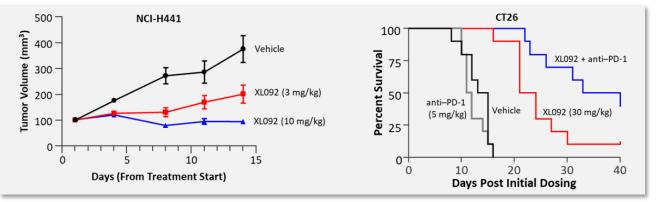
- Potent inhibitor of MET, VEGFR2, AXL and MER in biochemical / cellular assays
- Structure intended to modulate half-life
- 6-methylamide group provides a metabolic soft-spot

#### **Molecular Structure**

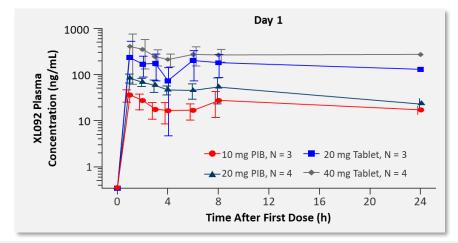
## *In Vitro*Profile

IC50's nM	MET	VEGFR2	AXL	MER
Biochemical	16.1	12.1	1.2	3.0
Cellular	15.4	1.6	3.4	7.2

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



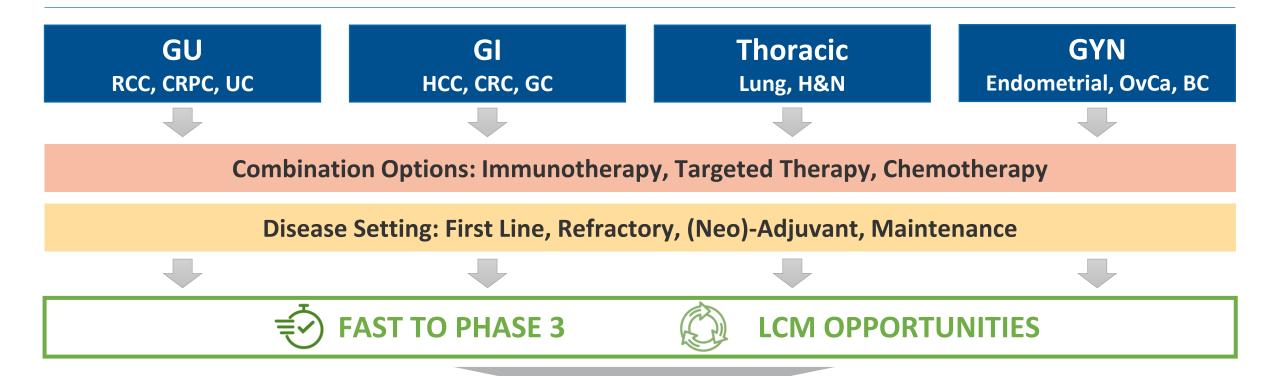
#### **Phase 1 Clinical Pharmacokinetics**



- Exposure increased with increasing doses for PIB and tablet formulation at steady state
- Mean terminal T<sub>1/2</sub> of 20-28 hours



## **Broad & Rapid Development for XL092 in a Wide Range of Solid Tumors**



- Develop XL092 with potential to be part of future standard of care in evolving treatment landscapes
- Pursue differentiated opportunities from cabozantinib based on XL092's differentiated therapeutic profile



## Extensive Development Plan Supported by XL092's Differentiated Clinical Profile and >15 Years of TKI Clinical Experience – Plan to Initiate Late Stage XL092 Studies in 2021

#### **XL092 Development Strategy**

#### **Potential Tumors / Settings**

#### **Combination Approaches**

#### **FAST TO MARKET**

High unmet need indications with **potential for accelerated development** 

## Endometrial Sa

**CRC** 

Sarcoma

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

**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 Treatment Today**



XL092 + ICI + ICI

XL092 + New MOA

XL092 + ICI + New MOA

XL092 + PDL-1 + CTLA-4

XL092 + PDL-1 + Novel ICI

XL092 + PDL-1 + Novel Biologic

XL092 + PDL-1 + Novel Small Mol.



## Other Early-stage Pipeline Assets Progressing into Clinical Development

#### XL102

- Small molecule, CDK7-inhibitor (formerly AUR102)
- Part of collaboration and licensing agreement with Aurigene established in 2019
- FDA acceptance of IND and in-licensed from Aurigene in December 2020
- Phase 1 trial initiation expected in 2021

#### **XB002**

- Biologic, TF-targeting ADC (formerly ICON-2)
- Part of collaboration and licensing agreement with Iconic Therapeutics established in 2019
- In-licensed from Iconic in December 2020
- IND filing planned once drug product release assays are finalized
- Phase 1 trial initiation expected in 2021



## XL102 and XB002 Phase 1a/b Plans

#### **New INDs Cohort Expansion Dose Escalation Ovarian Cancer XL102 Single Agent Triple-negative BC** (Advanced Solid Tumors) Hormone-receptor positive BC *XL102-101 (CDK7 Inhibitor)* **mCRPC** Phase 1 FIH Study **XL102 Combination Therapy** Hormone-receptor positive BC + Fulvestrant (HR+ BC) (+ Fulvestrant) + Abiraterone/Prednisone **mCRPC** (mCRPC) (+ Abiraterone/Prednisone) **NSCLC Ovarian Cancer** *XB002-101 (TF-ADC)* **Cervical Cancer XB002 Single-Agent Phase 1 FIH Study** (Advanced Solid Tumors) **Urothelial Cancer Pancreatic Cancer Head & Neck Cancer**



## **Discovery and Early Development Pipeline:**

Encompassing Multiple Modalities & Mechanisms Across Small Molecules and Biologics

SMALL MOLECULES		
Program Name	Origin	Mechanism / Target
XL092	EXELIXIS°	TKI; MET/VEGFR/AXL/MER-targeting
XL102 (formerly AUR102)	A U R I G E N E  Accelerating Discovery	CDK7-inhibitor
EXEL-4329	<b>SSTI</b> ®	Casein Kinase 1 Alpha Activator
BIOLOGICS		
XB002 (formerly ICON-2)	ICONIC THERAPEUTICS	ADC; TF-targeting
ADC Platform	Catalent.	ADCs; Targets Undisclosed
ADC Platform	NBE therapeutics	ADCs; Targets Undisclosed
Novel Biologics Platform	jī invenra	Multi-specific Antibodies; Targets Undisclosed



## **In Summary**

#### Strong commercial business poised for a return to revenue growth in 2021

Potential CheckMate -9ER approval could drive \$1.5B RCC revenue run-rate by 2022

#### Robust clinical development activity with big pharma scale

- COSMIC and CONTACT studies provide opportunity for cabozantinib label expansion and significant revenue growth
- XL092: broad development plan with potential to set new SOC with novel treatment regimens

#### Next wave of Exelixis medicines support our vision of becoming a multi-product company

- Phase 1 trials planned for XL102 and XB002 this year
- Potential for advancement of compounds currently in preclinical development
- Long-term growth potential of early-stage pipeline with differentiated assets

#### Building an innovative oncology pipeline with internal discovery and business development

- New small molecule and biologic compounds progressing towards development candidate status
- Strategic BD activity to supplement internal discovery efforts to grow and diversify future Exelixis pipeline



## **Anticipated Milestones for 2021**

Program	Milestone	
COSMIC-311	File sNDA for approval of cabozantinib in patients with radioactive iodine-refractory DTC	
COSMIC-312	Report top-line results for co-primary endpoints PFS and OS	
COSIVIIC-312	File sNDA for approval of cabozantinib + atezolizumab in 1L HCC, if data supportive	
COSMIC-021	File sNDA for accelerated approval of cabozantinib + atezolizumab in mCRPC, if data supportive	
COSMIC-313	Complete expanded enrollment in phase 3 trial of triplet cabozantinib, nivolumab + ipilimumab vs combination of nivolumab + ipilimumab in 1L RCC	
CONTACT-01/02/03	Continue enrollment in pivotal trials of cabozantinib + atezolizumab in NSCLC, mCRPC and RCC	
	Continue enrollment in dose escalation cohort of Phase 1b trial of XL092 + atezolizumab	
XL092	Initiate enrollment of ccRCC, nccRCC, HR+ BC and mCRPC expansion cohorts of Phase 1a/b	
	Initiate further Phase 1b platform trial(s) with expansion cohorts in other tumor types and combinations	
XL102	Initiate Phase 1 trial of single-agent and combination therapy in solid tumors	
XB002	Initiate Phase 1 trial of single-agent in solid tumors	
Preclinical	Advance up to two compounds currently in preclinical development	

mCRPC = metastatic castration-resistant prostate cancer

HR+ BC = hormone receptor positive breast cancer

NSCLC = non-small cell lung cancer



## **Q&A Session**





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