Exelixis and Ipsen
Financial Community & Media Briefing

ESMO 2016 Congress
Monday, October 10, 2016
Copenhagen

Exelixis, Inc.
(NASDAQ: EXEL)

Ipsen
(Euronext: IPN.PA;
ADR: IPSEY)

Exelixis Forward-Looking Statement

This presentation, including any oral presentation accompanying it, contains forward-looking statements, including, without limitation, statements related to: Exelixis' intent to submit a sNDA based on CABOSUN results and plan to provide a detailed update on timing for submission once the company has further clarity; the development path and clinical, therapeutic and commercial potential for cabozantinib; and launch plans for CABOMETYX in the EU. Words such as "intend," "will," "potential," "planned," or the negative of such terms or other similar expressions, identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, statements that refer to expectations, projections or characterizations of future events or their timing are forward-looking statements. These forward-looking statements 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: Exelixis' ability and the ability of its collaborators to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; risks related to the potential failure of cabozantinib to demonstrate safety and efficacy in clinical testing; risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the degree of market acceptance of CABOMETYX and the availability of coverage and reimbursement for CABOMETYX; the risk that unanticipated developments could adversely affect the commercialization of CABOMETYX; competition from other therapies; Exelixis' dependence on its relationship with Ipsen, including, the level of Ipsen's investment in the resources necessary to successfully commercialize cabozantinib in the territories where it is approved; Exelixis' dependence on third-party vendors; Exelixis' ability to protect the company's intellectual property rights; market competition; 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 August 3, 2016, and in Exelixis' future filings with the SEC. The forward-looking statements made in this presentation, including any oral presentation accompanying it, speak only as of the date on which the statements are made. Exelixis expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Exelixis' expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

Ipsen Forward-Looking Statement

Disclaimer

This presentation includes only summary information and does not purport to be comprehensive. Forward-looking statements, targets and estimates contained herein are for illustrative purposes only and are based on management's current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated in the summary information. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties, notably given that a new product can appear to be promising at a preparatory stage of development or after clinical trials but never be launched on the market or be launched on the market but fail to sell notably for regulatory or competitive reasons. The Group must deal with or may have to deal with competition from generic that may result in market share losses, which could affect its current level of growth in sales or profitability. The Company expressly disclaims any obligation or undertaking to update or revise any forward-looking statements, targets or estimates contained in this presentation to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based unless so required by applicable law.

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The implementation of the strategy has to be submitted to the relevant staff representation authorities in each country concerned, in compliance with the specific procedures, terms and conditions set forth by each national legislation.

Safe Harbor

The Group operates in certain geographical regions whose governmental finances, local currencies or inflation rates could be affected by the current crisis, which could in turn erode the local competitiveness of the Group's products relative to competitors operating in local currency, and/or could be detrimental to the Group's margins in those regions where the Group's drugs are billed in local currencies.

In a number of countries, the Group markets its drugs via distributors or agents: some of these partners' financial strength could be impacted by the crisis, potentially subjecting the Group to difficulties in recovering its receivables. Furthermore, in certain countries whose financial equilibrium is threatened by the crisis and where the Group sells its drugs directly to hospitals, the Group could be forced to lengthen its payment terms or could experience difficulties in recovering its receivables in full.

Finally, in those countries in which public or private health cover is provided, the impact of the financial crisis could cause medical insurance agencies to place added pressure on drug prices, increase financial contributions by patients or adopt a more selective approach to reimbursement criteria.

All of the above risks could affect the Group's future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today.

Tonight's Agenda

Introduction & Opening Comments
Lindsay Treadway, Public Affairs, Exelixis
Mike Morrissey, Ph.D., President and CEO, Exelixis
David Meek, CEO, Ipsen

CABOSUN Results Review
Toni K. Choueiri, M.D., Dana-Farber Cancer Institute

Regulatory Plans and Overview of Cabozantinib Presentations at ESMO
Gisela Schwab, M.D., President, Product Development and Medical Affairs, and CMO, Exelixis

Cabozantinib plus Nivolumab Phase 1 Results Review
Sumanta Pal, M.D., City of Hope

Panel Discussion (Moderated by Gisela Schwab)
Toni K. Choueiri, M.D.
Sumanta Pal, M.D.
Nizar Tannir M.D., University of Texas MD Anderson Cancer Center

Claude Bertrand, Ph.D., EVP of Research and Development and CSO, Ipsen

ESMO data press releases and webcast of this briefing available at www.exelixis.com and www.ipsen.com

CABOMETYX™ (cabozantinib) tablets: Approval Status

CABOMETYX is currently approved by the U.S. Food and Drug Administration for the treatment of advanced renal cell carcinoma (RCC) in patients who have received prior anti-angiogenic therapy

- Please see full U.S. prescribing information at: https://cabometyx.com/downloads/cabometyxuspi.pdf

CABOMETYX is approved in the EU for the treatment of advanced renal cell carcinoma in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy.

CABOMETYX™ (cabozantinib) tablets: Important Safety Information

- **Hemorrhage:** Severe hemorrhage occurred with CABOMETYX. The incidence of Grade ≥3 hemorrhagic events was 2.1% in CABOMETYX-treated patients and 1.6% in everolimus-treated patients. Fatal hemorrhages also occurred in the cabozantinib clinical program. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.

- **Gastrointestinal (GI) Perforations and Fistulas:** Fistulas were reported in 1.2% (including 0.6% anal fistula) of CABOMETYX-treated patients and 0% of everolimus-treated patients. GI perforations were reported in 0.9% of CABOMETYX-treated patients and 0.6% of everolimus-treated patients. Fatal perforations occurred in the cabozantinib clinical program. Monitor patients for symptoms of fistulas and perforations. Discontinue CABOMETYX in patients who experience a fistula that cannot be appropriately managed or a GI perforation.

- **Thrombotic Events:** CABOMETYX treatment results in an increased incidence of thrombotic events. Venous thromboembolism was reported in 7.3% of CABOMETYX-treated patients and 2.5% of everolimus-treated patients. Pulmonary embolism occurred in 3.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Events of arterial thromboembolism were reported in 0.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Fatal thrombotic events occurred in the cabozantinib clinical program. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or any other arterial thromboembolic complication.

- **Hypertension and Hypertensive Crisis:** CABOMETYX treatment results in an increased incidence of treatment-emergent hypertension. Hypertension was reported in 37% (15% Grade ≥3) of CABOMETYX-treated patients and 7.1% (3.1% Grade ≥3) of everolimus-treated patients. Monitor blood pressure prior to initiation and regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume CABOMETYX at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy. Discontinue CABOMETYX if there is evidence of hypertensive crisis or severe hypertension despite optimal medical management.

- **Diarrhea:** Diarrhea occurred in 74% of patients treated with CABOMETYX and in 28% of patients treated with everolimus. Grade 3 diarrhea occurred in 11% of CABOMETYX-treated patients and in 2% of everolimus-treated patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 diarrhea or Grade 3-4 diarrhea that cannot be managed with standard antidiarrheal treatments until improvement to Grade 1; resume CABOMETYX at a reduced dose. Dose modification due to diarrhea occurred in 26% of patients.

CABOMETYX™ (cabozantinib) tablets: Important Safety Information, continued

- **Palmar-Plantar Erythrodysesthesia Syndrome (PPES):** Palmar-plantar erythrodysesthesia syndrome (PPES) occurred in 42% of patients treated with CABOMETYX and in 6% of patients treated with everolimus. Grade 3 PPES occurred in 8.2% of CABOMETYX-treated patients and in <1% of everolimus-treated patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPES or Grade 3 PPES until improvement to Grade 1; resume CABOMETYX at a reduced dose. Dose modification due to PPES occurred in 16% of patients.

- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in the cabozantinib clinical program. Perform an evaluation for RPLS in any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

- **Embryo-fetal Toxicity:** CABOMETYX can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the last dose.

- **Adverse Reactions:** The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, nausea, decreased appetite, PPES, hypertension, vomiting, weight decreased, and constipation.

- **Drug Interactions: Strong CYP3A4 inhibitors and inducers:** Reduce the dosage of CABOMETYX if concomitant use with strong CYP3A4 inhibitors cannot be avoided. Increase the dosage of CABOMETYX if concomitant use with strong CYP3A4 inducers cannot be avoided.

- **Lactation:** Advise a lactating woman not to breastfeed during treatment with CABOMETYX and for 4 months after the final dose.

- **Reproductive Potential: Contraception—**Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the final dose. **Infertility —**CABOMETYX may impair fertility in females and males of reproductive potential.

- **Hepatic Impairment:** Reduce the CABOMETYX dose in patients with mild (Child-Pugh score [C-P] A) or moderate (C-P B) hepatic impairment. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

CABOSUN Results Review

Toni K. Choueiri, M.D., Dana-Farber Cancer Institute

Abstract LBA30

CABOzantinib versus SUNitinib (CABOSUN) as initial targeted therapy for patients with metastatic renal cell carcinoma (mRCC) of poor and intermediate risk groups

ALLIANCE A031203 Trial

Toni K. Choueiri MD, Susan Halabi PhD, Ben Sanford MS, Olwen Hahn MD, M. Dror Michaelson MD, Meghara Walsh RN, Thomas Olencki MD, Joel Picus MD, Eric Small MD, Shaker Dakhil MD, Daniel George MD, and Michael J. Morris MD

Presented at the ESMO 2016 Congress, Copenhagen

Cabozantinib and the CABOSUN Trial

- Cabozantinib is an oral inhibitor of tyrosine kinases including MET, AXL, and VEGF receptors[1]
  - Approved in 2016 in the US and EU for previously-treated RCC
- The phase 2 CABOSUN trial evaluated cabozantinib compared to sunitinib in treatment-naïve poor and intermediate risk RCC patients[2]
  - Poor and intermediate risk groups have inferior clinical outcomes relative to favorable-risk patients
- Primary endpoint
  - Progression-free survival (PFS) assessed by investigator
- Secondary endpoints
  - Overall survival (OS)
  - Objective response rate (ORR) by investigator-assessment
  - Safety

[1] Yakes FM et al., Mol Cancer Ther, 2011
[2] NCT01835158

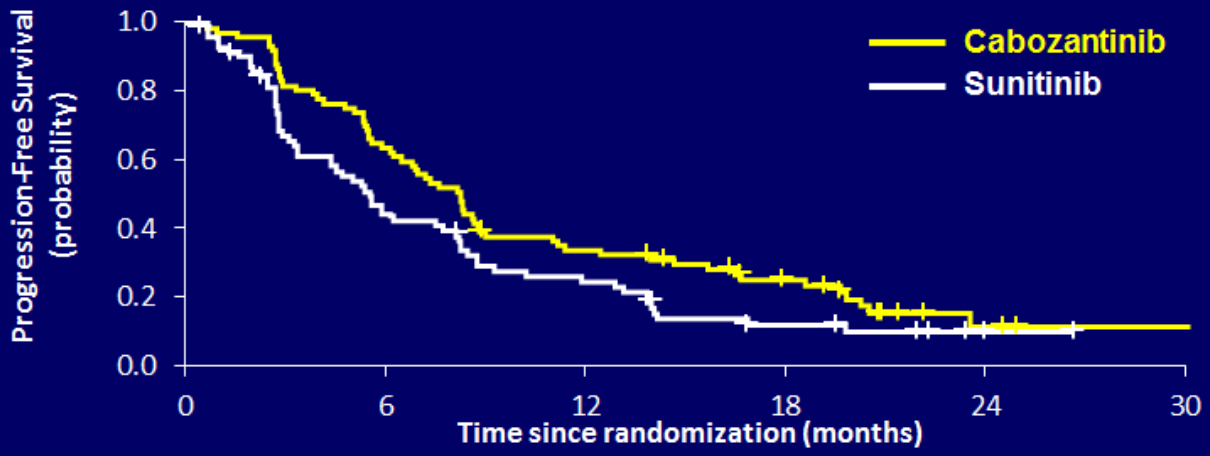
CABOSUN Patient Population

Study	Risk Groups (%)				ECOG 2 (%)	Bone Mets (%)
	System	Favorable	Intermediate	Poor		
CABOSUN	IMDC	0	81	19	13	36
RECORD3[1]	MSKCC	30	56	14	6	23
COMPARZ[2]	IMDC	25	55	18	NR	18

- Compared to typical Phase 3 first line RCC populations:
  - No patients with favorable prognosis
  - Higher rate of ECOG PS 2, poor prognosis patients
  - Higher rate of bone metastasis
    - Associated with poor prognosis

[1]Motzer et al JCO 2014 [2]Motzer et al NEJM 2013
NR, not reported

CABOSUN Efficacy



ORR* (95%CI)	
Cabozantinib (N=79)	**Sunitinib** (N=78)
46% (34-57%)	**18% (10-28%)**

Arm	PFS Events	Median PFS (95% CI), mo	HR (95% CI)*
Cabozantinib	**64**	**8.2 (6.2, 9.0)**	**0.69 (0.48-0.99)**
Sunitinib	**61**	**5.6 (3.4, 8.1)**	**p-value (one-sided) = 0.012**

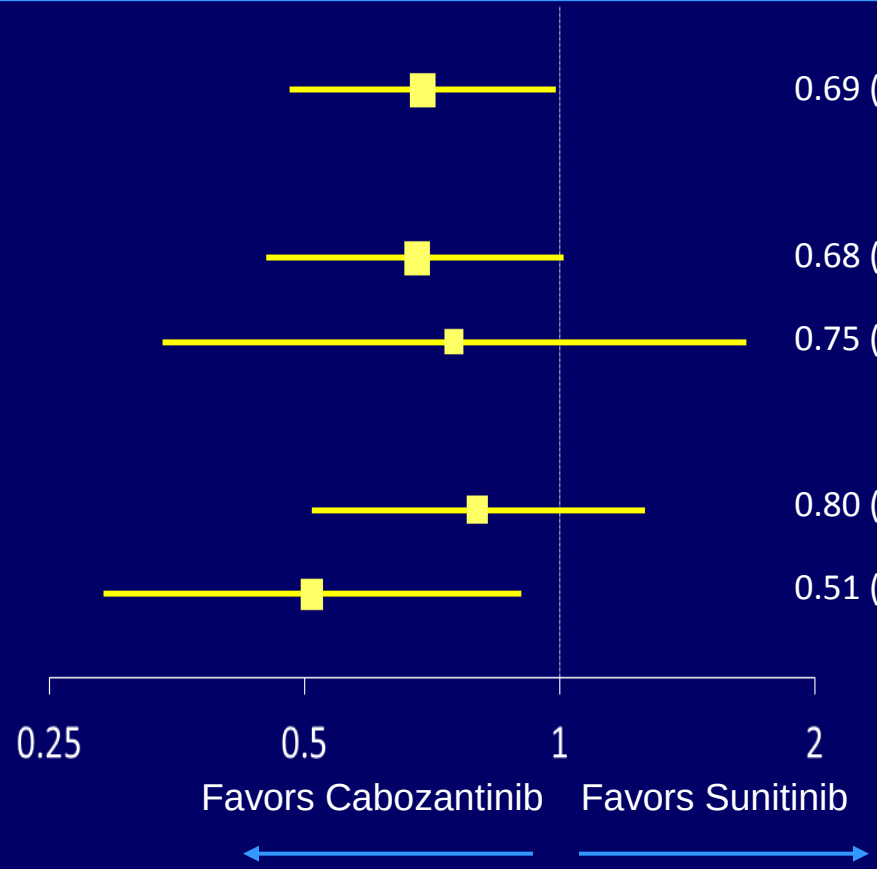
Arm	Deaths	Median OS (95% CI), mo	HR (95% CI)*
Cabozantinib	**37**	**30.3 (14.6, 35.0)**	**0.80 (0.50, 1.26)**
Sunitinib	**41**	**21.8 (16.3, 27.0)**	

Presented at the ESMO 2016 Congress, Copenhagen

* Investigator assessed

PFS Subgroup Analysis

	N	Median PFS (mo)		HR (95%CI)
		Cabozantinib	Sunitinib	
All Patients	157	8.2	5.6	0.69 (0.48-0.99)
IMDC Risk Group				
Intermediate	127	8.4	6.2	0.68 (0.45-1.01)
Poor	30	6.3	2.8	0.75 (0.34-1.66)
Bone Metastases				
No	100	8.7	7.6	0.80 (0.51-1.26)
Yes	57	6.3	3.4	0.51 (0.29-0.90)



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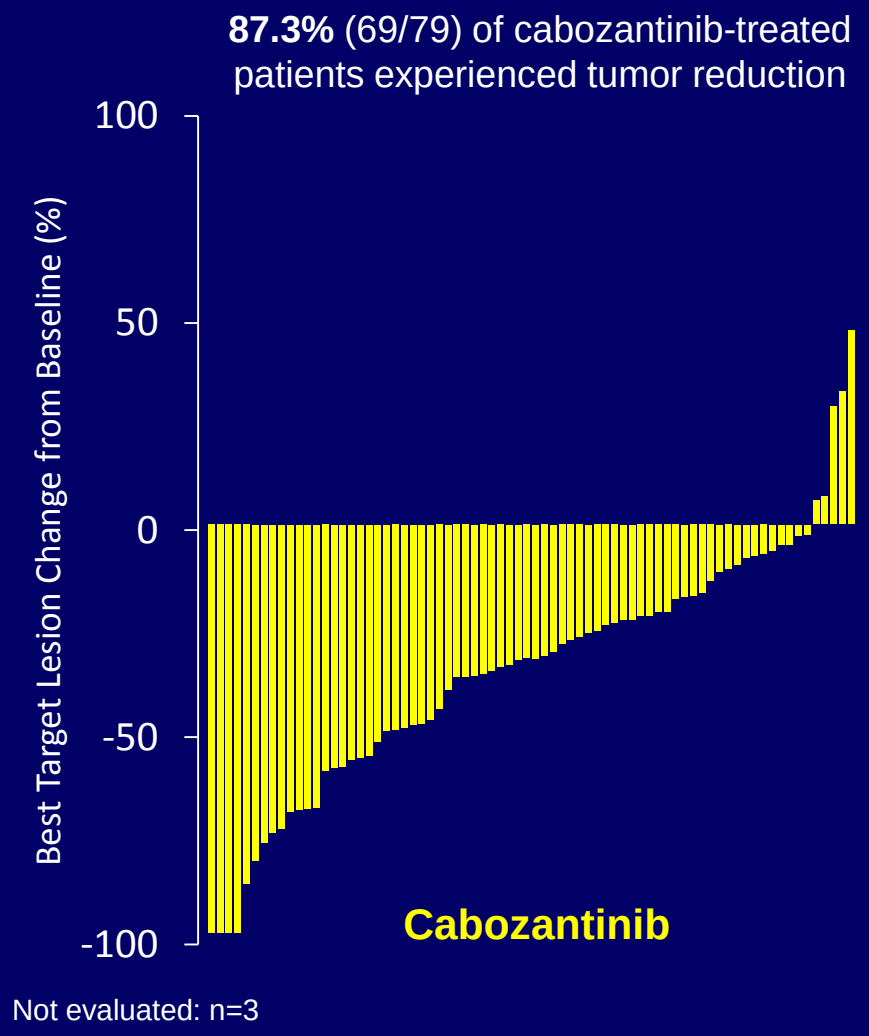
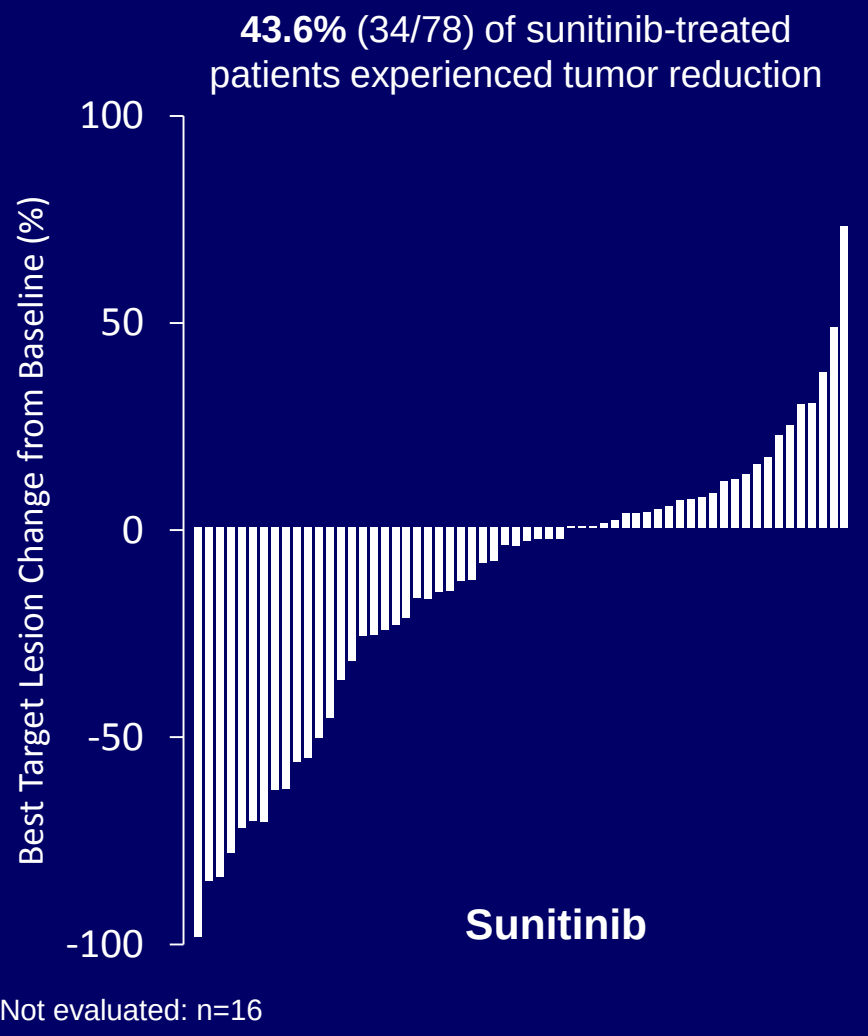
Best Target Lesion Change from Baseline



Not evaluated: n=3



Not evaluated: n=16

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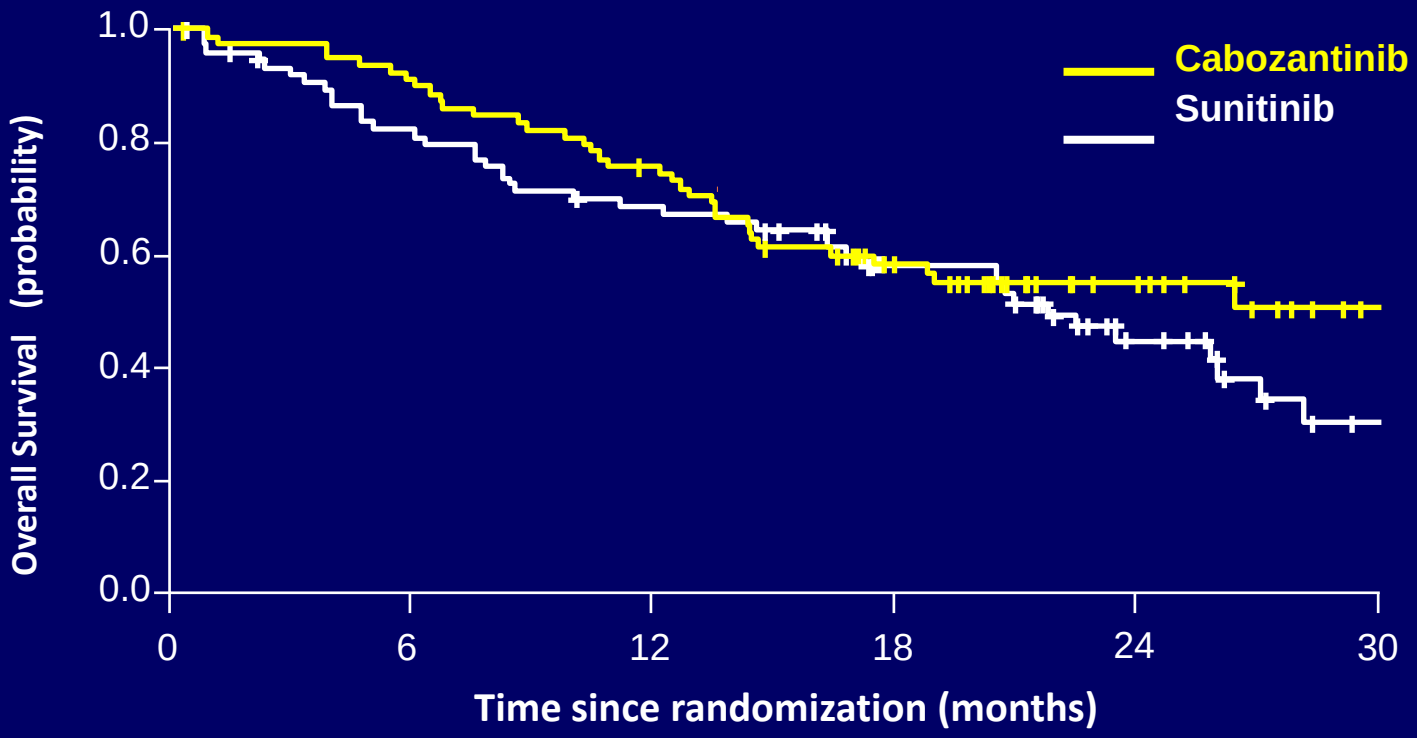
Overall Survival



No. at Risk						
Cabozantinib	79	71	58	35	16	5
Sunitinib	78	60	49	34	17	4

Arm	Deaths	Median Survival (95% CI), mo	HR (95% CI)*
Cabozantinib	**37**	**30.3 (14.6, 35.0)**	**0.80 (0.50, 1.26)**
Sunitinib	**41**	**21.8(16.3, 27.0)**	

* Adjusted for bone metastases and IMDC risk group; median follow-up for OS: 22.8 mo

CABOSUN Safety

	Cabozantinib	Sunitinib
Median number of 6 week cycles (range)	5 (0-19)	2 (0-17)
Any Grade 3/4 adverse event (%)	65	68
Dose reductions (%)	58	49
Discontinuation due to adverse event (%)	20	21
Most frequent Gr 3/4 adverse events	Hypertension (28%) Diarrhea (10%) PPES (8%) Fatigue (6%)	Hypertension (22%) Fatigue (15%) Diarrhea (11%) Thrombocytopenia (11%) Oral mucositis (6%)

- Greater exposure in cabozantinib arm
- Similar rates of adverse events and discontinuations between the cabozantinib and sunitinib arms

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RCC Treatment Implications

- Sunitinib is a standard-of-care therapy in first-line mRCC
  - 8-11mo median PFS for VEGFR TKIs in standard first-line trials[1,2]
- Pts with intermediate/poor-risk disease have worse prognosis
  - Median PFS of 5.6mo for intermediate/poor risk pts on first targeted therapy[3]
- Cabozantinib improved PFS and ORR compared to sunitinib in intermediate/poor risk pts
  - Median PFS of 8.2mo for cabozantinib vs 5.6mo for sunitinib
  - ORR of 46% for cabozantinib vs 18% for sunitinib
  - Similar safety profile
- Cabozantinib represents a potential first-line treatment option in patients with advanced RCC

[1]Motzer R et al, NEJM 2007
[2]Motzer R et al, NEJM 2013
[3]Ko J et al, BJC 2014

Presented at the ESMO 2016 Congress, Copenhagen

Regulatory Plans & Overview of Cabozantinib Presentations at ESMO

Gisela Schwab, M.D., President, PD & MA, and CMO, Exelixis

CABOSUN Regulatory Plans

Exelixis intends to submit an sNDA based on CABOSUN results.

- Exelixis is working with the Alliance to transfer the complete CABOSUN clinical database to Exelixis. We have also initiated the image collection process from the Alliance sites for a read by an Independent Radiology Committee (IRC).

- Once we have all the CABOSUN results in house, we will prepare the data sets and analyses consistent with regulatory expectations for a supplemental NDA (sNDA).

- Timing for the sNDA submission is dependent on a number of factors. We will provide a detailed update once we have further clarity.

Our partner Ipsen is in discussions with the EMA to define the submission of the variation simultaneously with the U.S. submission.

Cabozantinib Presentations at ESMO

Abstract Topic	Indication	Format
Phase 2 CABOSUN Study in Treatment-naïve Poor and Intermediate Risk RCC patients	RCC	Oral
METEOR: Outcomes by Metastatic Site and Tumor Burden	RCC	Poster
METEOR: Analysis of Regional Differences	RCC	Poster
METEOR: Trial Design, the "Trial within a Trial"	RCC	Poster
METEOR: Quality of Life Analysis	RCC	Poster
Phase 1 of Cabozantinib + Nivolumab in GU Tumors	GU Tumors	Poster Discussion
Phase 2 Study in Metastatic Urothelial Carcinoma	Bladder	Poster
Phase 2 Study in Patients with High-Grade Uterine Sarcoma (TIP)	HGUS	Poster

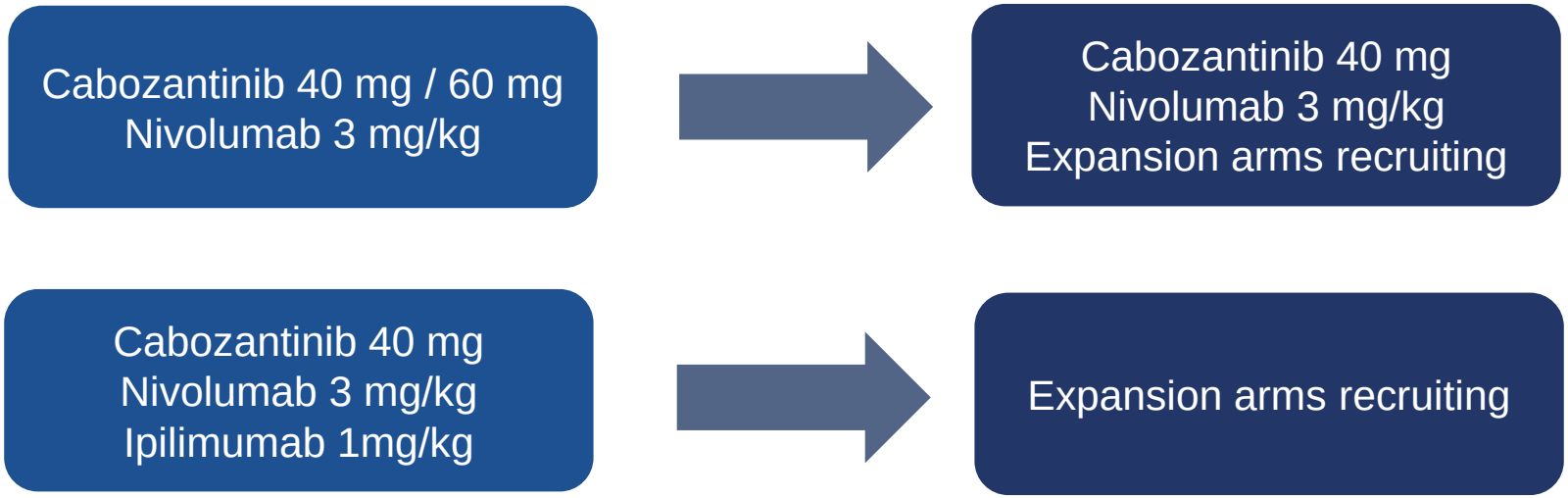
Cabozantinib Plus Nivolumab Phase 1 Results Review

Sumanta Pal, M.D., City of Hope

Cabozantinib in Combination with Checkpoint Inhibitors

A phase 1b trial of cabozantinib plus nivolumab, or plus nivolumab and ipilimumab in patients with genitourinary tumors

– Sponsored by NCI-CTEP, with Dr. Andrea Apolo as principal investigator



Expansion cohorts focus on urothelial and renal cell carcinomas

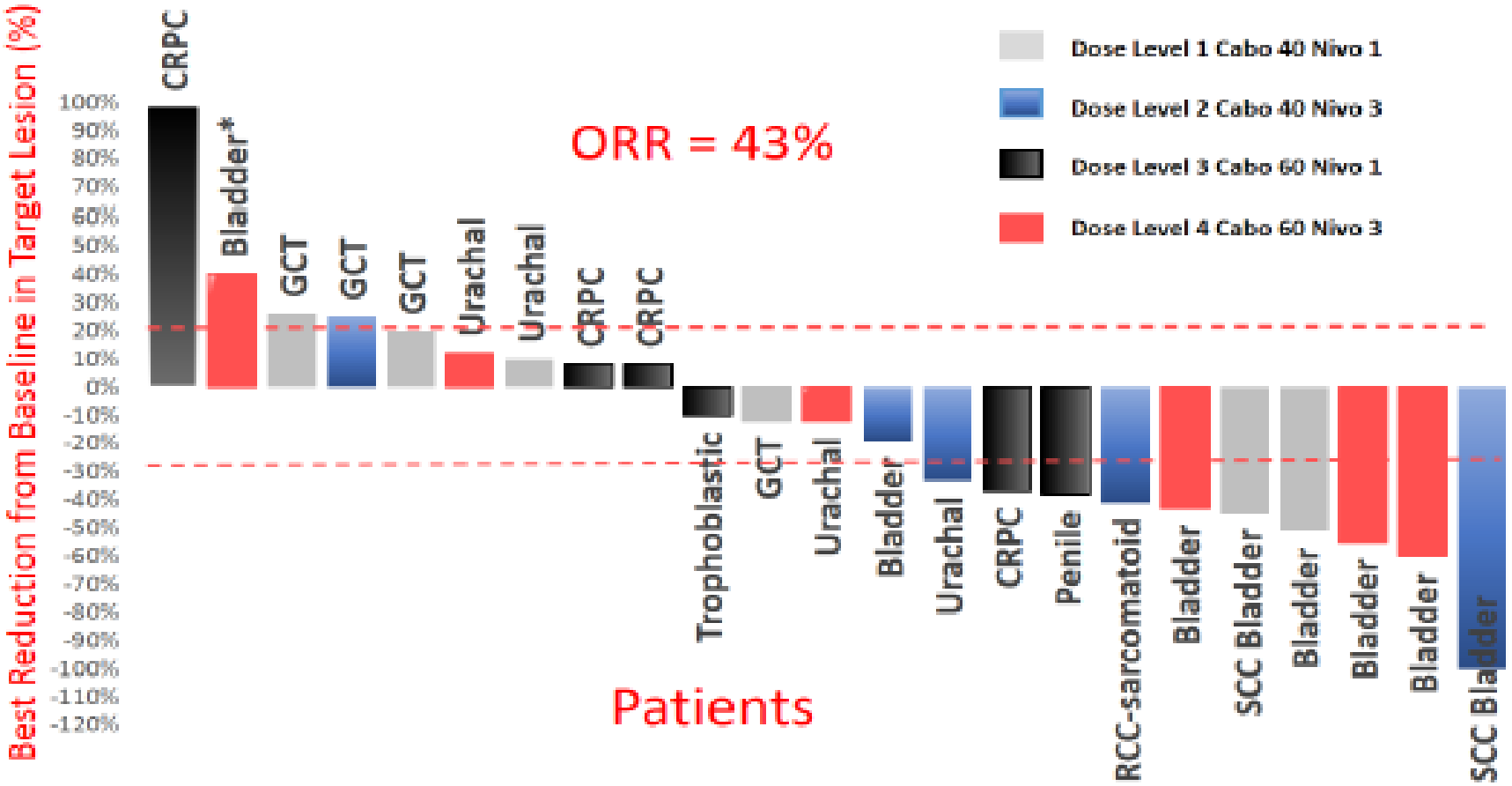
Patient Characteristics and Prior Treatment

Table 2: Patient Characteristics of Part I, Cabozantinib + Nivolumab

Patient Characteristics	N = 24
Age	
Median	55
Range	(35-75)
Sex	
Male	21
Female	3
Karnofsky Performance Status	
90%	9
80%	12
70%	3
Tumor type	
Urothelial carcinoma	7
Urachal adenocarcinoma	4
Squamous cell carcinoma of the bladder or urethra	3
Castration-resistant prostate cancer	4
Renal cell carcinoma—sarcomatoid	1
Trophoblastic	1
Germ cell	4
No. of prior therapies for metastatic disease	(range 1-6)
1	2
2	8
3	4
4 or more	10

Patient Response: Cabozantinib plus Nivolumab

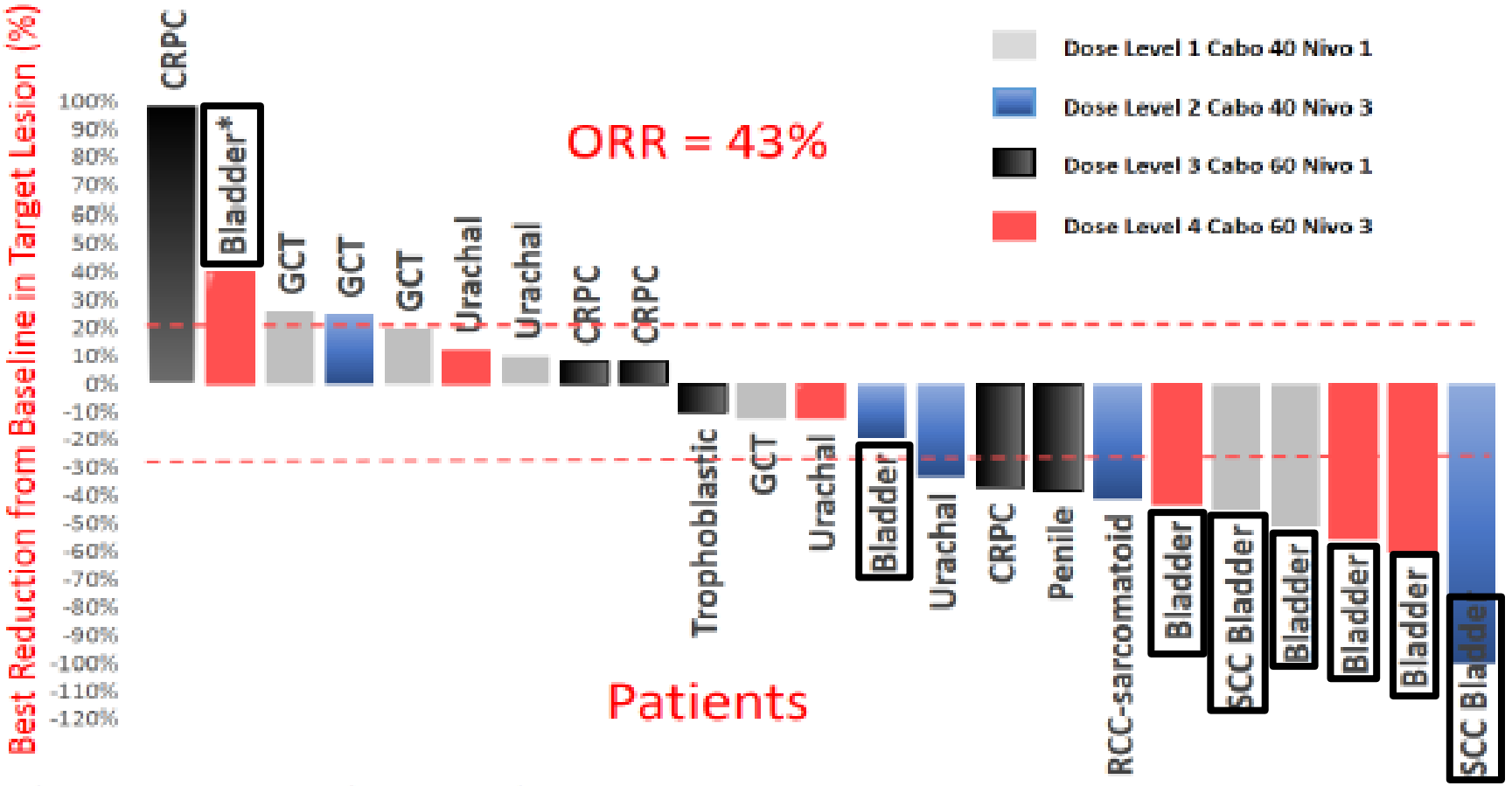
Figure 2: Best change in target lesions from baseline



*Solid tumor in lung became cavitary (no solid component), but outline became larger; categorized as stable disease.
CRPC: castration-resistant prostate cancer; GCT: germ cell tumor; ORR: overall response rate; SCC: squamous cell carcinoma; urachal: urachal adenocarcinoma

Patient Response: Cabozantinib plus Nivolumab

Figure 2: Best change in target lesions from baseline



*Solid tumor in lung became cavitary (no solid component), but outline became larger; categorized as stable disease.
CRPC: castration-resistant prostate cancer; GCT: germ cell tumor; ORR: overall response rate; SCC: squamous cell carcinoma; urachal: urachal adenocarcinoma

Cabozantinib in Combination with Checkpoint Inhibitors

The combination of cabozantinib and nivolumab was safe and well-tolerated

Grade 3 AEs >10%:

- Decreased neutrophil count 17%
- Thromboembolic event 13%
- Fatigue 13%

One grade 4 lipase increase – no other grade 4 or 5 AEs

No grade 3 or higher liver enzyme elevation

Recommended Phase 2 dose is cabozantinib 40 mg plus nivolumab 3 mg/kg

Two expansion cohorts - urothelial carcinoma and renal cell carcinoma - are actively accruing

IPSEN
Innovation for patient care

EXELIXIS®

Panel Discussion

Dr. Toni K. Choueiri
Dr. Sumanta Pal
Dr. Nizar Tannir
Dr. Claude Bertrand

Moderated by Dr. Gisela Schwab, Exelixis

Question & Answer Session

*Please direct questions to **ltreadway@exelixis.com.** Alternatively, you may fill out the form below the video stream.*

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