From Novel Science to Clinical Development: Stories from Small Biotechs – Exelixis, Inc.

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Cancer Progress by Defined Health
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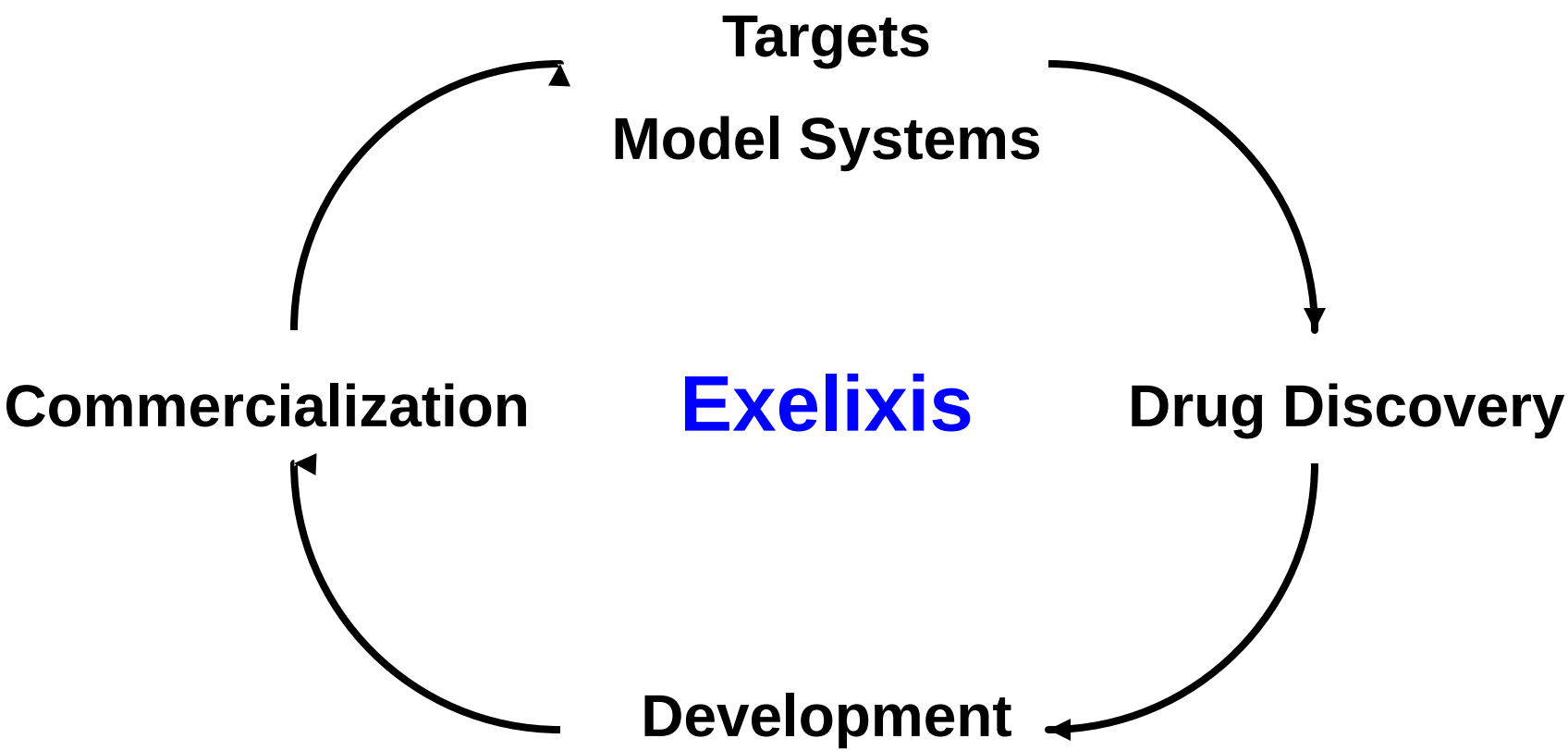
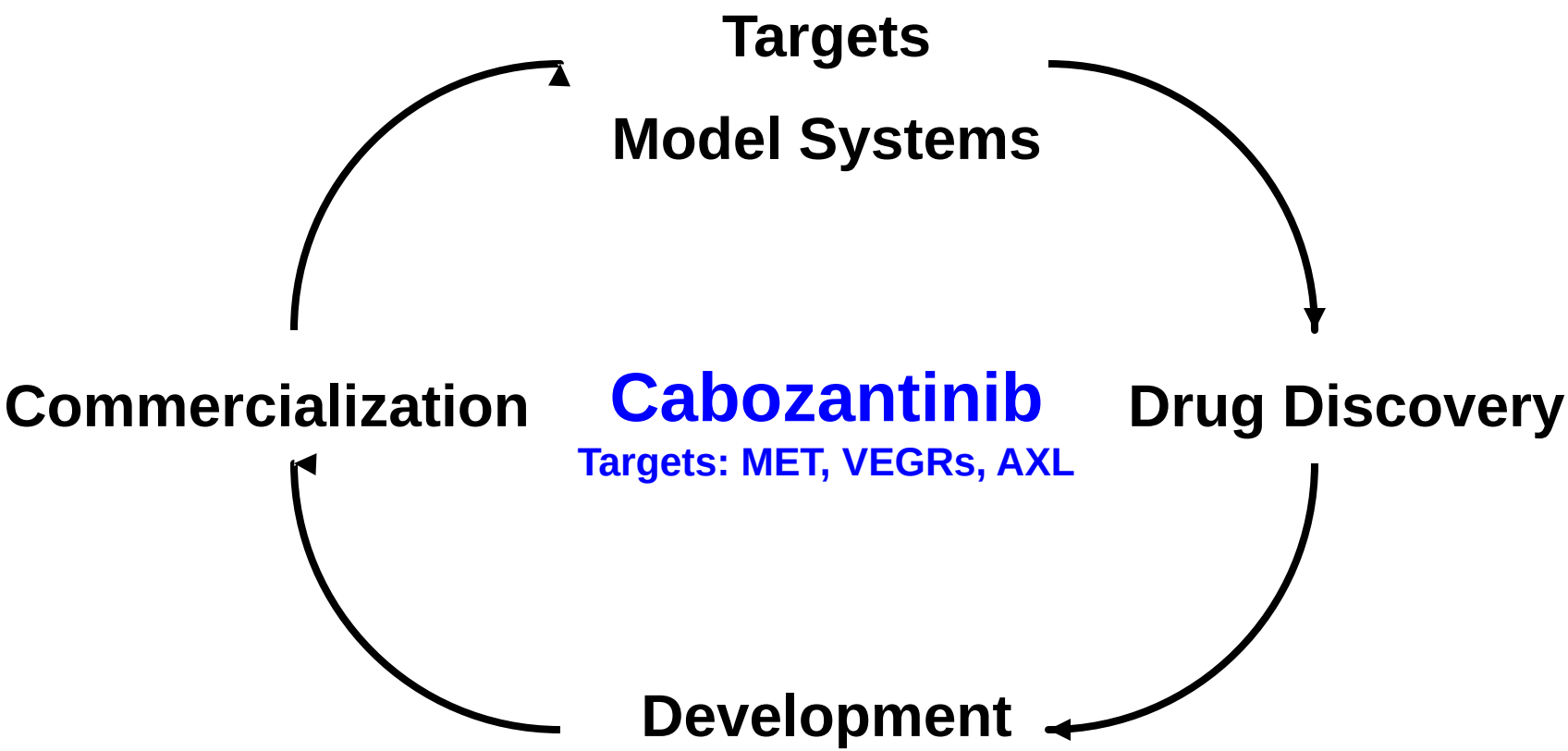
Integrated Approach



20 INDs in 8 Year Span

Cabozantinib



Rationale for Cabozantinib in RCC Matching Tumor Biology and Target Profile

- Drugs targeting VEGF and its receptors, or the mammalian target of rapamycin (mTOR), are standard therapies in RCC
- Inactivation of the von Hippel-Lindau tumor suppressor protein in clear cell RCC results in upregulation of VEGF, MET, and AXL[1]
- Increased MET and AXL expression associated with poor prognosis and resistance to VEGFR inhibitors in RCC[1,2]

[1] Zhou L et al., Oncogene, 2015
[2] Ciamporcero E et al., Mol Cancer Ther, 2014

Activity of Everolimus and Axitinib in Patients Who Have Received Prior Sunitinib Only

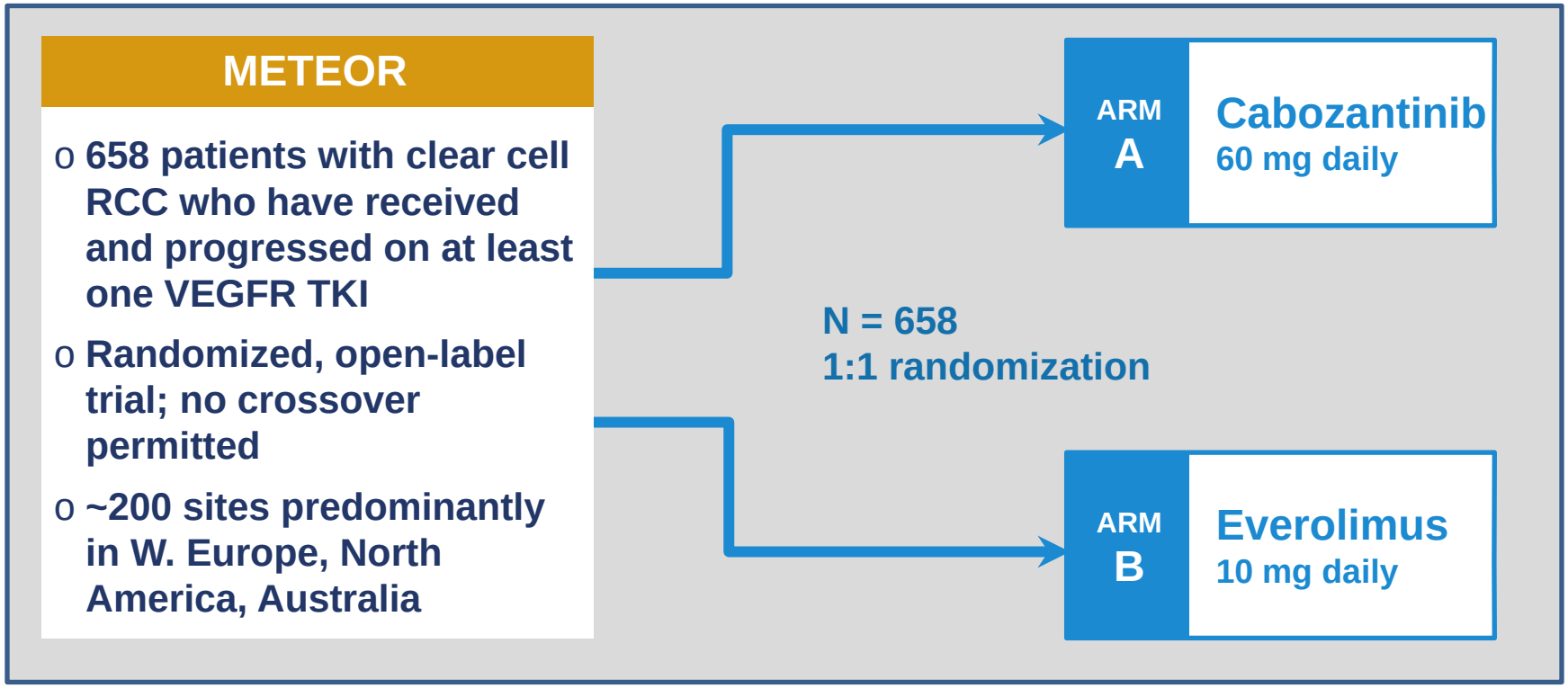
- RCC treatment landscape limited to VEGF(R) or mTOR targeting (2013)
- Majority of agents approved based on PFS benefit
- Activity in previously treated patients limited

	RECORD-1 (everolimus) ***(N=124,45% of all pts)***	**AXIS (axitinib)** ***(N=194, 26% of all pts)***
Response Rate	1-2%	11%
PFS (months)	3.9[1]	4.8
FKSI scores (disease-related symptoms)	Minimal impact vs. placebo[2]	Similar to sorafenib[3]
Discontinuation due to AEs[4]	14%	9%

Illustrates unmet need in second line RCC

1. Motzer et al, Cancer 2010 2. Beaumont et al, *Oncologist* 2011 3.Cella et al, *ASCO meeting* 2011
4. Updated Package Inserts for everolimus and axitinib (accessed May 13, 2012)

METEOR Phase 3 Pivotal Trial Design

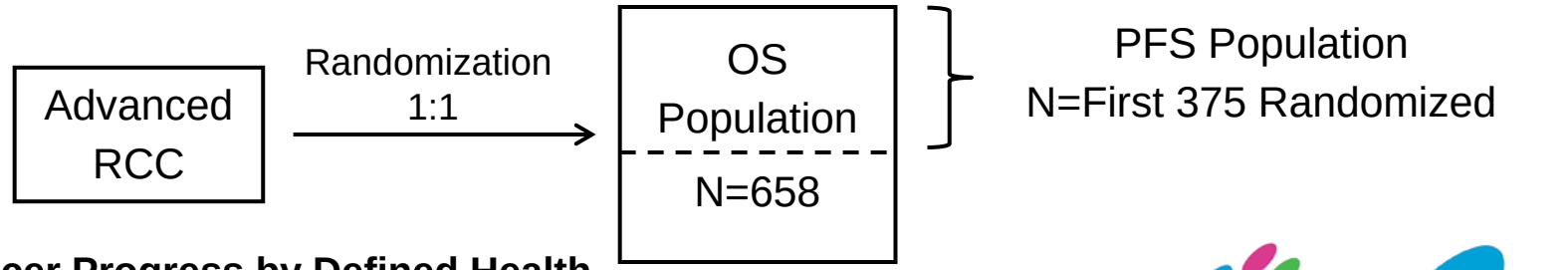


Endpoints:

- **Primary:** Progression-Free Survival, conducted once 259 events from the first 375 patients enrolled occurred
  - Statistical modeling assumptions for primary endpoint: 5.0 months for everolimus, 7.5 months for cabozantinib
  - Designed to provide 90% power to detect a hazard ratio (HR) of 0.667 with a two-sided alpha of 0.05
- **Secondary:** Overall Survival and Objective Response Rate

Changing Competitive Environment in RCC

- Nivolumab vs everolimus 2nd/3rd line RCC phase 3 study with Overall Survival endpoint was already ongoing
- Speed and comprehensive efficacy package were key drivers for trial design for cabozantinib in RCC
  - Moved from phase 1 with durable ORR and long PFS to phase 3
  - Powered Phase 3 METEOR trial for PFS and OS
  - PFS as primary endpoint first (n = 375)
  - ORR as secondary endpoint (n = 658)
  - OS as key secondary endpoint with longer follow up



Competitive Profile and Commercialization

- Cabozantinib improved all three efficacy parameters as compared with everolimus in previously treated RCC
  - Progression free survival (July 2015) – HR 0.58, $p < 0.001$
  - Objective response rate (July 2015) – $p < 0.001$
  - Overall survival (February 2016) – highly significant
- Regulatory filings completed in US and EU Dec ’15/Jan ’16; OS results submitted during review
  - Granted Priority Review and Breakthrough Therapy Designation in US and accelerated review status in EU
- Exelixis plans to commercialize in US – prepared to be launch-ready by April 1, 2016
- Partnership with Ipsen signed Feb 29, 2016 for all territories outside the United States, Canada, and Japan