

OUR VISION: COMBINING TO CURE WITH BEST-IN-CLASS CANCER THERAPIES

NYSE: RCUS

JANUARY 2021

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RCUS Investment Thesis

- **Well-positioned to unlock the value of our pipeline**
  - ~$785M cash and funding into at least 2023
  - 10-year Gilead partnership provides resources and expertise to efficiently and more fully exploit multiple unique intra-portfolio opportunities
  - Recently announced collaboration with AstraZeneca for registrational trial, PACIFIC-8, further validates the therapeutic potential of domvanalimab, Arcus's novel anti-TIGIT antibody
- **Advanced pipeline of products that target 3 of the most important and highly pursued IO pathways: TIGIT, Adenosine, and PD-1**
  - Essential Backbones:
    - **AB154 (Domvanalimab)**: anti-TIGIT mAb – rapidly advancing in randomized combinations
    - **Zimberelimab**: anti-PD-1 mAb with clear line-of-sight to commercialization, enables portfolio combination strategies
  - Adenosine Axis:
    - **AB928 (Etrumadenant)**: $A_{2a}R$ / $A_{2b}R$ antagonist – first and only dual antagonist in the clinic
    - **AB680**: CD73 inhibitor – first small-molecule in the clinic; exceptional potency
- **Initial signs of clinical activity from our early Phase 1/1b trials are being followed by randomized studies/cohorts in order to generate clear evidence of clinical activity; significant readouts from multiple studies expected in 2021**

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Essential Backbone Agents

- **PD-1/PD-L1 Axis**
  - Essential to fully leverage other programs and enable development and commercialization opportunities
  - Zimberelimab has profile similar to that of pembrolizumab: preclinically and clinically
  - Path to zimberelimab single-agent approval to be disclosed in 4Q 2020
- **TIGIT/CD155 Axis: Arcus early investment/commitment to success**
  - Domvanalimab (Ph2): FcR-silent; potential advantages in solid tumors
  - AB308 (IND 4Q20): FcR-capable; potential advantages in hematology
  - Arcus is well positioned in the TIGIT space: only company known to have both types of antibodies

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ATP/Adenosine Axis: One of the Most Ubiquitous Pathways Associated with Immunosuppressive Tumor Microenvironment

- **Arcus's early and broad investment in modulating the pathway**
- **Potential best-in-class adenosine receptor antagonists designed and optimized for oncology setting**
- **Etrumadenant (Ph2): first & only clinical agent that blocks A_{2a} and A_{2b} receptors**
  - Multiple potential biological advantages relative to selective A_{2a} receptor blockers
  - Growing evidence of A_{2b} role in both TME immunosuppression and cancer cell-intrinsic biology
- **AB680: first and most advanced small-molecule CD73 inhibitor in the clinic**
  - Small molecule best modality for tumor-associated enzyme inhibitor (e.g., better tumor penetration)
  - AB680 capable of complete inhibition of both membrane bound *and* soluble forms of CD73; the most advanced antibodies are not capable of fully inhibiting the enzymatic activity of CD73
  - IV and oral formulations in development

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Approaching Multiple Randomized Data Readouts in 2021+



[1]Clinical collaboration with AstraZeneca; AZ will be the primary sponsor of PACIFIC-8.
* +/- biologic
CRT: chemoradiotherapy; Zim: zimberelimab; Dom: domvanalimab; Etruma: Etrumadenant; Rego: regorafenib
Gem: gemcitabine; FOLFOX: (folinic acid, fluorouracil; oxaliplatin); Nab-pac: nab-paclitaxel; Doce: docetaxel;
Carbo: carboplatin; Pem: pemetrexed

Anticipated Upcoming Clinical Milestones

Program	Molecule	Milestone
TIGIT/CD155 Axis	**Dom (AB154)** (TIGIT mod.IgG1)	• ARC-7: Preliminary data in 1H21; Presentation at medical conference in 2021
	AB308 (TIGIT wt IgG1)	• IND filing 4Q20; Initiation of Phase 1/1b in 1H21

Adenosine Axis	**Etruma (AB928)** ($A_{2a}R/A_{2b}R$)	• **Randomized Phase 1b/2**
		  • ARC-4: Preliminary randomized data from Phase 2 portion; presentation at medical conference in 2021
		  • ARC-6: Preliminary data with presentation at medical conference in 2021
		  • ARC-7: Preliminary data in 1H21; Presentation at medical conference in 2021
		  • ARC-9: Initiation of Phase 1b/2 platform study in 4Q20
		• **Phase 1/1b**
		  • ARC-2: Presenting preliminary data at SABCS in 4Q20 (December)
		  • ARC-3: Presenting preliminary biomarker data at SITC in 4Q20 (November)

	AB680 (CD73)	• ARC-8: Preliminary dose-escalation data at ASCO-GI in 1Q21 (January)
PD-1/PD-L1 Axis	**Zim** (PD-1)	• ARC-7: Preliminary data in 1H21; Presentation at medical conference in 2021

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Partnerships that Greatly Expand & Accelerate Opportunities Inherent in Arcus's Expansive Portfolio

GILEAD

- **10-year "all-in" collaboration with well aligned partner**
  - Gilead obtained immediate rights to zim; option to license investigational products in current and future programs
- **Preserves Arcus's independence and provides strategic flexibility**
  - Enables aggressive development in highly competitive areas
- **Allows Arcus to maintain substantial commercial rights over pipeline with ability to accelerate and expand associated opportunities**
  - 50/50 profit share on Gilead-option programs in the U.S.
- **Provides mechanism for Arcus to fund its portion of co-development costs**
  - Ongoing R&D support and opt-in/milestone payments

AstraZeneca

- **Further validates Arcus's position at forefront of anti-TIGIT field**
  - Registrational PACIFIC-8 trial for dom plus Imfinzi expected to begin in 2021
- **Leverages AstraZeneca's leadership in the curative-intent Stage III NSCLC setting**
  - Imfinzi is the only immunotherapy approved for patients in this setting
- **Significant upside potential with optimized level of risk**
  - Retained economics on respective molecules; informed cost-sharing
- **Further builds on the Arcus-Gilead agreement**
  - Supports combinations and settings that maximize value and bring potential benefits to broadest patient population possible

Well-positioned to unlock the value of our pipeline
~$785M[1] cash and funding into at least 2023

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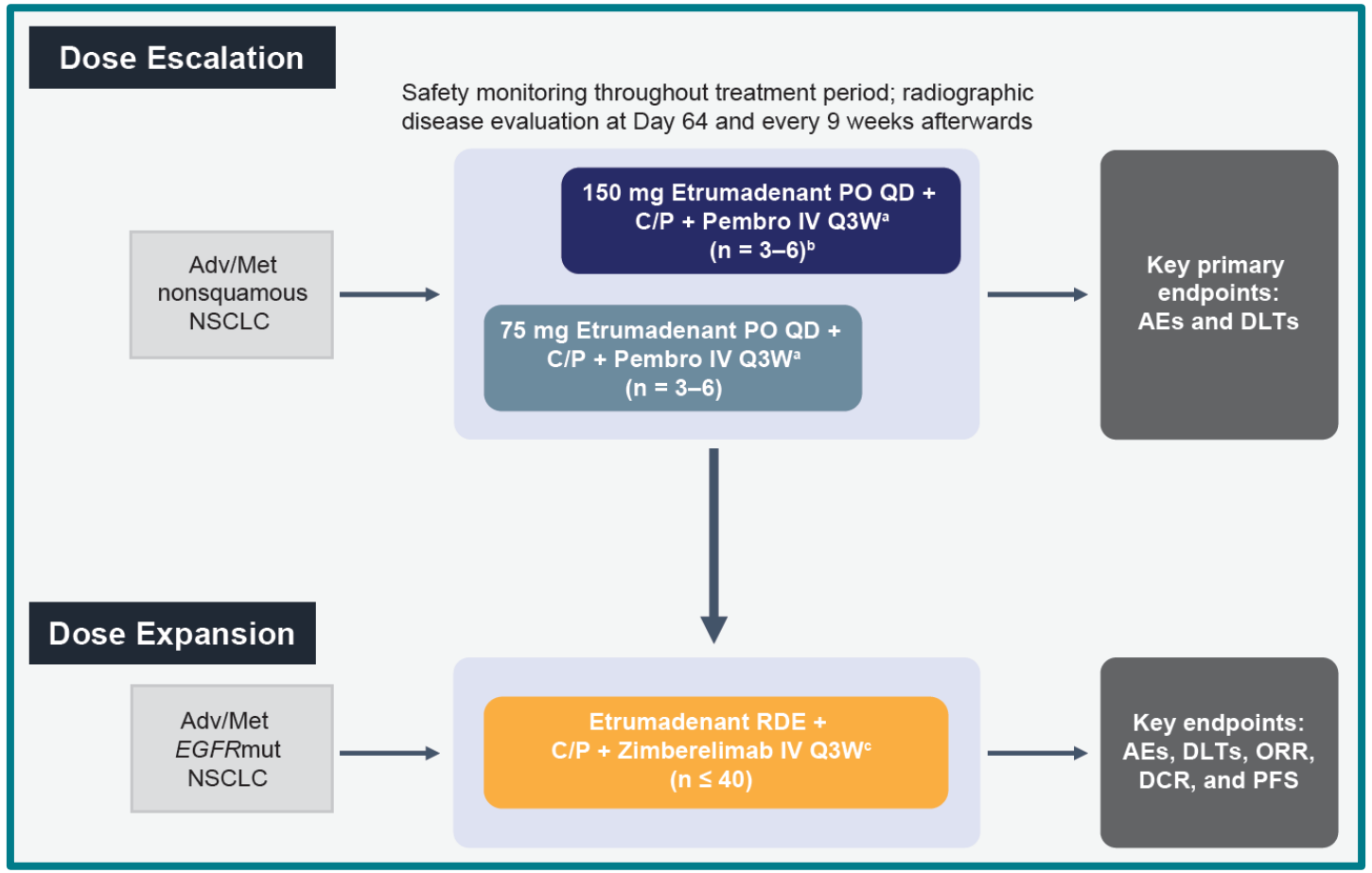
[1]As of September 30, 2020

CLINICAL-STAGE ADENOSINE PROGRAMS

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ARC-4 Study to Evaluate Etruma (AB928) + Zim + Chemotherapy in *EGFR*mut Non-Small Cell Lung Cancer

- **Study design schema for dose-escalation and dose-expansion of Etruma + anti-PD-1 + Carboplatin/Pemetrexed in NSCLC patients**
- **Dose-expansion phase:**
  - Participants must have a sensitizing EGFR mutation and failed treatment with 1 TKI (or 1-2 TKIs for tumors with T790M mutation)
  - Previous treatment with chemotherapy or PD-1/PD-L1 therapy is not allowed
  - Potential to open control arm after futility assessment
- **Preliminary data presented at ESMO 2020**



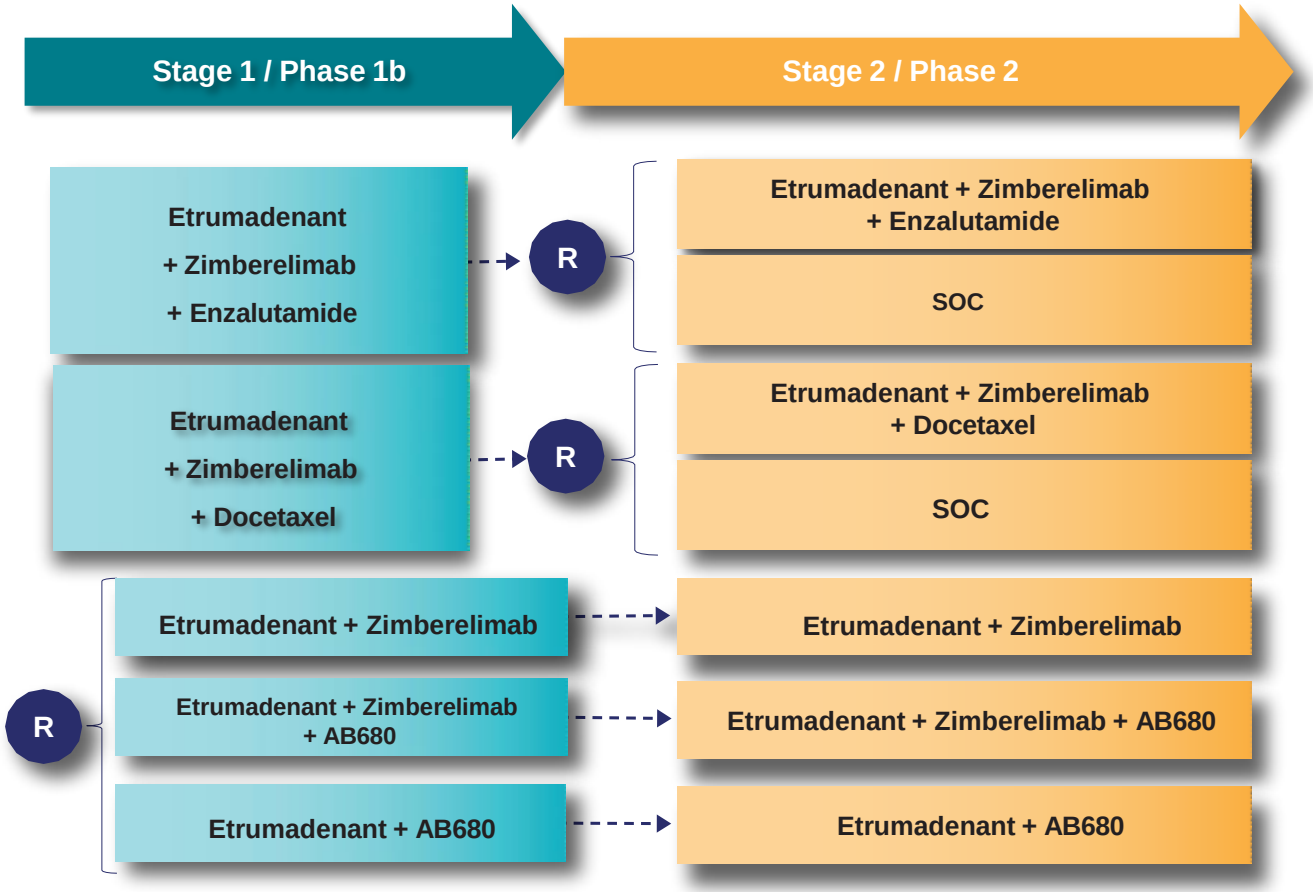
C/P: carboplatin/pemetrexed; RDE: recommended dose for escalation; TKI: tyrosine kinase inhibitor

A. Spira et al, ESMO (2020); presentation no.1309P; NCT03846310

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Platform Study to Evaluate Etruma (AB928) across Multiple Lines of Therapy in mCRPC

- **Platform study in mCRPC to assess the safety and efficacy of the addition of Etruma (AB928) + Zim to standard of care Enzalutamide and Docetaxel**
  - Supports early randomization and proof of concept if activity signal is seen in Stage 1
- **Evaluating Etruma novel combinations for late-line patients without available standard of care**
  - Opportunity for expansion of these cohorts based on initial signals

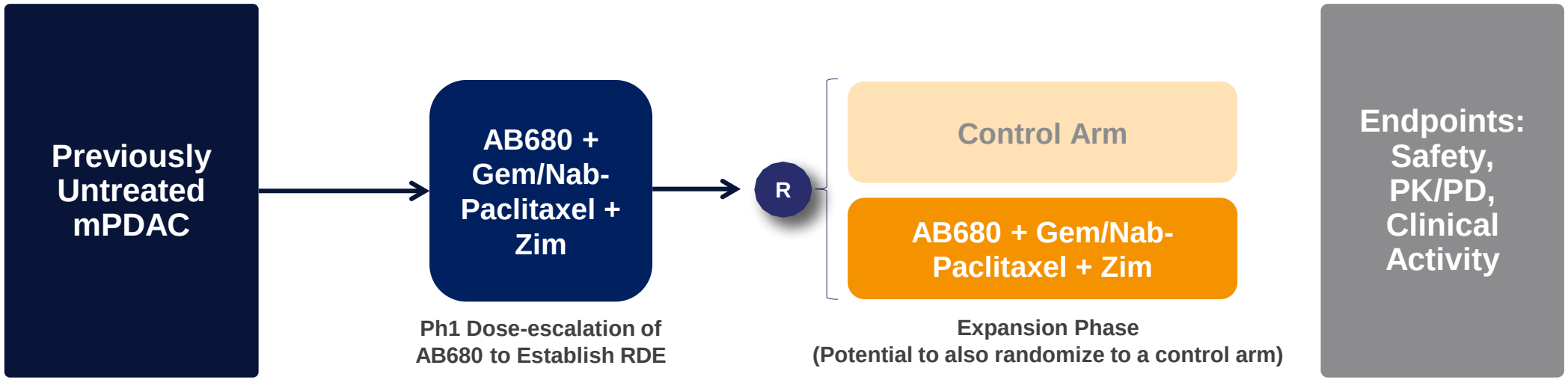


Subudhi e.t al, ESMO (2020); presentation no.687TiP; NCT04381832

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ARC-8 Phase 1/1b Evaluation of AB680 + Chemotherapy + Zim in 1L mPDAC

- **Evaluation of AB680 (CD73 small molecule inhibitor) in combination with zimberelimab (anti-PD-1) + gemcitabine/nab-paclitaxel in first line metastatic pancreatic cancer**
  - Phase 1 dose-escalation of AB680 to define a recommended dose for expansion (RDE) is ongoing
  - Phase 1b expansion anticipated to start in 2H2020 with potential to include a randomized control arm



- **Plans underway to evaluate AB680 in multiple combinations and indications once RDE achieved (e.g., mCRPC)**

Bendell et al, GI ASCO (2020); presentation no. TPS788; NCT04104672

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CLINICAL-STAGE TIGIT PROGRAMS

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Domvanalimab – Phase 1 Clinical Summary

- **Domvanalimab (Dom) is well tolerated in combination with zimberelimab (Zim) at all doses and regimens assessed thus far.**
- **To-date, no evidence of ADAs in any of the Ph1 samples for domvanalimab, nor has there been any evidence of ADAs in our clinical studies for zimberelimab.**
- **100% TIGIT occupancy on blood lymphocytes achieved at all timepoints at 0.5 mg/kg q2w and higher. Similar TIGIT occupancy has been seen with q3w and q4w regimens.**
- **Increased proliferation (Ki-67) of blood CD8 T cells, of a magnitude similar to what has been described for anti-PD-1 mAbs, observed in Ph1 subjects, both with domvanalimab single agent and in combination with zimberelimab.**
- **Ongoing evaluations of various dose-schedule combinations of domvanalimab and zimberelimab in our Ph1 study, which will be presented at an upcoming medical conference once complete.**

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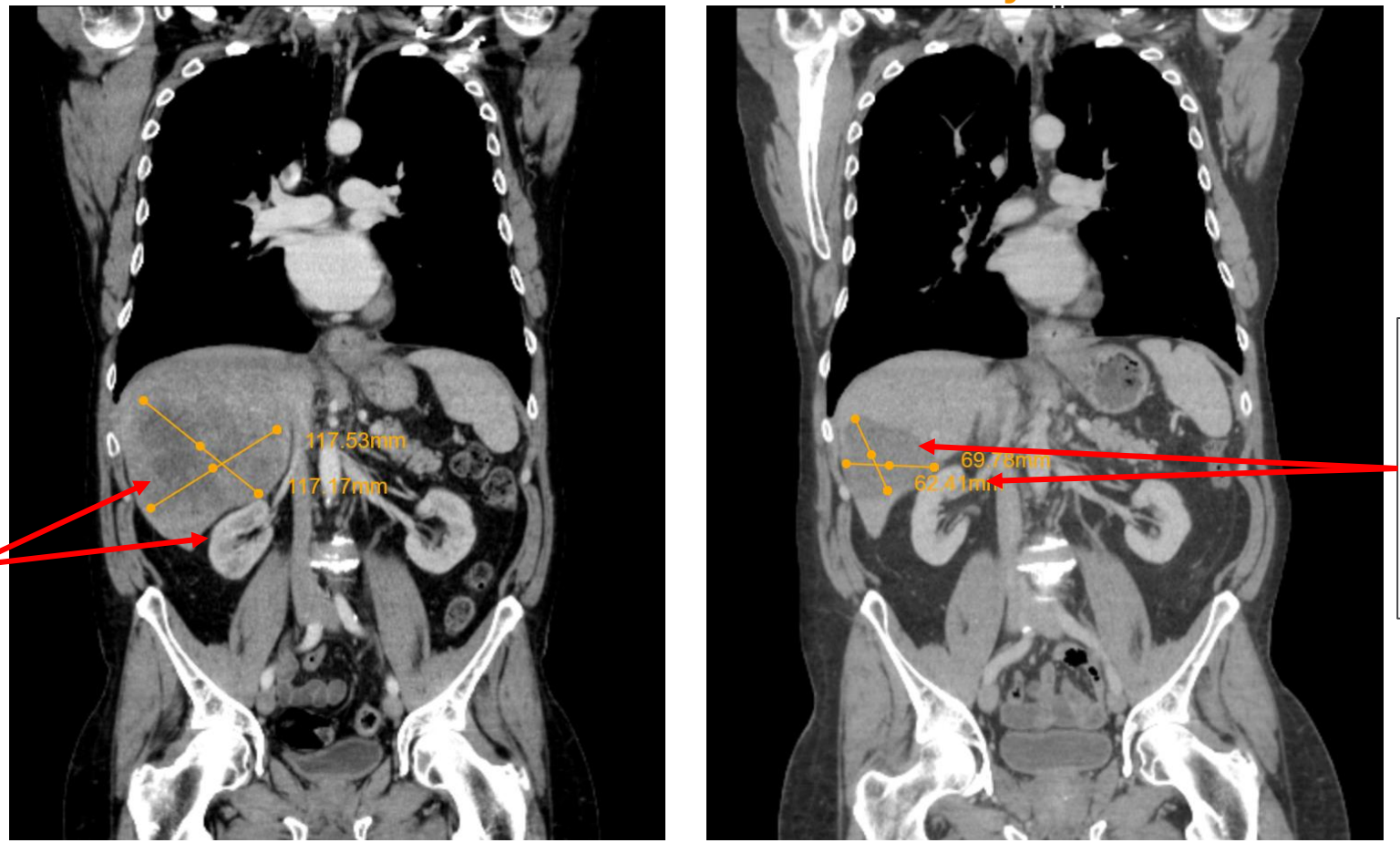
Ph1 Patient Example: Prolonged Confirmed Partial Response in a Late-line, Post-Checkpoint Inhibitor, Esophageal Cancer Patient

- **68 y.o. male with late-line metastatic esophageal cancer (CPS2)**
- **Patient remains on therapy with continued tumor shrinkage (cPR) at Cycle 9**

Prior therapies:
- FOLFOX
- Carbo/Pac
- Pembrolizumab

Baseline: very large metastatic right liver lobe lesion with right massive liver enlargement and compression of right kidney/renal vein

Baseline **Cycle 6**



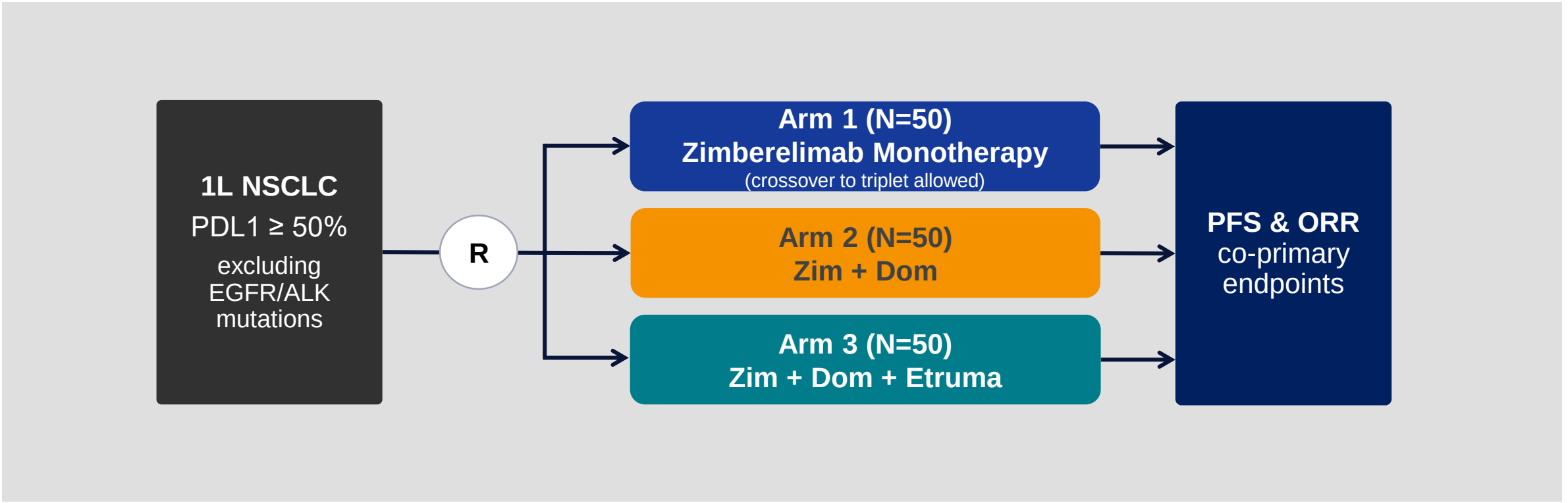
Cycle 6: significant tumor shrinkage and relief of liver enlargement & right kidney/vein compression

CSP: COMBINED POSITIVE SCORE (PD-L1 CELLS; PEMBRO APPROVAL IS IN CSP≥10 FOR ESOPHAGEAL CANCER; cPR: CONFIRMED PARTIAL RESPONSE

REPRESENTATIVE IMAGES COURTESY OF DR. AMITA PATNAIK (CO-DIRECTOR OF CLINICAL RESEARCH, THE START CENTER FOR CANCER CARE, SAN ANTONIO)

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Dom (TIGIT) + Zim (PD-1) + Etruma (A_{2a}/A_{2b}) vs. Dom + Zim vs. Zim in 1L NSCLC (PD-L1 ≥ 50%)

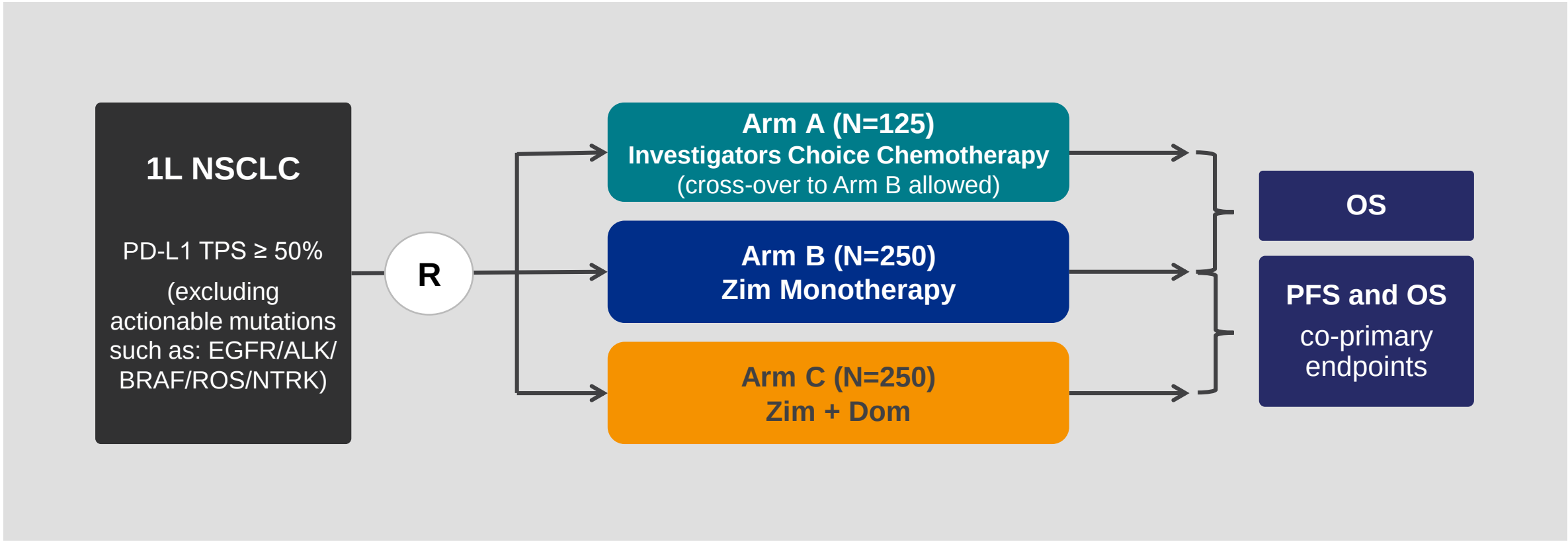


- **ARC-7 is the first study to investigate the triple combination of anti–PD-1, anti-TIGIT, and adenosine receptor antagonism including in patients who have progressed on PD-1 monotherapy for whom there is a high unmet need**
- **Ongoing enrollment in the US and Asia**

Chaudhry et al, ESMO (2020); presentation no.1419TiP; NCT04262856

Phase 3 Study Design

Enables potential approval of BOTH Zim mono and Zim + Dom Combination



- **Reviewed and aligned with the US and EU health authorities**
- **ARC-7 is ongoing in the US and Asia; intended to provide data supportive of ARC-10**

NCT#: pending

Two New INDs Expected in 2H21

HIF-2α Inhibitor

Transcription factor

HIF-2α is a master transcriptional regulator of multiple genes involved in tumor progression

Cancer cell intrinsic target;
potential non-oncology indications

PI3Kγ Inhibitor

Glycolipid kinase

PI3Kγ is required for the immunosuppressive activity of tumor-infiltrating macrophages and myeloid-derived suppressor cells

Immune (TAM, MDSC) target

AXL Inhibitor

Tyrosine kinase

AXL overexpression is associated with tumor resistance to chemotherapy and IO drugs

Cancer cell intrinsic target

PAK4 Inhibitor

Serine kinase

PAK4 overexpression is responsible for T-cell exclusion from immune desert tumors

Cancer cell intrinsic target

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