

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

CORPORATE OVERVIEW

APRIL 2021

NYSE: RCUS

Forward-looking Statements/Safe Harbor

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2021 Will Be a Pivotal Year for Arcus

- **Rapidly advancing five clinical-stage product candidates**
  - Essential backbone antibodies:
    - **AB154 (Domvanalimab)**: Anti-TIGIT mAb (FcR silent) – randomized interim-analysis read-out for ARC-7 planned in 2Q:21 (in 1L NSCLC, PD-L1 ≥ 50%); Initiated ARC-10, our registrational trial to support both Dom + Zim and Zim monotherapy approvals
    - **AB308:** Anti-TIGIT mAb (FcR enabled) to target heme malignancies; First patient dosed April 2021
    - **AB122 (Zimberelimab)**: Anti-PD-1 mAb with clear line-of-sight to commercialization; enables portfolio combination strategies
  - Two internally discovered small molecules targeting the adenosine axis:
    - **AB928 (Etrumadenant)**: First dual $A_{2a}R$ / $A_{2b}R$ antagonist to enter the clinic
    - **AB680**: First small-molecule CD73 inhibitor to enter the clinic; both IV and oral formulations in development
- **Six Arcus sponsored randomized trials with preliminary data from several of these randomized trials expected in 2021**
- **Advancing additional small molecule programs**
  - HIF-2*α* inhibitor anticipated to enter clinical development in 2H2021
- **Well-positioned to unlock the value of our pipeline**
  - ~$735M in cash as of 12/31/20; the addition of $220 million in proceeds from Gilead's equity investment in February 2021 provides funding at least through 2023
  - "All-in" Gilead partnership provides significant financial and other resources to more fully exploit our portfolio
  - Clinical collaboration with AstraZenca for PACIFIC-8 (Phase 3 trial in Stage III NSCLC) further validates the therapeutic potential of domvanalimab; initiation of registrational trial expected in 2H21

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Broad Clinical Program Targeting Major Cancers, Including Those Not Responsive to PD-(L)1 Therapy



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, Durva: durvalumab; Enza: enzalutamide
NSCLC: non-small cell lung cancer; CRPC: castrate-resistant prostate cancer; CRC: colorectal cancer; PDAC: pancreatic ductal adenocarcinoma
[1]Clinical collaboration with AstraZeneca; AZ will be the primary sponsor of PACIFIC-8.
* +/- biologic

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Multiple Important Readouts Are Expected In 2021

	COMBINATION / ARMS	SETTING	MILESTONE	ANTICIPATED TIMING
ARC-8	**AB680** + **Zim** + Gem/Nab-pac	Phase 1/1b Trial in **1L Pancreatic Cancer**	– Initial dose-escalation data – Additional data from dose-escalation / expansion	✓ **January 2021 (ASCO GI)** ▪ **2H21**
ARC-7	**Zim** + **Dom** *vs.* **Zim** *vs.* **Zim** + **Dom** + **Etruma**	Randomized Phase 2 Trial in **1L NSCLC (PD-L1 ≥ 50%)**	– Conduct of interim analysis – Presentation of IA data	▪ **2Q21** ▪ **2H21**
ARC-4	**Etruma** + **Zim** + Carbo/Pem *vs.* **Zim** + Carbo/Pem	Randomized Phase 1/2 Trial in **TKI R/R EGFR+ NSCLC**	– Initial randomized data	▪ **2H21**
ARC-6	**Etruma** + **Zim** + SOC *vs.* SOC	Randomized Phase 2 Trial in **2L/3L Metastatic castrate-resistant prostate cancer (mCRPC)**	– Preliminary data from an initial cohort – Initial randomized data	▪ **2Q21** ▪ **2H21**
ARC-9	**Etruma** + **Zim** + FOLFOX *vs.* SOC	Randomized Phase 2 Trial in **2L/3L/3L+ Colorectal cancer**	– Initial randomized data for 2L/3L cohorts; single-arm data for 3L+	▪ **1H22**

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

GILEAD

10-year "all-in" collaboration

- $175mm upfront payment + $200mm equity investment at closing
- Option rights: Gilead obtained immediate rights to zim + an option to license current and future molecules
- Opt-in payments: $200-275mm for certain clinical-stage programs and $150mm for earlier-stage programs
- R&D cost sharing: 50/50 post-opt in
- Enables aggressive development plan while allowing Arcus to maintain 50% of U.S. commercial rights and economics
- In 1Q21, increased their equity stake to 19.5%, with $220mm investment in Arcus

TAIHO PHARMA

5-year collaboration for Japan and other territories in Asia (ex-China)

- Included initial upfront payments of $35mm and potential for additional option payments
- Milestones: Up to $275mm in development, regulatory and commercial milestones per program
- Royalties: Tiered from high-single digit to mid-teens on net sales
- Taiho's in-licensing of etruma & zim allows potential combinations across Taiho's full oncology portfolio
- Facilitates global development & commercialization of Arcus molecules

AstraZeneca

Clinical collaboration for domanavalimab plus durvalumab

- Companies to collaborate on PACIFIC-8, an AstraZeneca-sponsored trial
- Further validates Arcus's position at forefront of anti-TIGIT field
- Leverages AstraZeneca's leadership in the curative-intent Stage 3 NSCLC setting
- Retained economics on respective molecules
- Further builds on the Arcus-Gilead partnership while allowing for cost and risk-sharing on a large registrational trial
- Trial expected to initiate in 2H2021

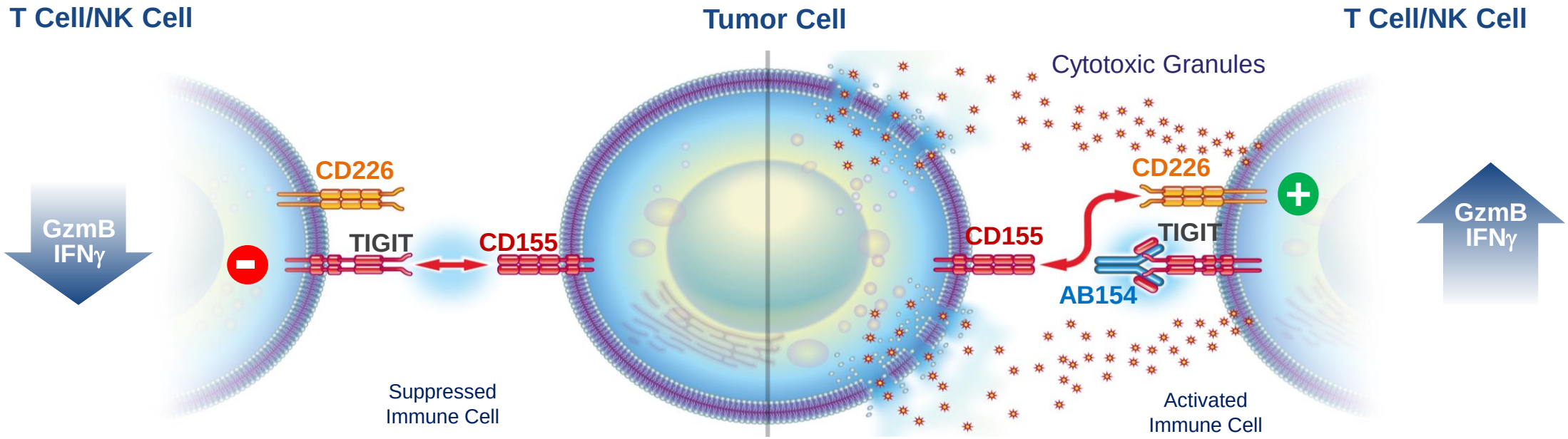
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DOMVANALIMAB

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Anti-TIGIT Antibodies Have the Potential to be the Next I-O Backbone

Dual Mechanism: Blocking TIGIT inhibits a critical immuno-suppressive pathway while promoting the CD226-CD155 immune-activating pathway



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Anti-TIGIT Antibody Portfolio Positions Arcus as a Pioneer in the TIGIT Field

Domvanalimab's advancement into a registrational study coupled with AB308's recent IND clearance reinforces Arcus as a leader in the development of anti-TIGIT therapies

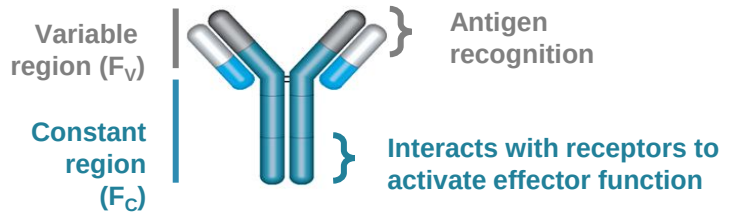
Domvanalimab (FcR-silent)

- Blocks the TIGIT receptor on T-cells to prevent binding of CD155; does NOT deplete TIGIT-bearing immune cells
- No evidence of ADAs (which can impact clinical efficacy) to date
- 100% TIGIT occupancy on blood lymphocytes achieved
- Increased proliferation (Ki-67) of blood CD8 T cells, of a magnitude similar to what has been described for anti-PD-1 mAbs
- Ongoing randomized phase 2 trial ***("ARC-7")***; Interim analysis (IA) in 2Q21; presentation of IA data in 2H21; Initiated Phase 3 trial evaluating Dom + Zim vs. Zim vs. chemotherapy ***("ARC-10")***

Potential best option for solid tumors

AB308 (FcR-enabled)

- Also blocks the CD155 interaction with TIGIT, critical for T cell activation
- Potential to deplete TIGIT-bearing cancer cells (e.g., myeloma, NHL)
- First patient dosed in April 2021; Initiated a "rapid dose-escalation" Phase 1/1b with the goal of being able to start a registrational trial by YE



Potential best option for heme malignancies

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

Domvanalimab Phase 1 Patient Example

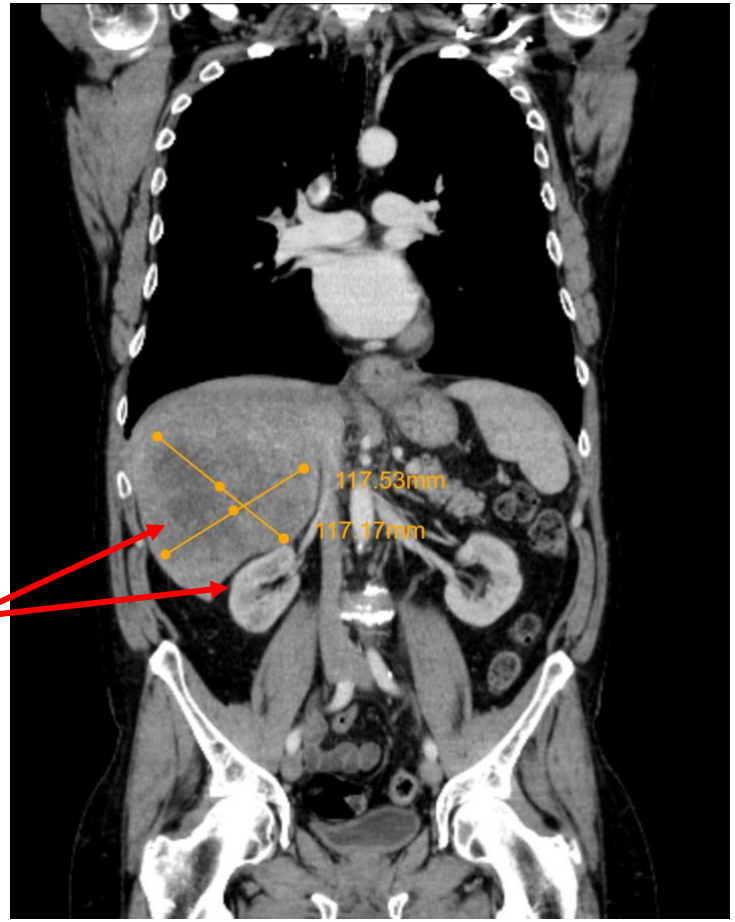
- **68 y.o. male with late-line metastatic esophageal cancer (CPS2)**
- **Patient remains on therapy with continued tumor shrinkage (cPR) at Cycle 12**

Prior therapies:
- FOLFOX
- Carbo/Pac/XRT
- Pembrolizumab

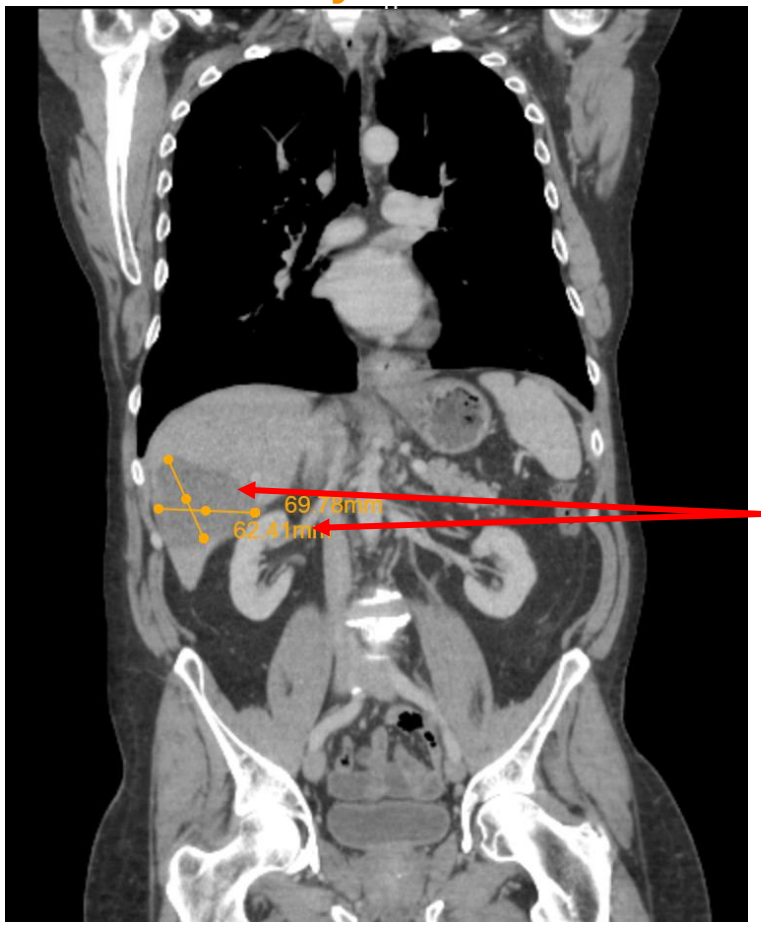
Best response to prior therapy: SD

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

Baseline



Cycle 6



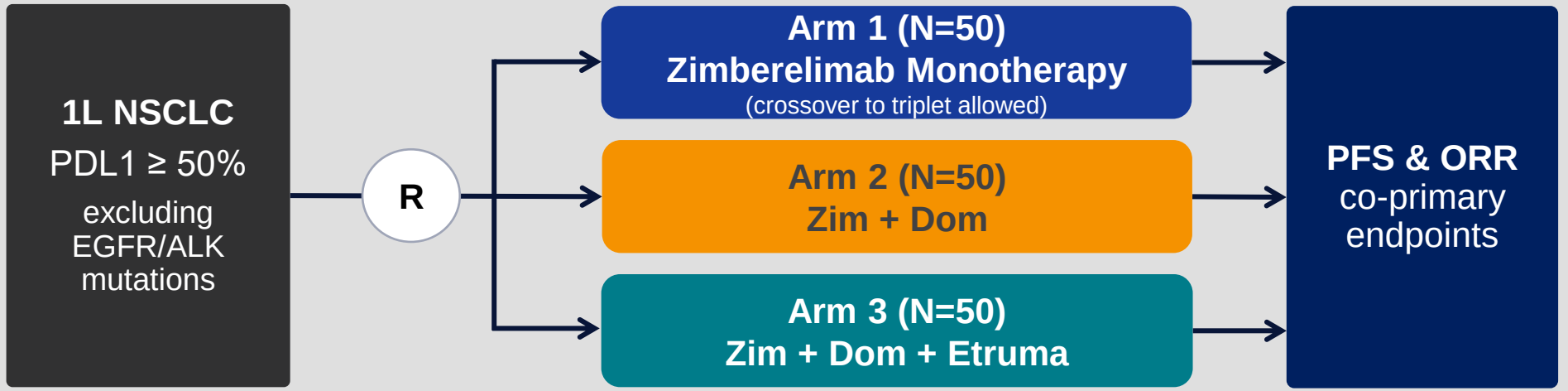
Cycle 6: significant tumor shrinkage and relief of liver enlargement & right kidney/vein compression

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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ARC-7 Randomized Phase 2 Study to Evaluate Dom + Zim vs. Zim vs. Etruma + Dom + Zim in 1L NSCLC (PD-L1 ≥ 50%)

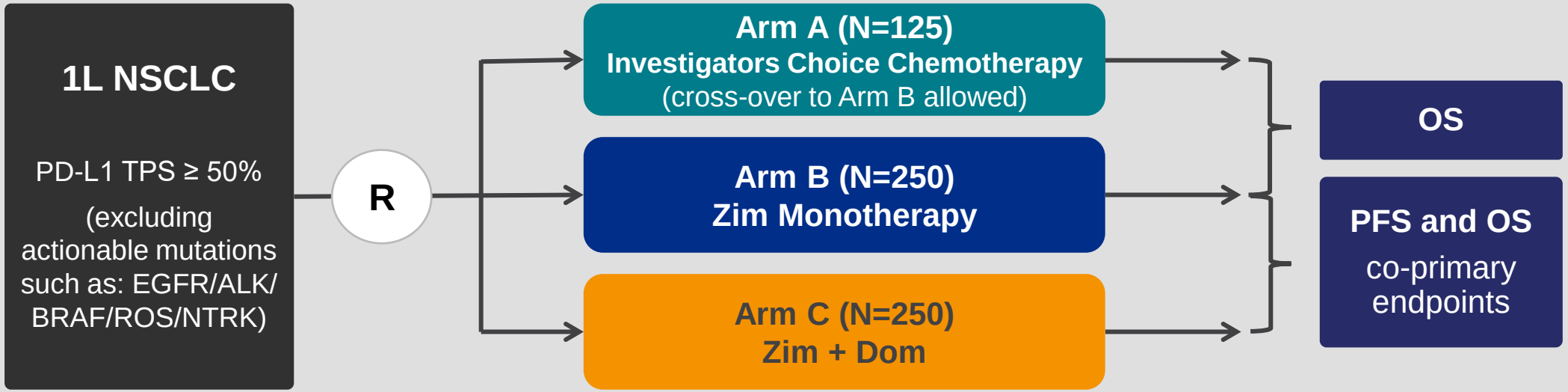


Interim analysis to be conducted in 2Q:21;
IA data expected to be presented in 2H:21

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

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ARC-10 Phase 3 Trial to Evaluate Dom + Zim vs. Zim mono vs. Chemo in 1L NSCLC (PD-L1 ≥ 50%)



Enables potential approval of BOTH Zim mono and Zim + Dom combination; Initiated in 1Q21

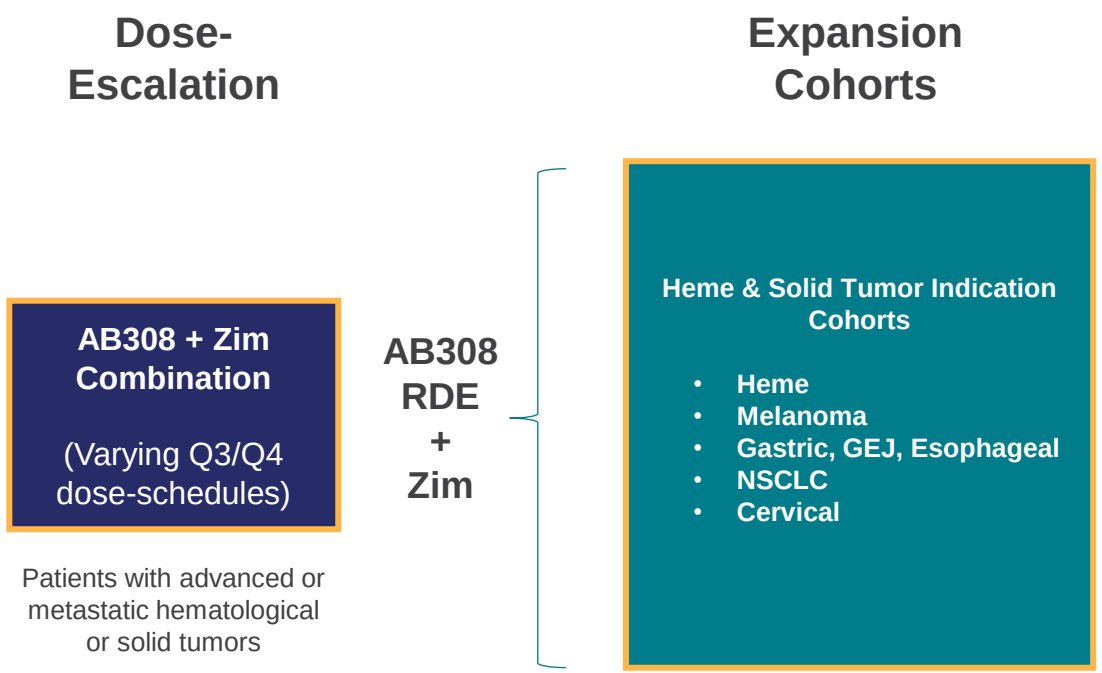
NCT#: NCT04736173

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ARC-12 Phase 1/1b Trial to Evaluate Safety & Tolerability of AB308 + Zim in Advanced Malignancies

- **Key elements of the design:**
  - Leverages Arcus's anti-TIGIT antibody development experience to expeditiously establish the safety, PK and PD of AB308 in combination with zimberelimab
  - Multiple parallel dose-schedules to optimize earliest Q3W and Q4W dose combinations could enable pivotal trials as early as year-end 2021



First patient dosed April 2021;
Rapid dose-escalation to support potential pivotal trials YE21

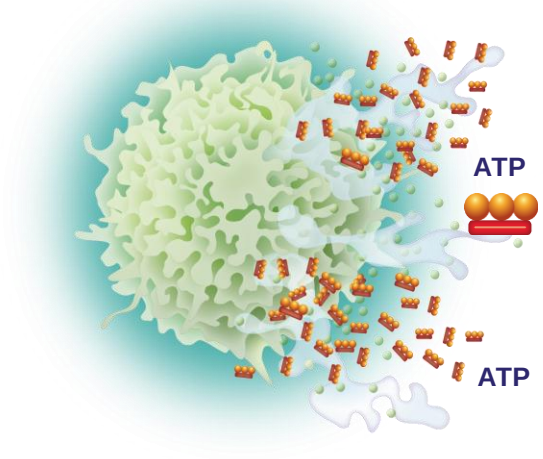
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ADENOSINE PROGRAMS

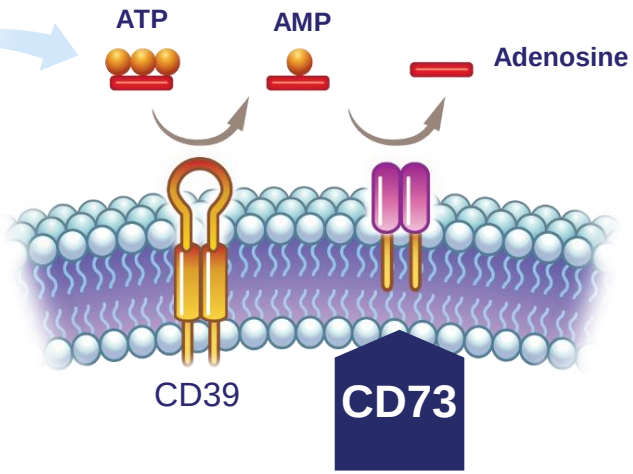
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The Adenosine Axis Plays a Well-Established and Critical Role in Suppression of the Immune Response

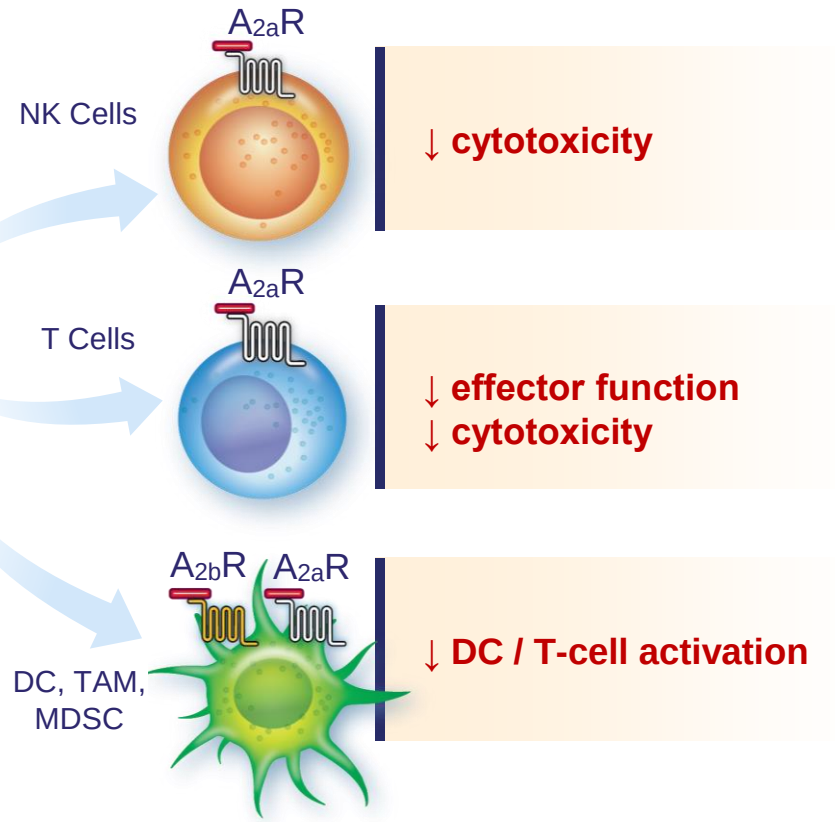
Extracellular ATP is released by dying cells, particularly when triggered by immunogenic chemotherapy



Adenosine is generated from ATP by the enzymatic action of CD39 and CD73



Adenosine production leads to significant **immunosuppression** in the tumor microenvironment



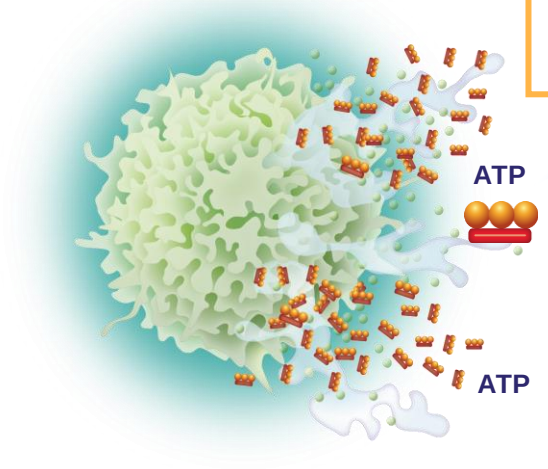
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Arcus is a Leader in the Development of Therapeutics that Target the Adenosine Axis

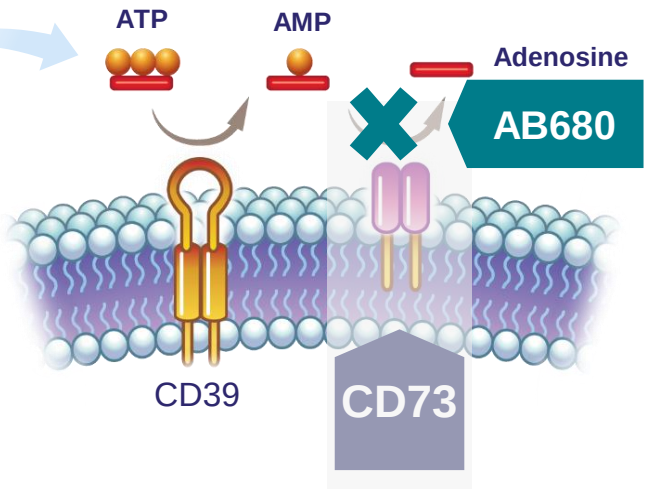
AB680 inhibits CD73, an enzyme that plays a key role in the conversion of AMP to adenosine, while Etrumadenant blocks the adenosine 2a and 2b receptors

Etruma blocks adenosine from binding to **$A_{2a}R$** and **$A_{2b}R$**, **blocking immunosuppression**

Extracellular ATP is released by dying cells, particularly when triggered by immunogenic chemotherapy



AB680 blocks the function of CD73, preventing the conversion of AMP to adenosine



NK Cells



Etruma

↑ cytotoxicity

T Cells



Etruma

↑ effector function
↑ cytotoxicity

DC, TAM, MDSC



Etruma

↑ DC / T-cell activation

Etruma: Dual $A_{2a}R/A_{2b}R$ receptor antagonist; **AB680**: Small-molecule CD73 inhibitor

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We Are Pursuing a Broad Development Plan for Etruma

		COMBINATION / ARMS	SETTING	STATUS
Ongoing randomized studies	ARC-4	**Etruma** + **Zim** + Carbo/Pem *vs.* **Zim** + Carbo/Pem	Randomized Phase 1/2 Study in **TKI R/R EGFR+ NSCLC**	– Initial randomized data expected 2H21
	ARC-6	**Etruma** + **Zim** + SOC *vs.* SOC	Randomized Phase 2 Study in **2L/3L Metastatic castrate-resistant prostate cancer (mCRPC)**	– Futility analysis passed for the “chemo combo” cohort – Preliminary data from an initial cohort expected 2Q21 – Initial randomized data expected 2H21
	ARC-9	**Etruma** + **Zim** + FOLFOX *vs.* SOC	Randomized Phase 2 Study in **2L/3L/3L+ Colorectal cancer**	– Initial randomized data for 2L/3L cohorts and single-arm data for 3L+ expected 1H22
Initial studies	ARC-2	**Etruma** + PLD	Phase 1/1b Study in **TNBC** or **Ovarian cancer**	– Results presented at SABCS 2020
	ARC-3	**Etruma** + FOLFOX	Phase 1/1b Study in **Colorectal cancer**	– Initial results presented at SITC 2020 – OS / PFS data at AACR 2021

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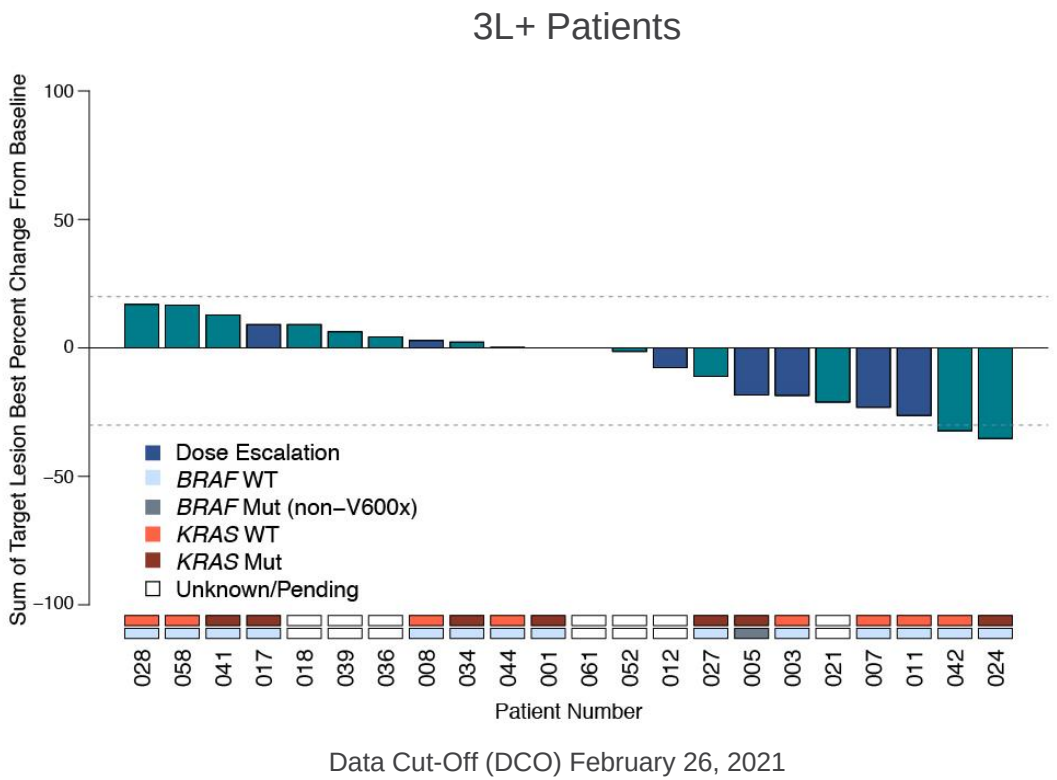
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Etruma Has Generated Early Clinical POC Data in Multiple Settings Characterized by High Levels of CD73

Setting	Combination	Conference Presented	Key Highlights	Next Steps
NSCLC ARC-4	**Etruma** +Pembro/ Zimberelimab (anti-PD-1) + Chemotherapy	ESMO 2020	**31% ORR** (4/13) including in a TKI-R/R patient that had failed 3 prior lines of therapy; **46% SD** 6 of the 7 patients in the 150mg etruma dose expansion cohort were still on drug at the time of data cutoff (150mg RDE)	Randomized portion of ARC-4 is enrolling in TKI R/R EGFR+ patients Initial data expected 2H21
1-3L mCRC ARC-3	**Etruma** + FOLFOX	SITC 2020 and AACR 2021	**In 1L: 53.3% ORR and 43% SD**; 5/15 patients went on to curative surgery **In 3L+: 8.7% ORR and 4.2 months median Time on Treatment** (2x+ what is observed with trifluridine and tipiracil or regorafenib) High levels of intra-tumoral CD73 and high TMB were associated with better outcomes in 3L+ patients	PFS and OS data to be presented at AACR 2021 Randomized Phase 2 ***ARC-9*** study (Etruma combinations in 2L and 3L CRC) initiated
1L+ TNBC ARC-2	**Etruma** + PLD	SABCS 2020	Responses with doublet observed in patients failing 1L treatment	Plans for future development under evaluation

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In Phase 1/1b Study Etruma Compares Favorably to SOC for PFS and OS in 3L+ mCRC Setting



Data Cut-Off (DCO) February 26, 2021

- **Patients had received at least 2 prior lines of therapy (median of 3 prior lines and a range of 2 to 7) and 87% of which had received prior FOLFOX**
- **Median progression-free survival (PFS) of 4.2 months, double the data reported for current standard-of-care (SOC) therapies**
  - Median PFS of 2.0 and 1.9 months for trifluridine-tipiracil and regorafenib, respectively[1,2]
- **Median overall survival (OS) of 13.6 months compares favorably to reported data for current SOC therapies**
  - Median OS of 7.1 and 6.4 months, for trifluridine-tipiracil and regorafenib, respectively[1,2]
- **Observed high 8-week and 16-week disease control rates of 86% and 46%, respectively**
- **Combination was well tolerated; no additive toxicity observed**

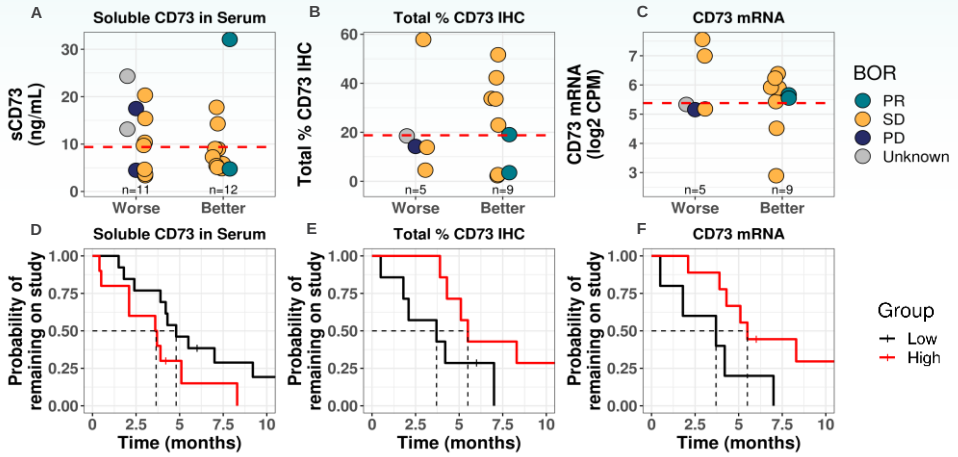
Advanced into ARC-9 randomized Phase 2 study in 1Q21 based on encouraging results; Initial data expected in 1H22

M. Cecchini et al, AACR (2021); Poster No. CT129; NCT03720678
1. Maher RJ, et al. *N Eng J Med*. 2015;372(20):1909-1919.
2. Grothey A, et al. *Lancet.* 2013; 381(9863):303-312.

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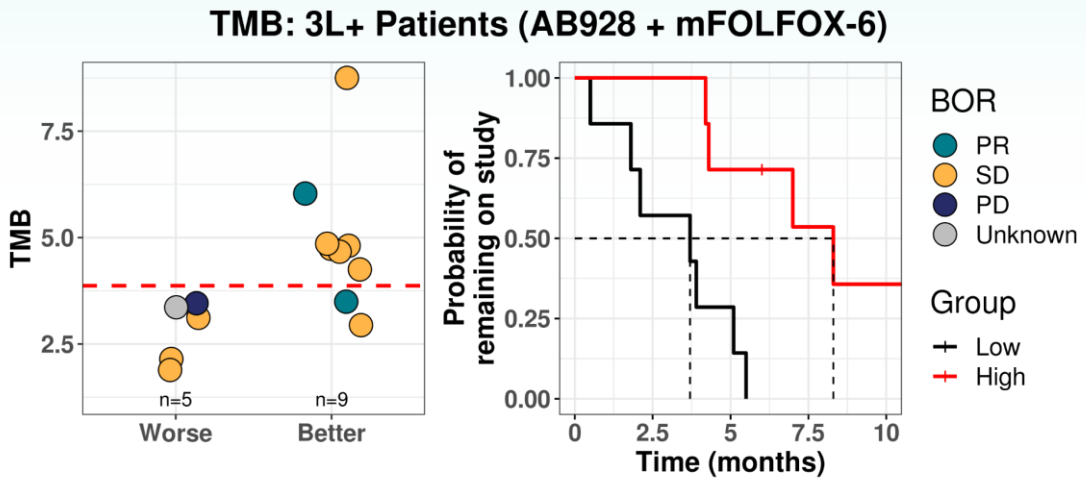
In mCRC: Early Data in 3L+ Patients Reveal Potential Biomarkers Predictive of Response to Etruma

Intra-tumoral CD73 Appears to Be Associated with a Better Clinical Outcome(1)



Baseline soluble CD73 (sCD73) in serum and tumor CD73 gene/protein measurements in 3L+ mCRC.
Top panel shows dot plots for clinical outcome on the x-axis (as defined in Fig. 1B) and on the y-axis for (A) sCD73 by ELISA, (B) total percent CD73 protein by tumor biopsy multi-plex IHC, and (C) CD73 mRNA by tumor biopsy RNA-seq. Red dashed lines denote cut-points that maximize sensitivity and specificity[4] for prediction of clinical outcome given each CD73 measurement. (D,E,F) Corresponding Kaplan-Meier (KM) curves denoting time in months on the x-axis and probability of remaining on study on the y-axis. The cut-points used for the KM curves are defined by the red dashed lines in panels A-C. Interestingly, our trend is in the opposite direction to prior studies that identified CD73 (protein and mRNA) as a strong negative prognostic/predictive (FOLFOX) biomarker in CRC[5,6], perhaps reflective of an AB928-mediated effect in the present study.

Tumor Mutation Burden (TMB) Is Associated with Better Clinical Outcome



Tumor Mutation Burden (TMB) in 3L+ mCRC patients.
(A) Dot plot with TMB on the y-axis in 3L+ mCRC patients and clinical outcome on the x-axis. Red dashed line shows the cut-point[4] for TMB that best discriminates clinical outcome. (B) KM curves (probability of remaining on treatment) on the y-axis, stratified by cut-point defined in A. TMB is strongly associated with better clinical outcome and duration on treatment in 3L+ patients treated with AB928 + mFOLFOX-6. In contrast, TMB is not associated with outcome in 1L ARC-3 patients or 1L patients in TCGA[13] treated with FOLFOX regimens (data not shown).

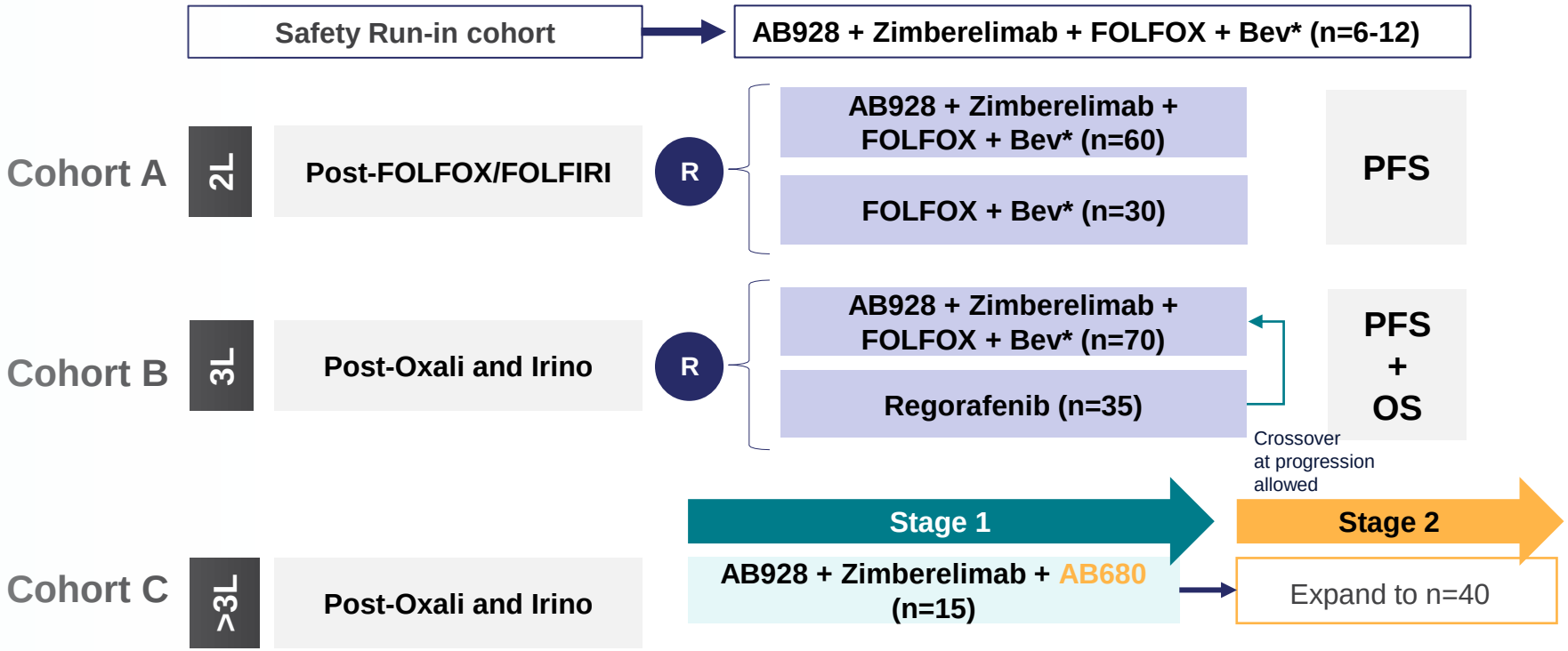
(1) Prior studies have identified CD73 (protein and mRNA) as a strong negative prognostic biomarker in CRC. Because patients in this study with higher intra-tumoral CD73 had better clinical outcomes, CD73 may be a potentially important biomarker for response to Etruma.

A. Udyavar et al, SITC (2020); Abstract No. 338; NCT03720678

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Randomized Phase 2 Study to Evaluate Etruma Combinations in 2L / 3L+ mCRC

- **Randomized Phase 2 study evaluating Etruma + Zim + chemo combinations in 2L/3L mCRC**
- **Based on results from the ARC-3 study in 1-3L+ mCRC; Primary differences:**
  - Addition of Zim to the combination
  - More homogenous patient population
  - Active comparator (chemo in 2L; regorafenib in 3L)
- **Initiated in 1Q21; Initial data presentation in 1H22**

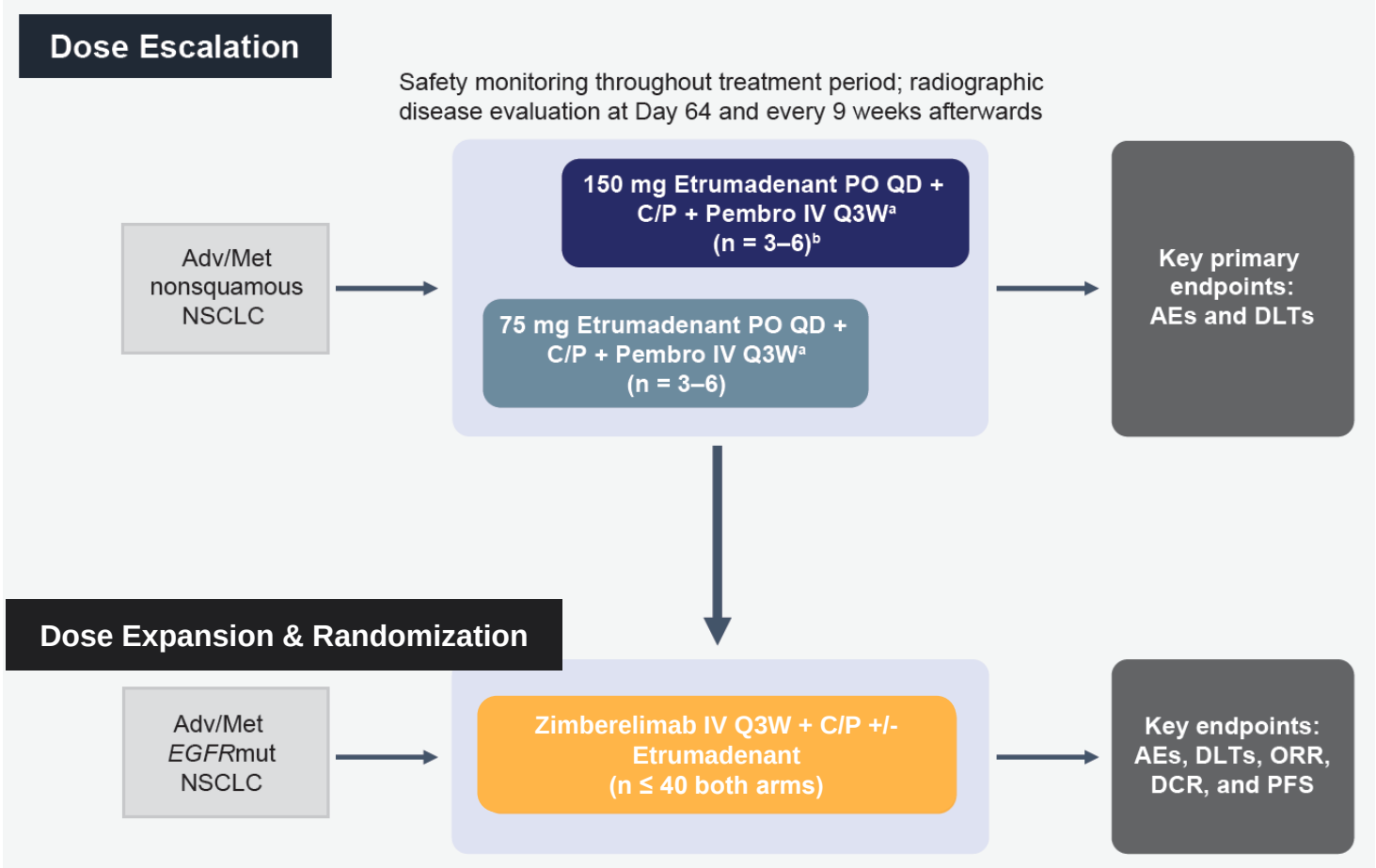


*Bev will be included for all patients in whom it is not contraindicated

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ARC-4 Ongoing Phase 1/2 Study to Evaluate Etruma + Zim + Chemotherapy in *EGFR*mut NSCLC

- **Dose-escalation and dose-expansion study to evaluate Etruma + Zim + Carboplatin / Pemetrexed in NSCLC**
- **Dose-expansion / randomization 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
  - Control arm of Zim + chemotherapy was opened after passing the futility assessment
- **Randomized portion is ongoing with initial data to be presented 2H21**



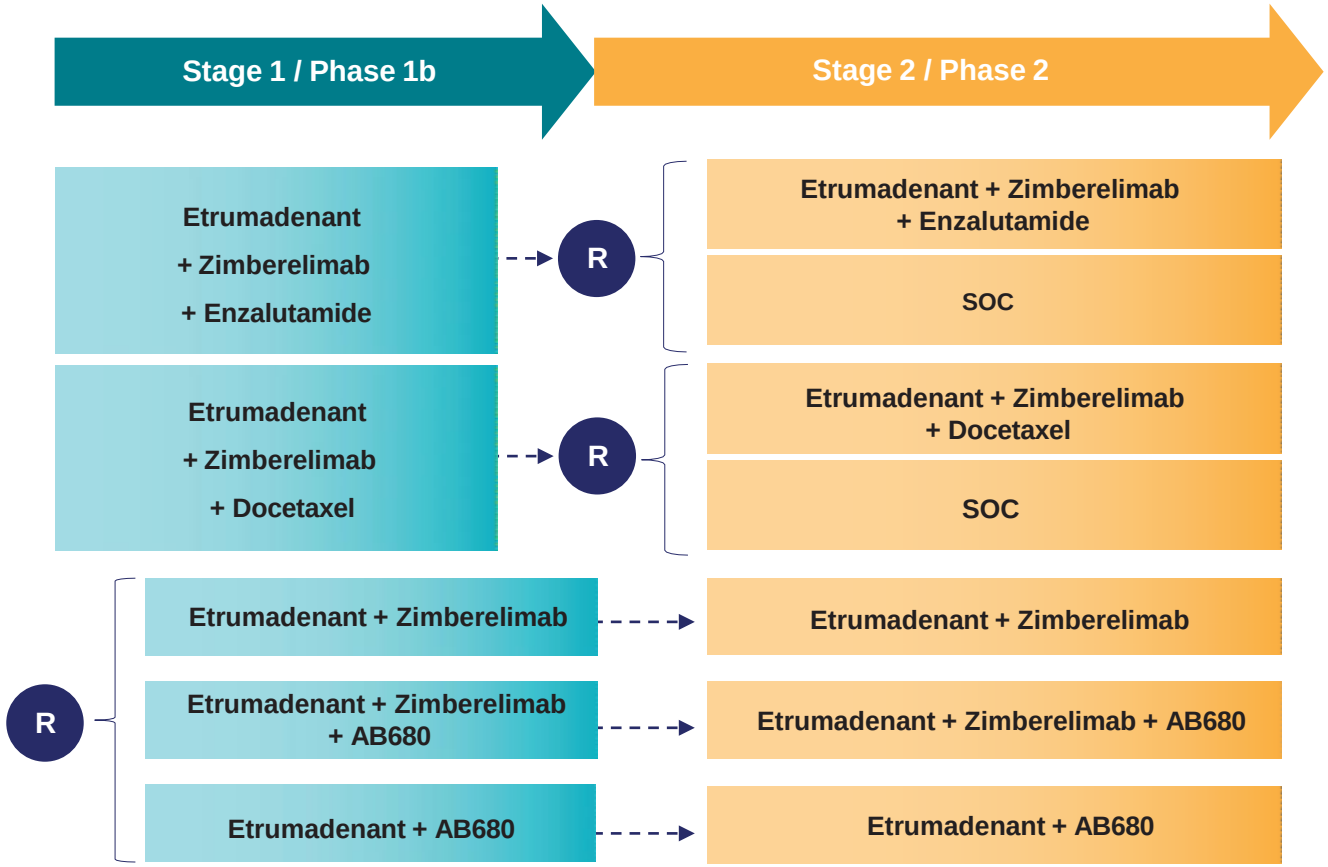
C/P: carboplatin/pemetrexed; RDE: recommended dose for escalation; TKI: tyrosine kinase inhibitor

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

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Ongoing Phase 1b/2 Platform Study to Evaluate Etruma across Multiple Lines of Therapy in mCRPC

- Randomized Phase 2 portion evaluates Etruma + Zim combined with Enzalutamide or Docetaxel vs. those SOC agents alone in mCRPC
- The Etruma + Zim + Docetaxel cohort has passed the Stage 1 futility bar and advanced to Stage 2 (randomization)
- Preliminary data from an initial cohort expected to be presented in 2Q21
- Also evaluating novel Etruma combinations (e.g. with AB680) in late-line patients

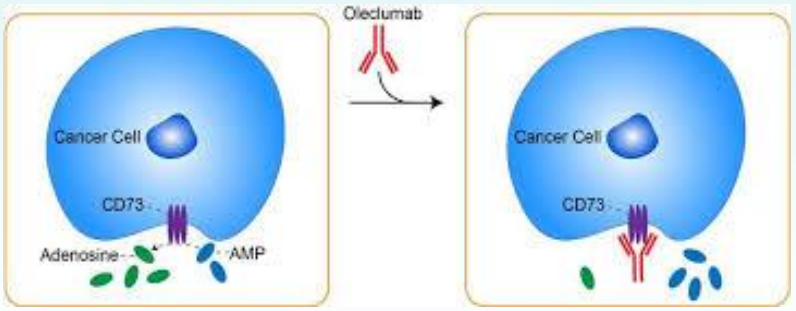


Subudhi e.t al, ESMO (2020); presentation no.687TiP; NCT04381832

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AB680 Is the First Small-molecule CD73 Inhibitor to Enter Clinical Development

CD73 Antibodies Have Limitations



The most advanced antibodies in the clinic are being developed by AZN (Oleclumab) and BMS

- Antibodies are unlikely to achieve a small molecule's permeability of tumor tissue (important since adenosine exerts its biology where it is formed by CD73)
- Antibodies are unable to completely inhibit CD73 enzymatic activity and are even less effective against soluble CD73

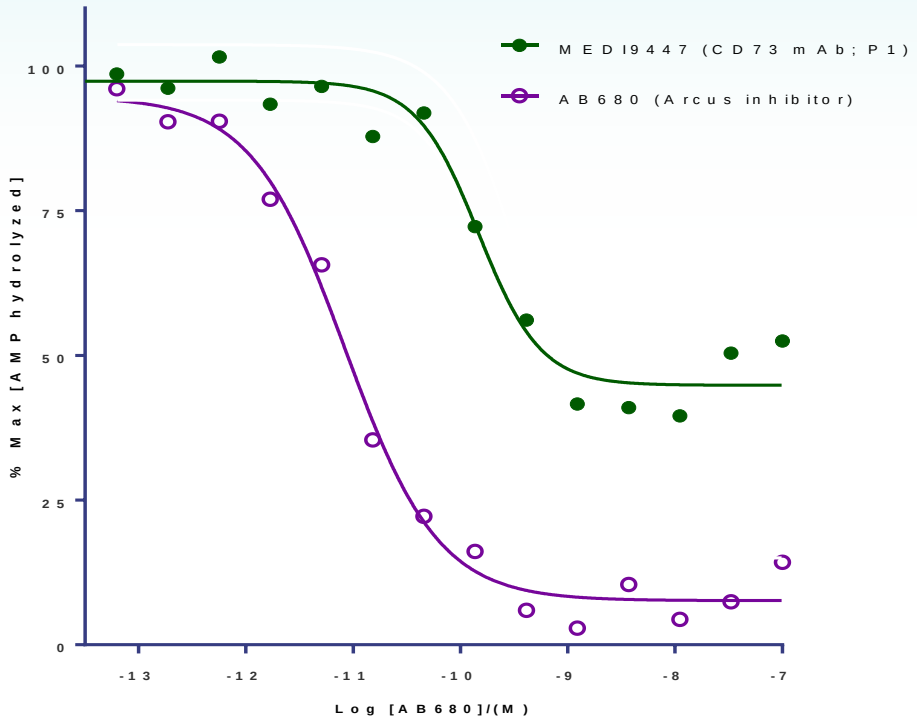
AB680 (Small Molecule)

- ✓ First small-molecule inhibitor of CD73 to enter the clinic
- ✓ **Extremely potent and selective against both tumor and soluble CD73** and orders of magnitude more potent than CD73 antibodies
- ✓ Established safety profile as a single agent in healthy volunteers and in combination with chemo/anti-PD-1 in pancreatic cancer patients
- ✓ PK/PD profile has shown complete target coverage 24/7 in humans
- ✓ Pursuing development of both IV and oral formulations

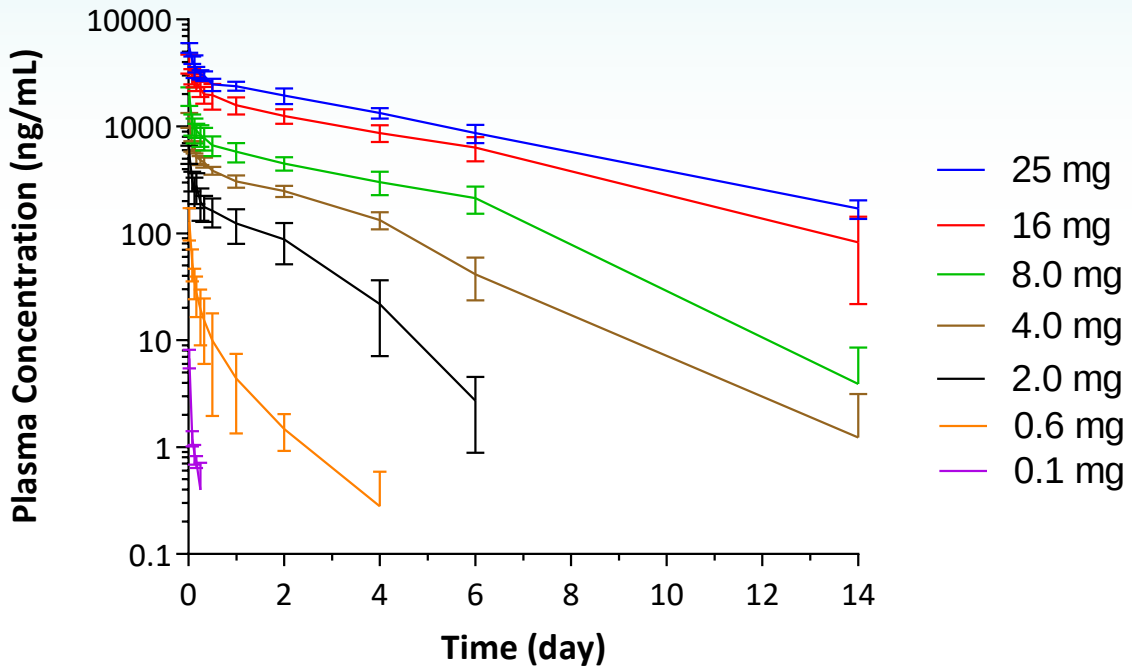
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AB680 Has Displayed Excellent Pharmacological Properties

AB680 Potently Inhibits CD73 Enzymatic Activity on CD8+ T Cells (IC_{50} = 0.008 nM)



AB680 Displays Excellent PK Profile in Healthy Human Volunteers Consistent with q2w Dosing

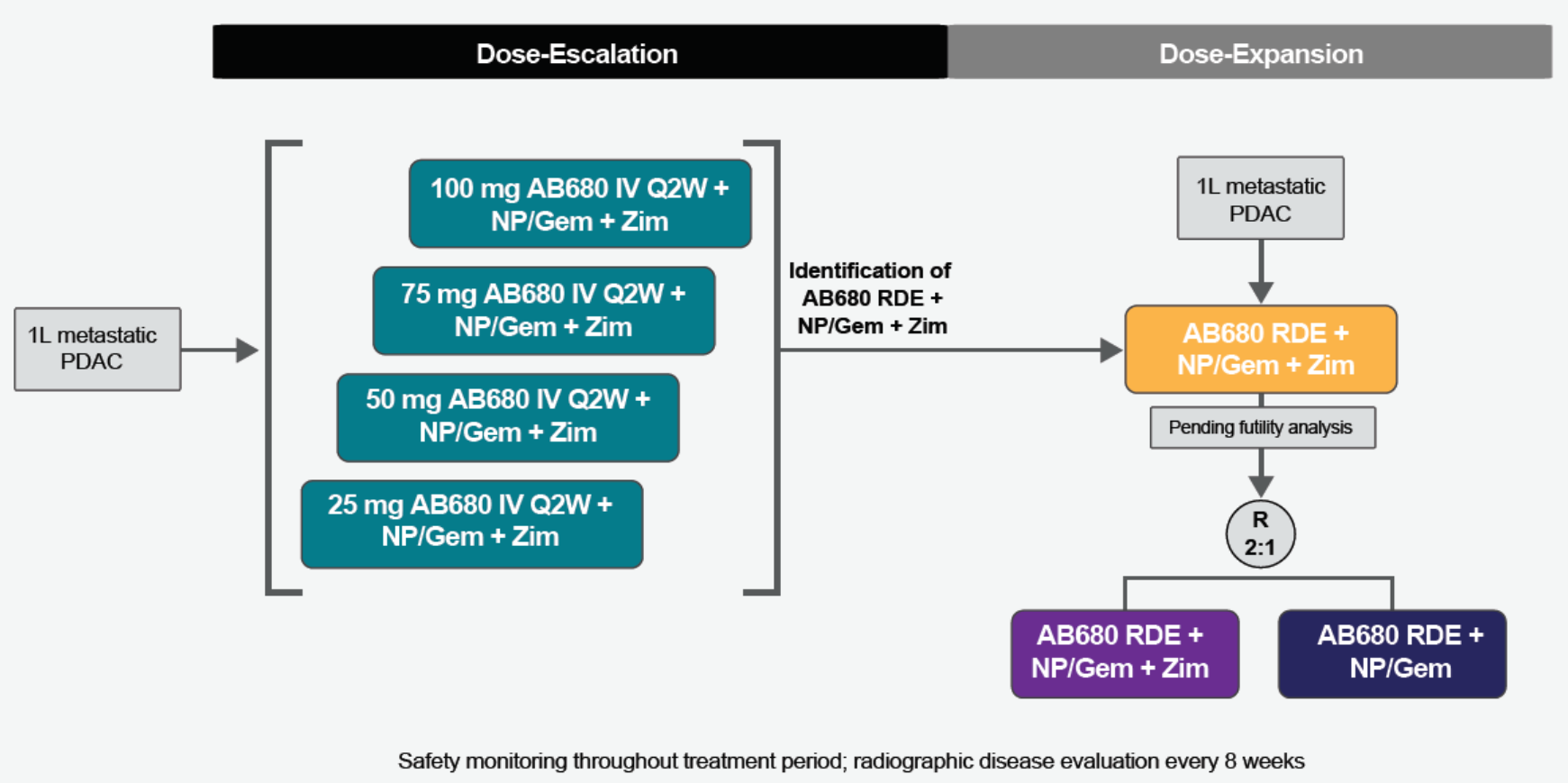


[a] MEDI9447 synthesized by Arcus based on the following publication and patent application: Hay et al., OncoImmunology (2016) 5, e1208875; Patent Appl. US 2016/0129108.

AB680 was administered (30-60 min) by i.v. infusion on day 0

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Ongoing Phase 1/1b Trial of AB680 + Zim + Gem/NP in 1L Metastatic Pancreatic Cancer



Randomized Portion Initiated 1Q21

IV, intravenously; Gem, gemcitabine; NP, nab-paclitaxel; PDAC, pancreatic ductal adenocarcinoma; Q2W, every 2 weeks; R, randomization; RDE, recommended dose for expansion; Zim, zimberelimab.

Presented at ASCO-GI 2021 (GA Manji et al. Abstract #404)

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Preliminary Dose-Escalation Data Demonstrate Early Signs of Clinical Activity for AB680



- ✓ AB680, in combination with NP/Gem and zimberelimab, has a manageable safety profile consistent with that expected for each agent alone and demonstrated early signals of clinical activity
- ✓ AB680 combination therapy **in 17 efficacy-evaluable patients resulted in a 41% objective response rate (7/17)**[1] which compares favorably with chemotherapy (23% ORR for NP/Gem)[2]
- ✓ **83% (10/12) of evaluable patients from the first three cohorts continue on treatment as of DCO of 12/9/20** with a median time on treatment of 180 days
- ✓ 100mg q2w was selected as the recommended dose for expansion (RDE), which is currently ongoing

Presented at ASCO-GI 2021 (GA Manji et al. Abstract #404)

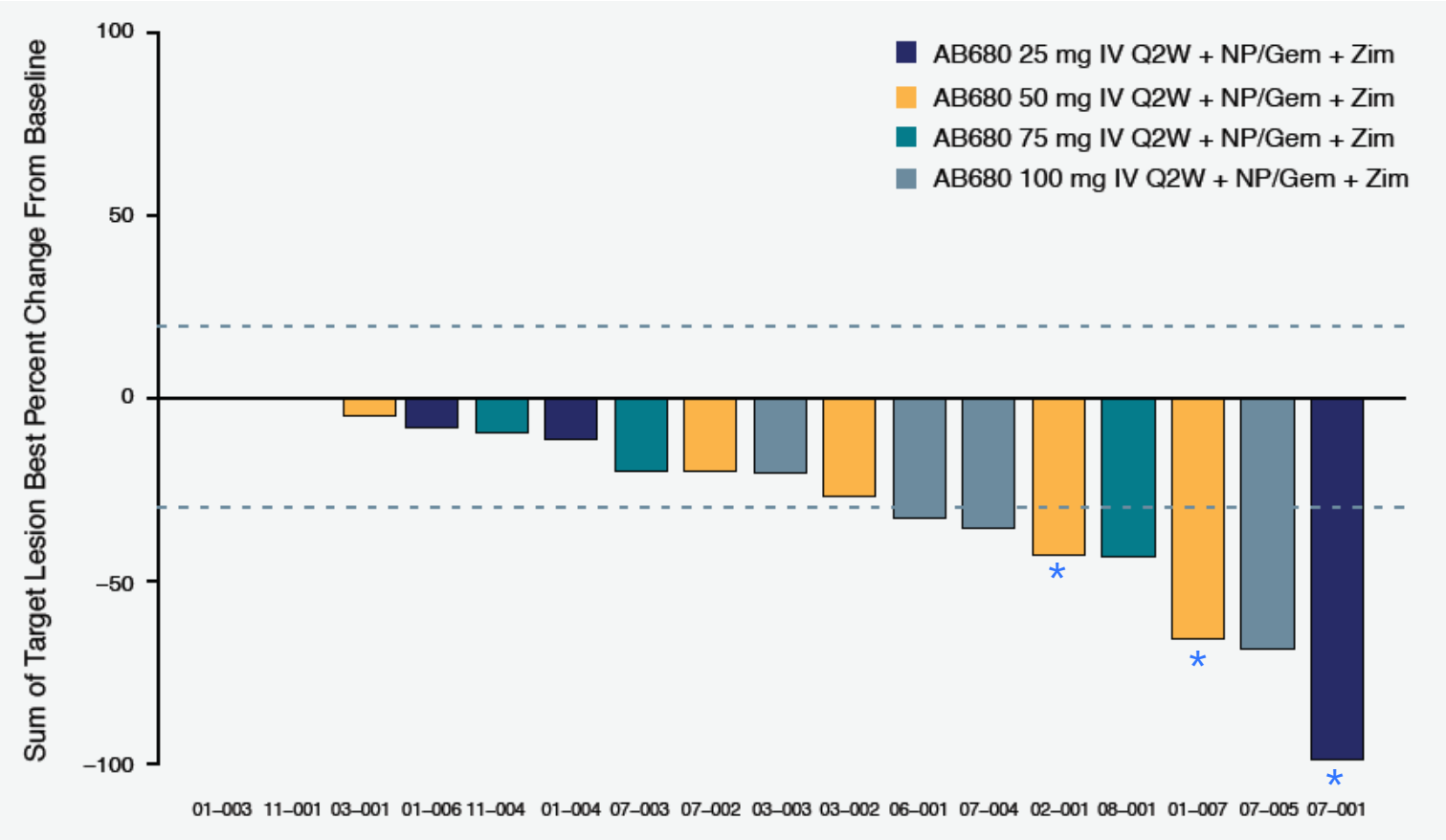
[1]Of the partial responses (PRs), 3 are confirmed responses and of the 4 unconfirmed responders, 3 responded at the first tumor assessment and the fourth responded at the second tumor assessment, and all remain on study

[2]Von Hoff DD, et al NEJM 369(18):1691-1703 (2013)

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Waterfall Plot of Best Percent Change from Baseline in Sum of Target Lesions

88% (15/17) of Evaluable Patients in the Dose-Escalation Portion Experienced Tumor Shrinkage



IV, intravenously; NP/Gem, nab-paclitaxel/gemcitabine; Q2W, every 2 weeks; Zim, zimberelimab.

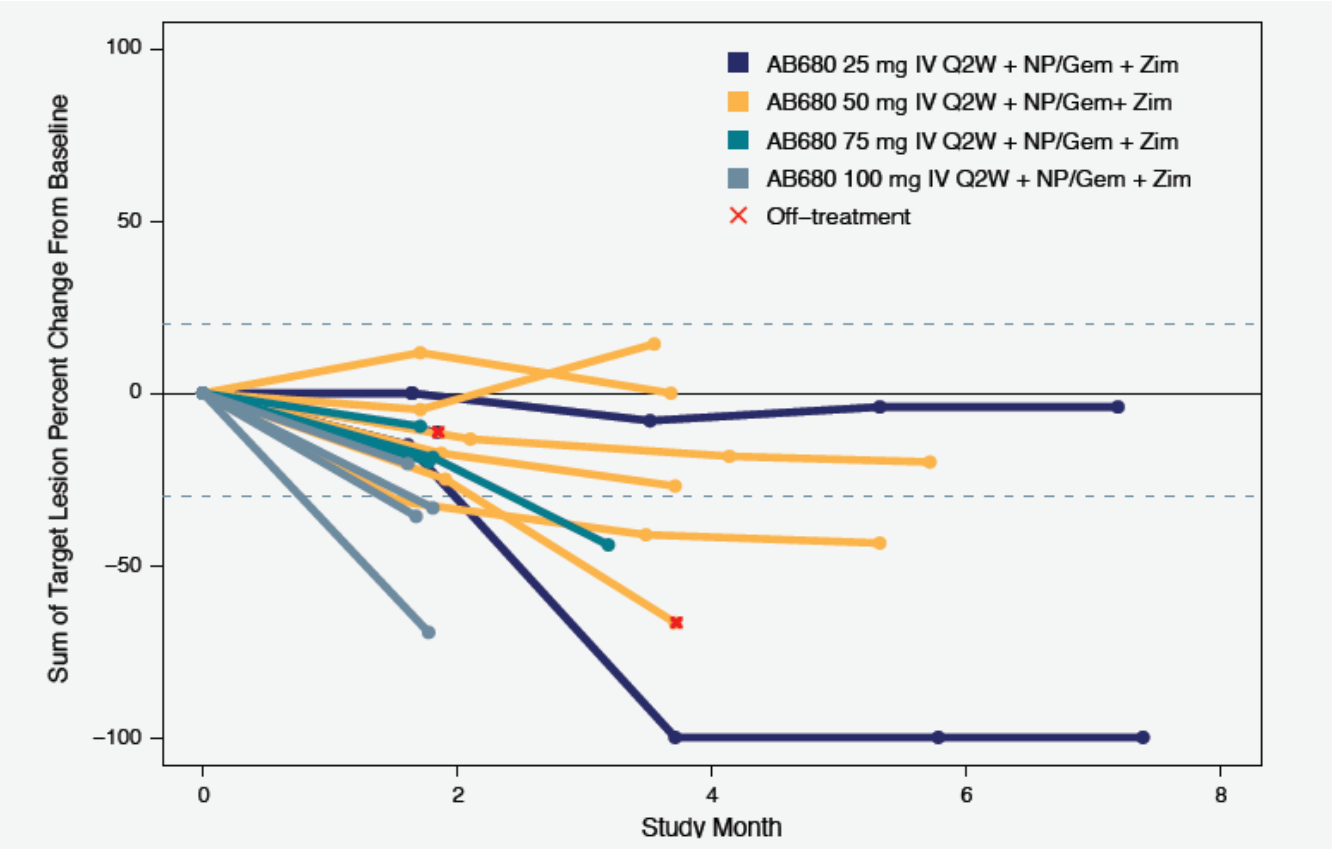
Presented at ASCO-GI 2021 (GA Manji et al. Abstract #404); data as of Dec. 9, 2020

* Confirmed Response

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Spider Plot of Percentage Change from Baseline in Sum of Target Lesions

7 of 10 Patients with Stable Disease at First Disease Evaluation Experienced Further Shrinkage at the Next Evaluation



IV, intravenously; NP/Gem, nab-paclitaxel/gemcitabine; Q2W, every 2 weeks; Zim, zimberelimab.

Presented at ASCO-GI 2021 (GA Manji et al. Abstract #404); data as of Dec. 9, 2020

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ARC-8 Data Provide Important POC for the Molecule and Therapeutic Hypothesis

As CD73 is ubiquitous in cancer, AB680 has broad development potential

Recently Initiated Platform Trials with AB680

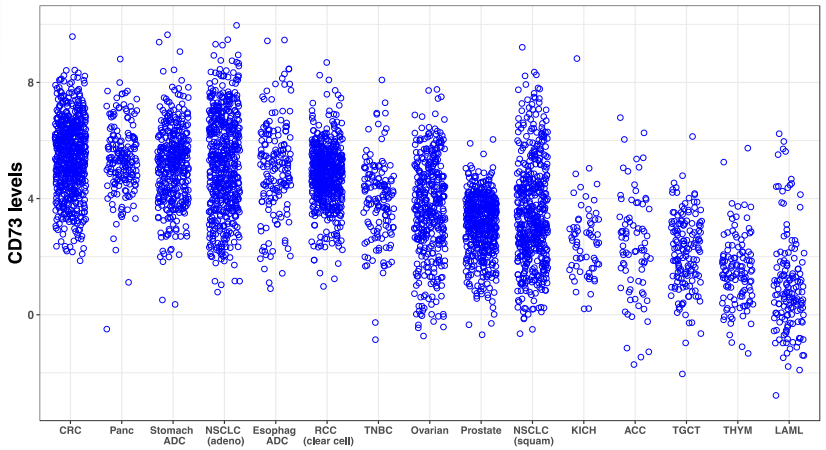
Objective: Efficiently explore the potential synergy between AB680 and Etruma

ARC-6 | **AB680** + Etruma +/- Zimberelimab arm

ARC-9 | **AB680** + Etruma + Zimberelimab arm

Additional Tumor Types

Objective: Evaluate AB680 in other tumor types associated with high levels of CD73, e.g. CRC, NSCLC, Gastric / Esophageal



Novel, Intra-portfolio Combinations

Objective: Rationally combine AB680 with other **Arcus-controlled molecules** and/or existing therapies

Setting	Potential Combination
Arcus Molecules	▪ Etruma ▪ Zim ▪ Dom ▪ Others
SOC	▪ Chemotherapy ▪ Radiation

30 Analysis of Tumor Cancer Genomic Atlas (TCGA) performed by Arcus

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ZIMBERELIMAB

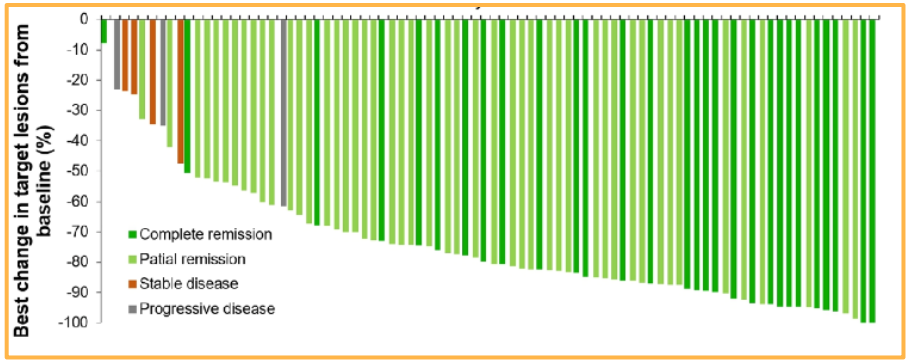
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Zimberelimab (anti-PD-1) Provides Flexibility & Optionality in Clinical Development

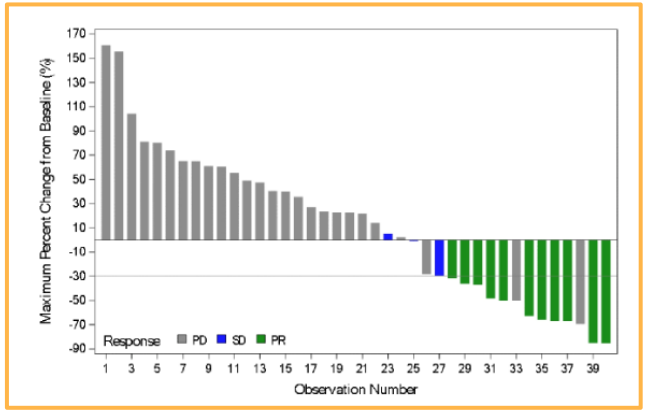
- **Zim was in-licensed by Arcus to fully enable portfolio combinations**
- **Zim partnerships with Gilead and Taiho facilitate global development and enable additional opportunities to broaden potential therapeutic combinations**
- **Demonstrated ORR similar to other checkpoint inhibitors[1]**
  - >90% ORR in late-line classic Hodgkin's lymphoma (cHL)
  - >20% ORR in late-line GI cancers (e.g., esophageal, cholangiocarcinoma and gastric)
- **Zim advanced into ARC-10 registrational study in 1Q21, Arcus's "two in one trial" supporting potential approvals of both zim monotherapy and in combination with dom**

Zim* Demonstrates Robust anti-Tumor Activity in R/R Classical Hodgkin's Lymphoma & Cervical Cancer (Data from Gloria Biosciences)

R/R Classical Hodgkin's Lymphoma



Advanced (2L+) Cervical Cancer



[1] Presentations by Gloria Biosciences at CSCO 2019. Gloria's studies conducted independently of Arcus.
* Also known as GLS-010 in China (Gloria Biosciences)

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PROGRAMS ADVANCING TOWARDS CLINICAL DEVELOPMENT

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Next Wave of Arcus's Clinical Programs Reflects Broadening of Portfolio to Include Cancer Cell Intrinsic Programs

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

AXL Inhibitor

Tyrosine kinase

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

Cancer cell intrinsic target

PAK4 Inhibitor

Serine kinase

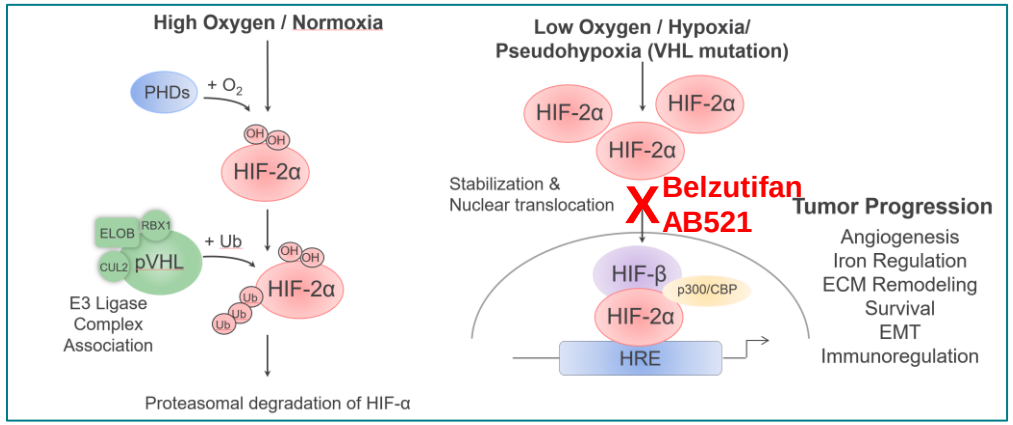
PAK4 overexpression is responsible for T-cell exclusion from immune desert tumors

Cancer cell intrinsic target

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HIF-2α Inhibitor Program – AB521

- **Genetic alterations in VHL are often causatively associated with increased HIF signaling and clear cell RCC development**
- **Clinical POC obtained in ccRCC and VHL disease with HIF-2α inhibitor belzutifan**
- **We have identified several novel, potent and selective HIF-2α inhibitors, of which AB521 is the most advanced – currently in preclinical development**
- **Opportunities to differentiate our program by combining with other portfolio molecules**
  - e.g., upregulation of CD73 (adenosine) by hypoxia is believed to be mediated by HIF-1α; thus, strong rationale to combine AB521 with etrumadenant or AB680 in RCC or several other tumor types characterized by a *hypoxia gene signature*



Assay	AB521	Belzutifan[1]
HIF-2α 786-O Luc. IC_{50} (nM)	10.0 ± 3.7	15.9 ± 7.4
HIF-2α SPA IC_{50} (nM)	19.1 (n=1)	31.2 ± 9.7
VEGF Secretion IC_{50} (nM)	30.5 ± 3.7	66.7 ± 37

[1]Data from Arcus test of molecule described as MK-6482 in Wehn et al., J Med Chem (2018) 61:9691

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