

The background of the slide is a blurred laboratory setting. On the left, a multi-well plate reader is visible, with a multi-well plate containing red liquid being processed. On the right, a scientist in a white lab coat and safety glasses is working at a bench, looking down at a piece of equipment. The overall color scheme is a soft blue overlay.

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

CORPORATE OVERVIEW

MAY 2021

NYSE: RCUS

Forward-looking Statements/Safe Harbor

This presentation contains forward-looking statements about Arcus Biosciences, Inc. (“we,” “Arcus” or the “Company”) made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements regarding events or results to occur in the future contained in this presentation are forward-looking statements, including statements about our strategy, advantages, expectations for the company, potential of our investigational products, upcoming milestones and associated timing, the anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca, and expectations regarding our available cash and investments. These forward-looking statements are subject to a number of risks, uncertainties and assumptions that may cause actual results to differ materially from those contained in any forward-looking statements we may make, including, but not limited to: the inherent uncertainty associated with pharmaceutical product development and clinical trials; delays in our clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials; risks associated with the impact of the COVID-19 pandemic; risks associated with our collaboration arrangement with Gilead including our dependence on Gilead for the successful development and commercialization of our investigational products; risks associated with preliminary or interim data, or results from early-stage studies and the applicability of the results described herein to our subsequent clinical trials; the unexpected emergence of adverse events or other undesirable side effects; differences in interpretation of our clinical trial results; changes in the competitive landscape; our limited operating history and our ability to manage our growth; and risks regarding our license and collaboration agreements and our ability to obtain and maintain intellectual property protection for our product candidates.

We operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially and adversely from those anticipated or implied in the forward-looking statements. Further information on these and other factors that could affect the forward-looking statements made herein are described in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission.

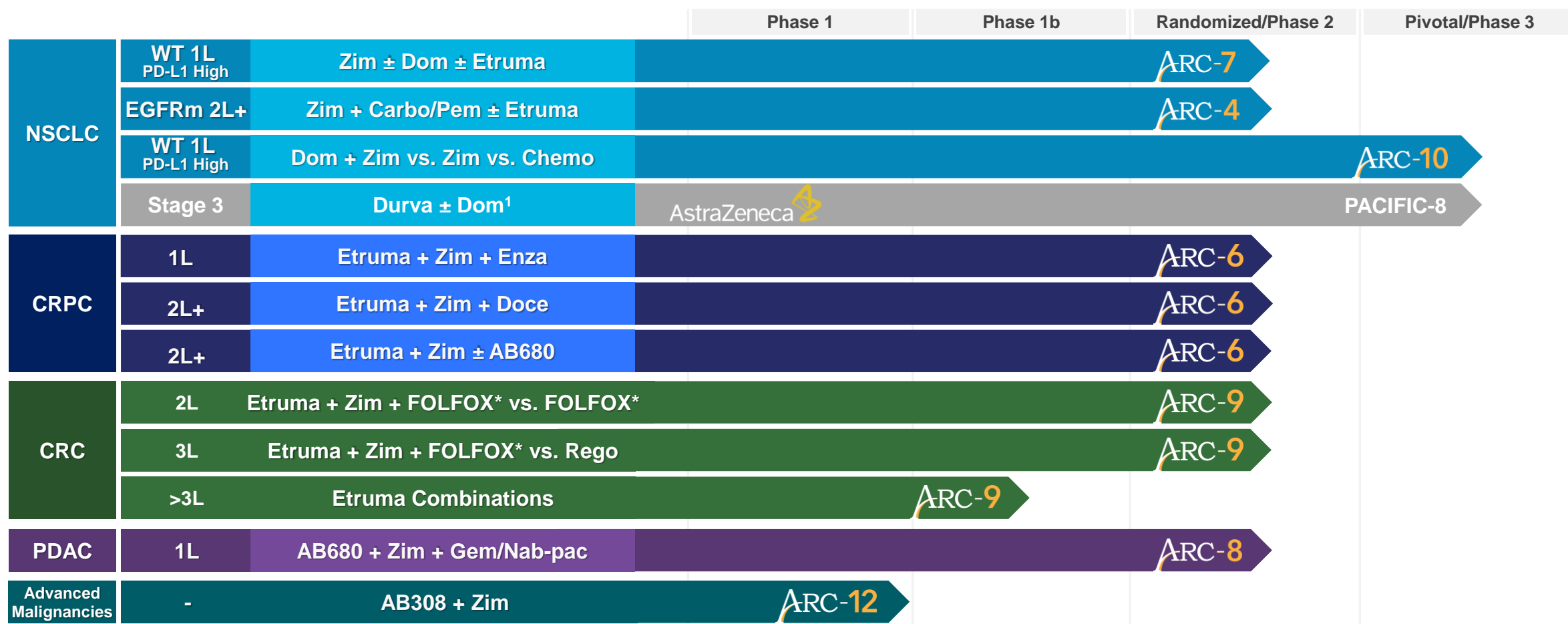
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2021 Will Be a Pivotal Year for Arcus

- **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 \geq 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**
 - ~\$885M in cash as of 3/31/21; includes \$220 million in proceeds from Gilead's equity investment in February 2021 and 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

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



Zim: zimberelimab; Dom: domvanalimab; Etruma: etrumadenant;

Carbo: carboplatin; Doce: docetaxel; Durva: durvalumab; Enza: enzalutamide; FOLFOX: (folinic acid, fluorouracil; oxaliplatin); Gem: gemcitabine; Nab-pac: nab-paclitaxel; Pem: pemetrexed; Rego: regorafenib

NSCLC: non-small cell lung cancer; CRPC: castrate-resistant prostate cancer; CRC: colorectal cancer; PDAC: pancreatic ductal adenocarcinoma

¹Clinical collaboration with AstraZeneca; AZ will be the primary sponsor of PACIFIC-8.

* +/- biologic

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	<ul style="list-style-type: none"> – Initial dose-escalation data – Additional data from dose-escalation / expansion 	<ul style="list-style-type: none"> ✓ 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%)	<ul style="list-style-type: none"> – Conduct of interim analysis – Presentation of IA data 	<ul style="list-style-type: none"> ▪ 2Q21 ▪ 2H21
●	ARC-4	Etruma + Zim + Carbo/Pem vs. Zim + Carbo/Pem	Randomized Phase 1/2 Trial in TKI R/R EGFR+ NSCLC	<ul style="list-style-type: none"> – Initial randomized data 	<ul style="list-style-type: none"> ▪ 2H21
●	ARC-6	Etruma + Zim + SOC vs. SOC	Randomized Phase 2 Trial in 2L/3L Metastatic castrate-resistant prostate cancer (mCRPC)	<ul style="list-style-type: none"> – Preliminary data from an initial cohort – Initial randomized data 	<ul style="list-style-type: none"> ▪ 2Q21: ASCO ▪ Early 2022
●	ARC-9	Etruma + Zim + FOLFOX vs. SOC	Randomized Phase 2 Trial in 2L/3L/3L+ Colorectal cancer	<ul style="list-style-type: none"> – Initial randomized data for 2L/3L cohorts; single-arm data for 3L+ 	<ul style="list-style-type: none"> ▪ 1H22

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



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



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



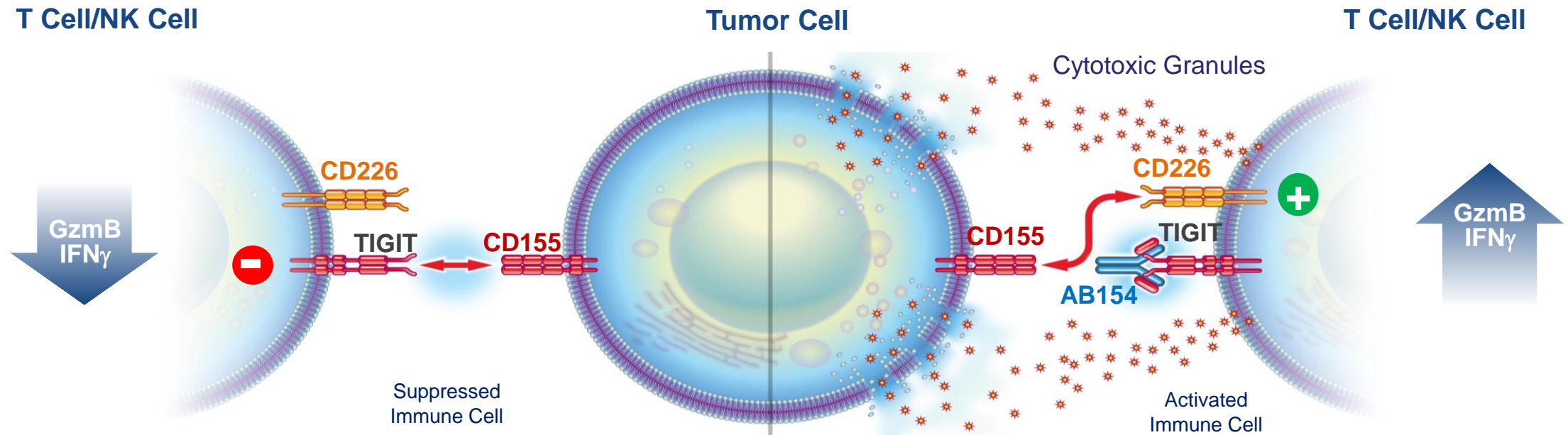
Clinical collaboration for domvanalimab plus durvalumab

- 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

DOMVANALIMAB

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



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

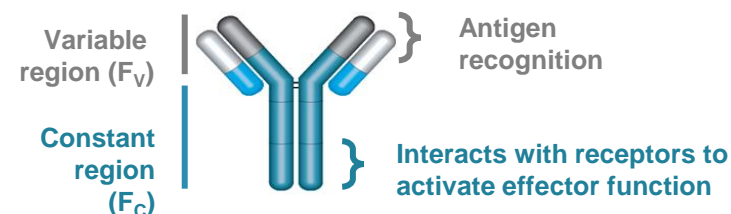
Domvanalimab (FcR-silent)

- 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” to facilitate advancement into a late-stage trial



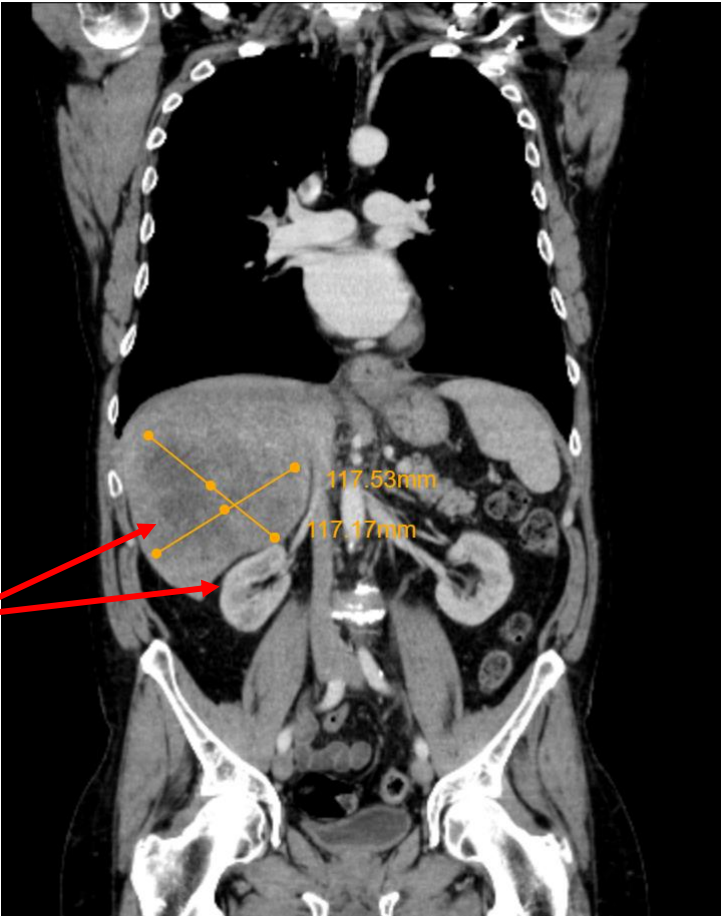
Potential best option for heme malignancies

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

Baseline



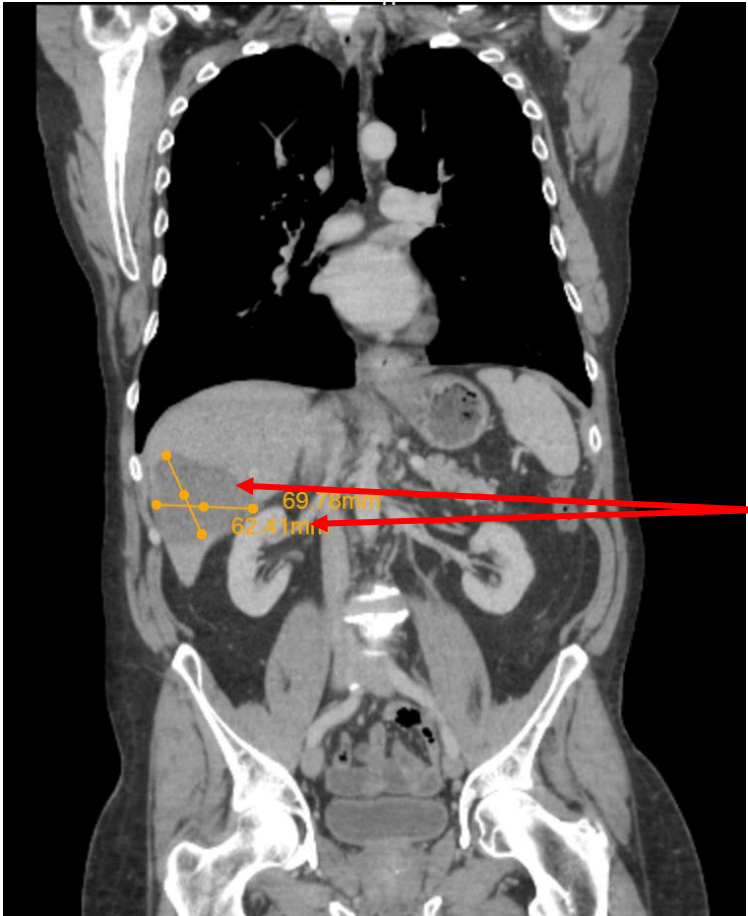
Prior therapies:

- 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

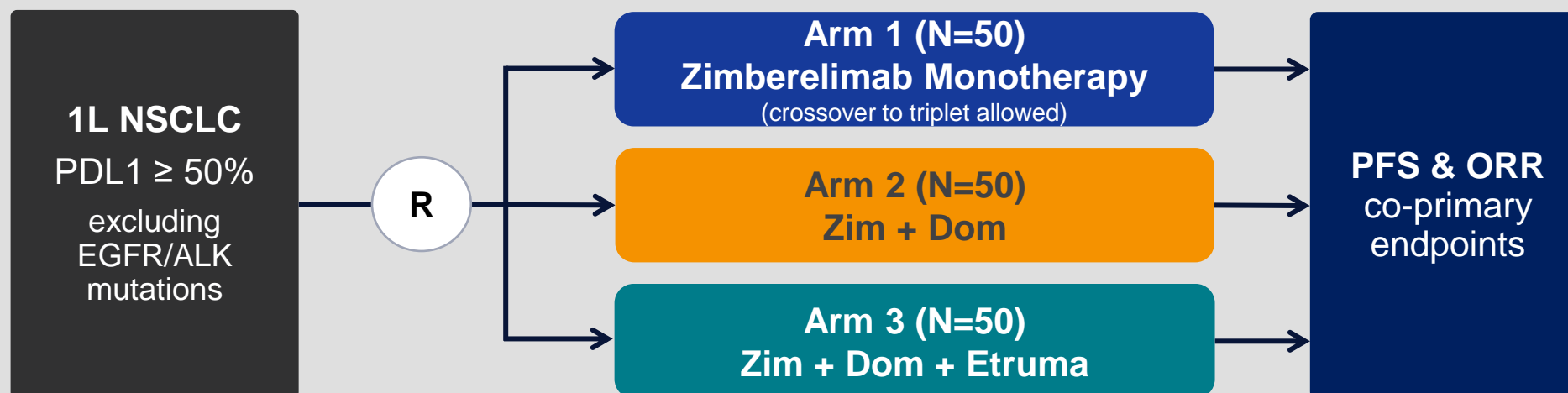
Cycle 6



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

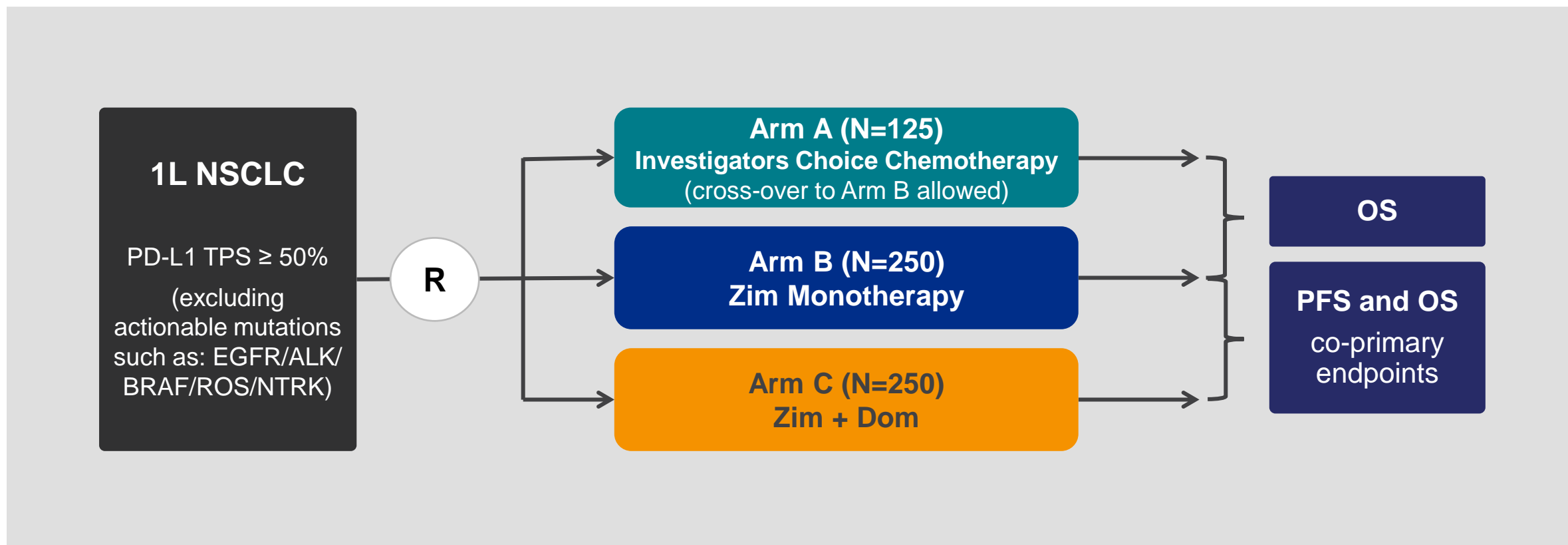
CSP: COMBINED POSITIVE SCORE (PD-L1) CELLS; PEMBRO APPROVAL IS IN CSP≥10 FOR ESOPHAGEAL CANCER; cPR: CONFIRMED PARTIAL RESPONSE

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



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

Phase 3 Trial to Evaluate Dom + Zim vs. Zim mono vs. Chemo in 1L NSCLC (PD-L1 $\geq 50\%$)



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

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 to facilitate advancement into a late-stage trial

Dose-Escalation

**AB308 + Zim
Combination**

(Varying Q3/Q4
dose-schedules)

Patients with advanced or
metastatic hematological
or solid tumors

**AB308
RDE
+
Zim**

Expansion Cohorts

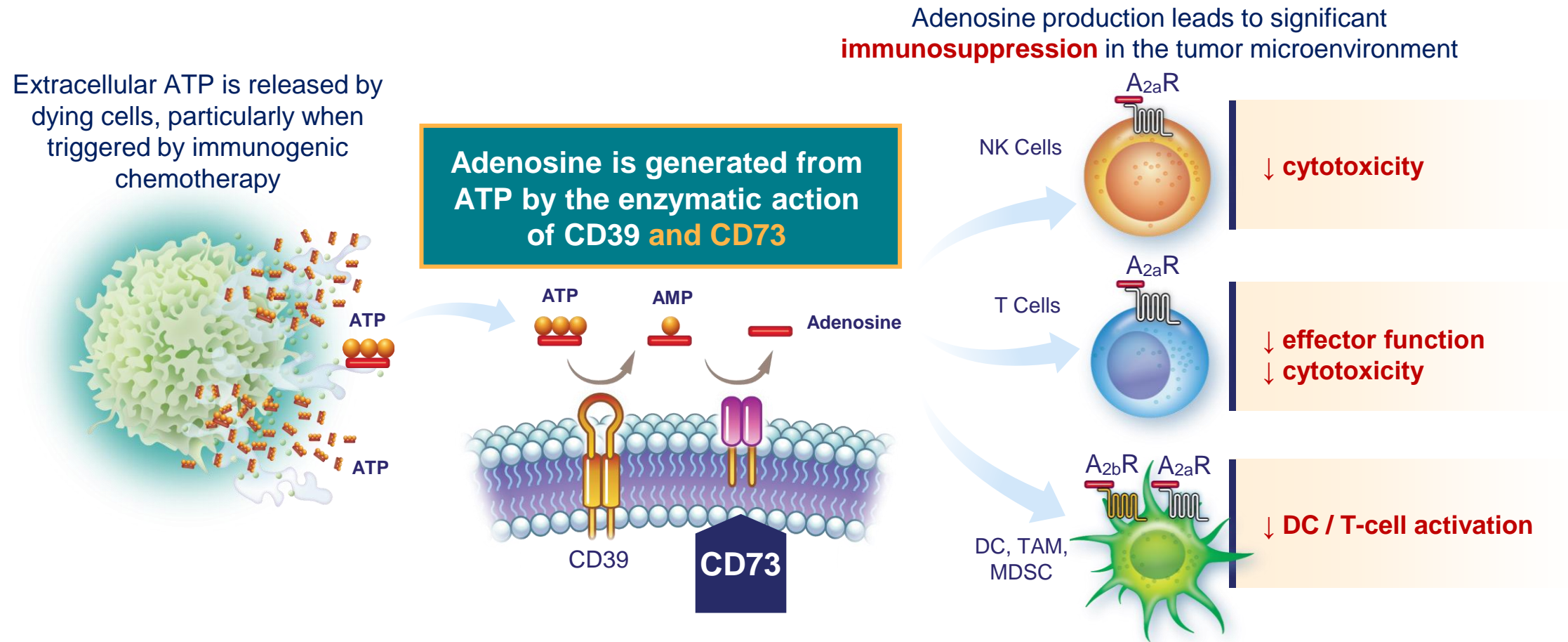
Heme & Solid Tumor Indication Cohorts

- Heme
- Melanoma
- Gastric, GEJ, Esophageal
- NSCLC
- Cervical

***First patient dosed April 2021;
Rapid dose-escalation to facilitate advancement into a late-stage trial***

ADENOSINE PROGRAMS

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



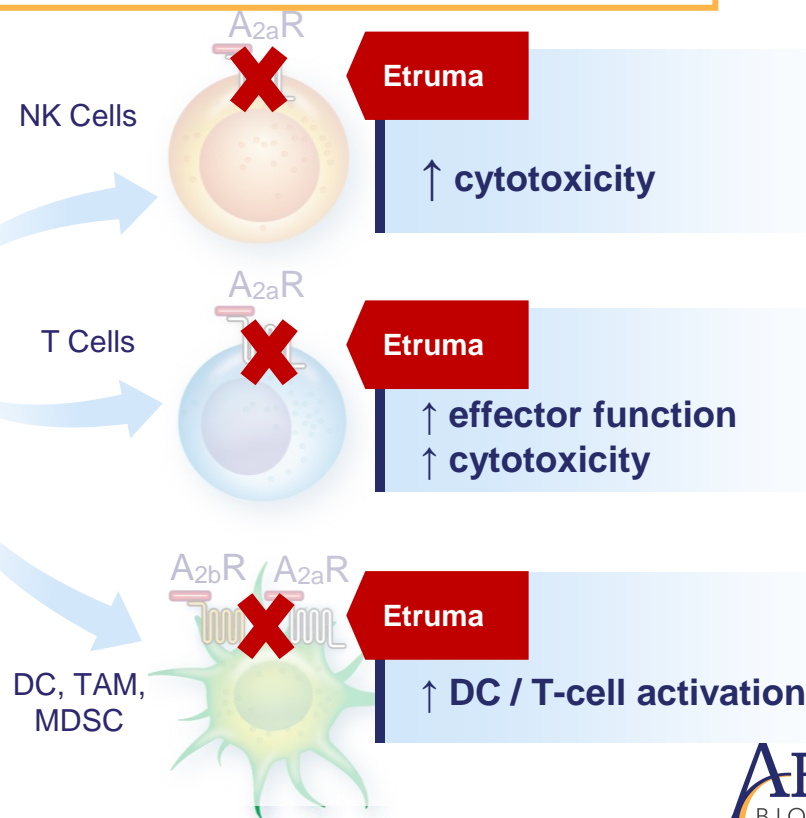
Arcus is a Leader in the Development of Therapeutics that Target the Adenosine Axis

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



We Are Pursuing a Broad Development Plan for Etruma

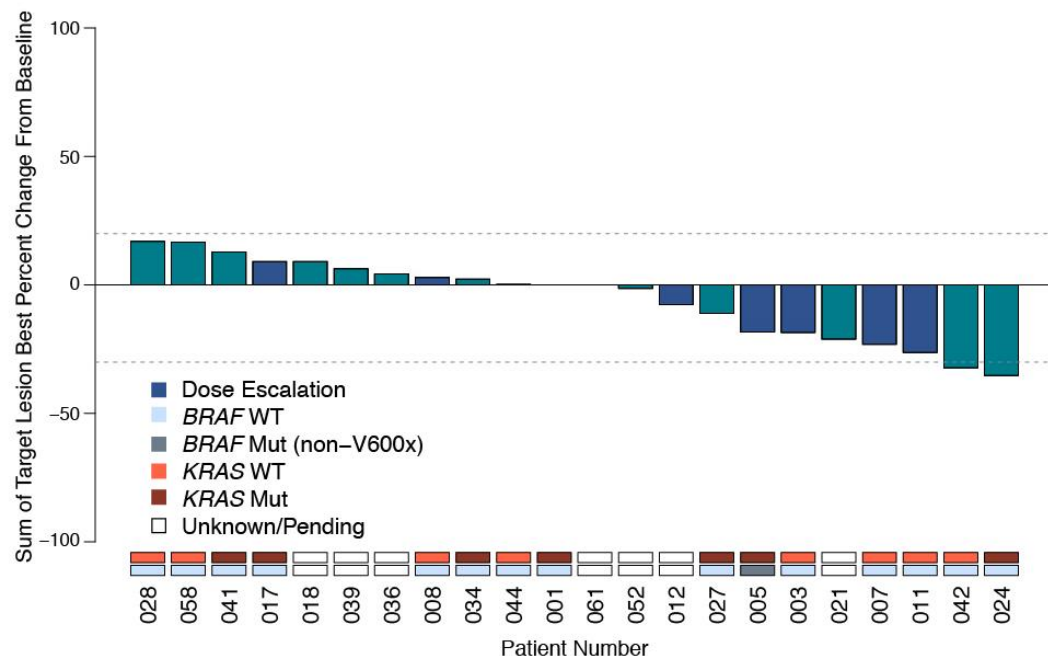
		COMBINATION / ARMS	SETTING	STATUS
Ongoing randomized studies	●	ARC-4 Etruma + Zim + Carbo/Pem vs. Zim + Carbo/Pem	Randomized Phase 1/2 Study in TKI R/R EGFR+ NSCLC	– Initial randomized data expected 2H21
	●	ARC-6 Etruma + Zim + SOC vs. SOC	Randomized Phase 2 Study in 2L/3L Metastatic castrate-resistant prostate cancer (mCRPC)	<ul style="list-style-type: none"> – Futility analysis passed for the “chemo combo” cohort – Preliminary data from an initial cohort at ASCO 2021 – Initial randomized data expected early 2022
	●	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	<ul style="list-style-type: none"> – Initial results presented at SITC 2020 – OS / PFS data presented at AACR 2021

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+: PFS of 4.2 months and OS of 13.6 months (~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 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

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

3L+ Patients



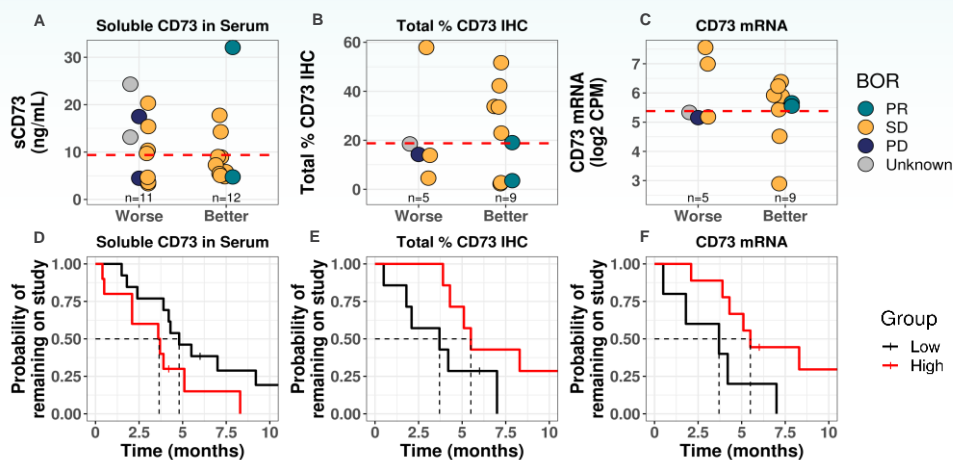
Data Cut-Off (DCO) February 26, 2021

- 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 (a randomized Phase 2 study) in 1Q21 based on encouraging results; Initial data expected in 1H22

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⁾

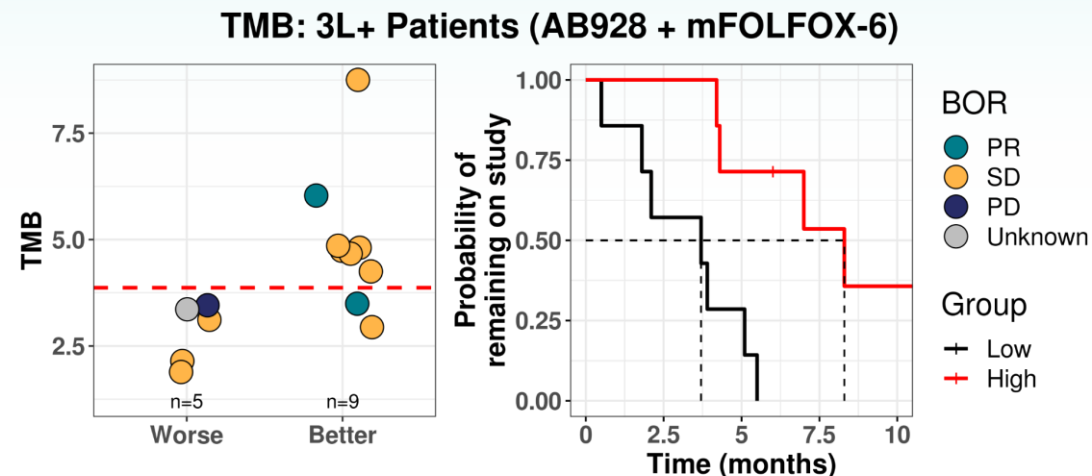


Baseline soluble CD73 (sCD73) in serum and tumor CD73 gene/protein measurements in 3L+ mCRC.

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 specificity⁴ 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.

(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.

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

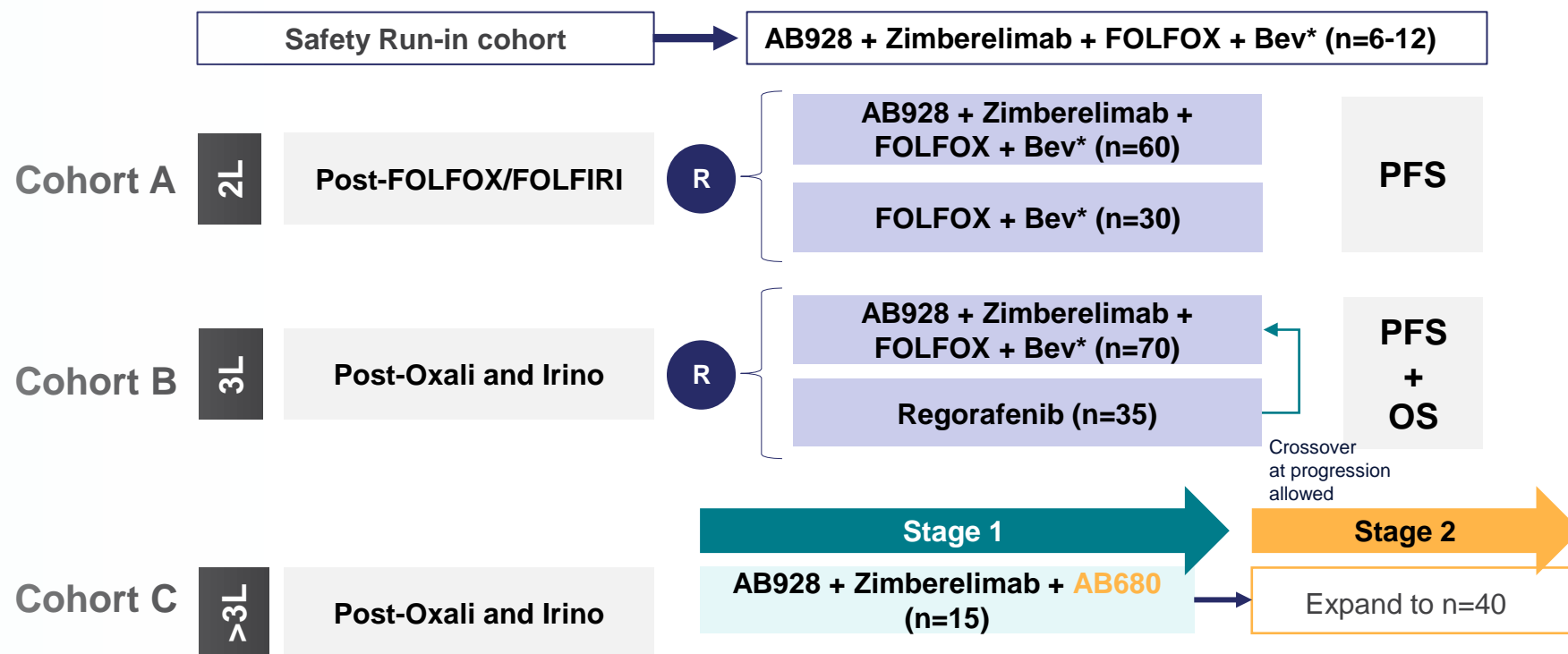


Tumor Mutation Burden (TMB) in 3L+ mCRC patients.

(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-point⁴ 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 TCGA¹³ treated with FOLFOX regimens (data not shown).

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

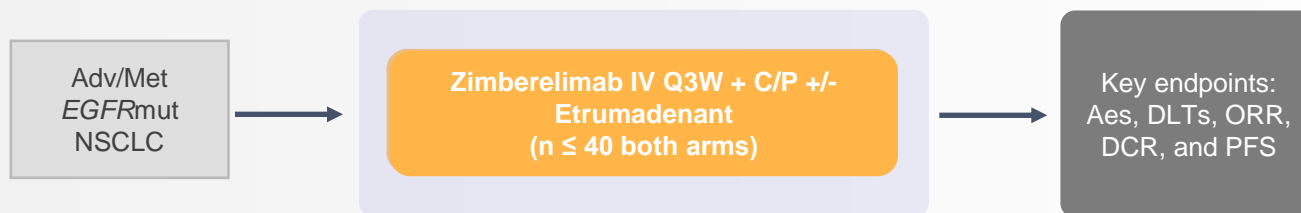


*Bev will be included for all patients in whom it is not contraindicated

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

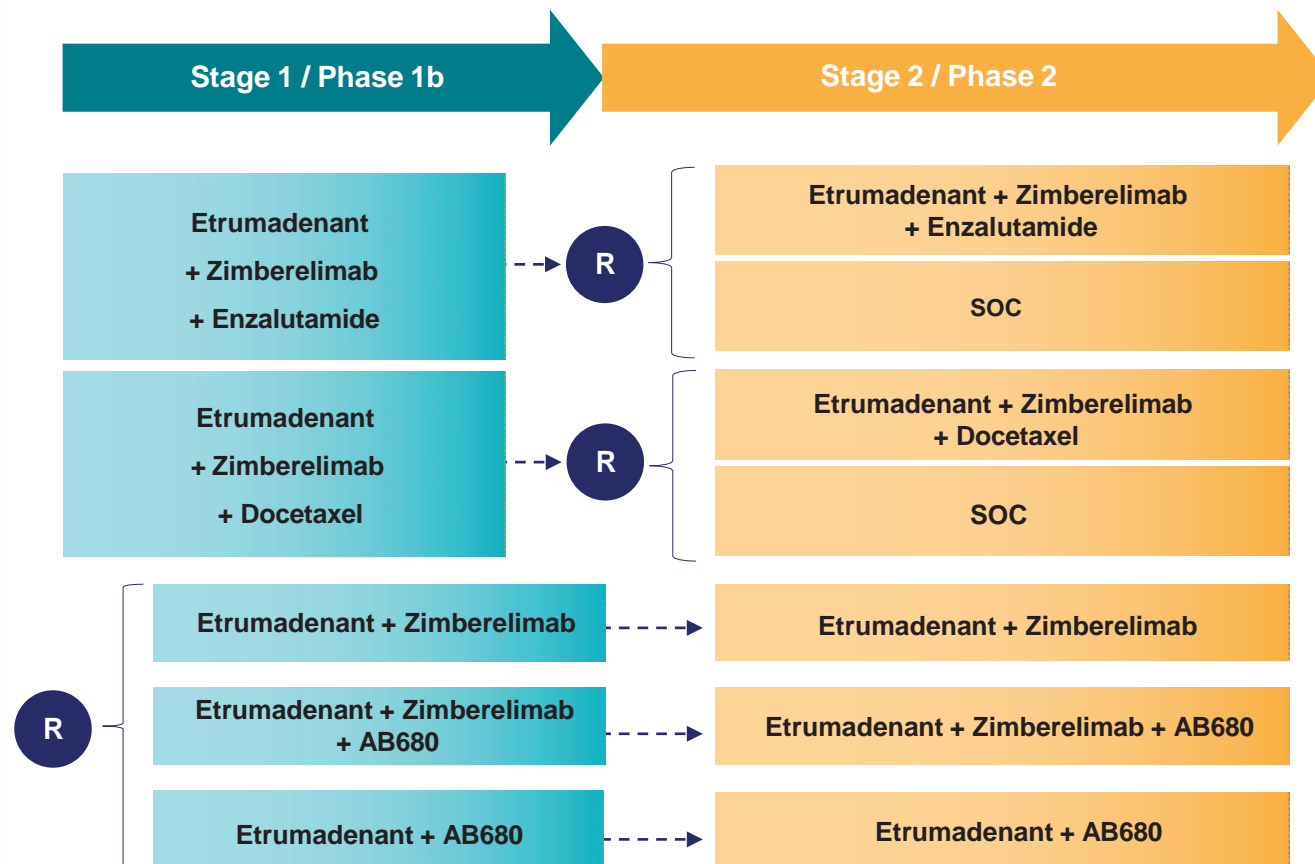
Dose Expansion & Randomization



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

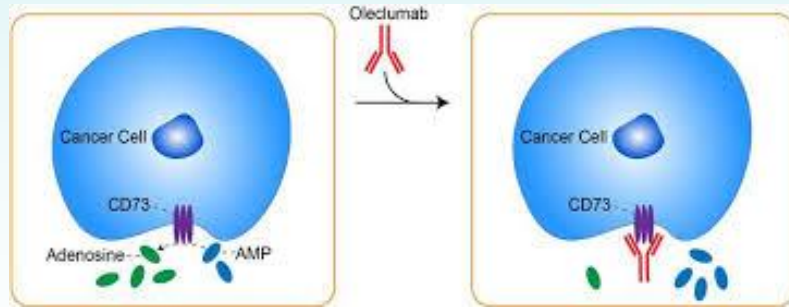
Ongoing Phase 1b/2 Platform Study to Evaluate Etruma across Multiple Lines of Therapy in mCRPC

- 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 to be presented in 2Q21
- Also evaluating novel Etruma combinations (e.g. with AB680) in late-line patients



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

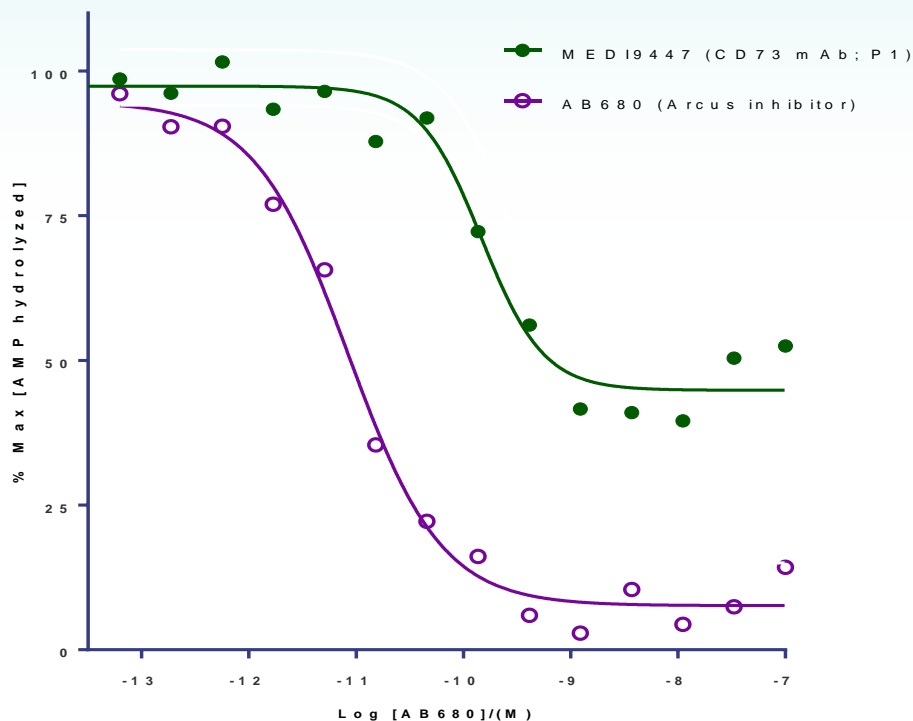
- Antibodies are unlikely to achieve a small molecule's permeability of tumor tissue (important since adenosine exerts its biology where it is formed by CD73)
- Antibodies are unable to completely inhibit CD73 enzymatic activity and are even less effective against soluble CD73

AB680 (Small Molecule)

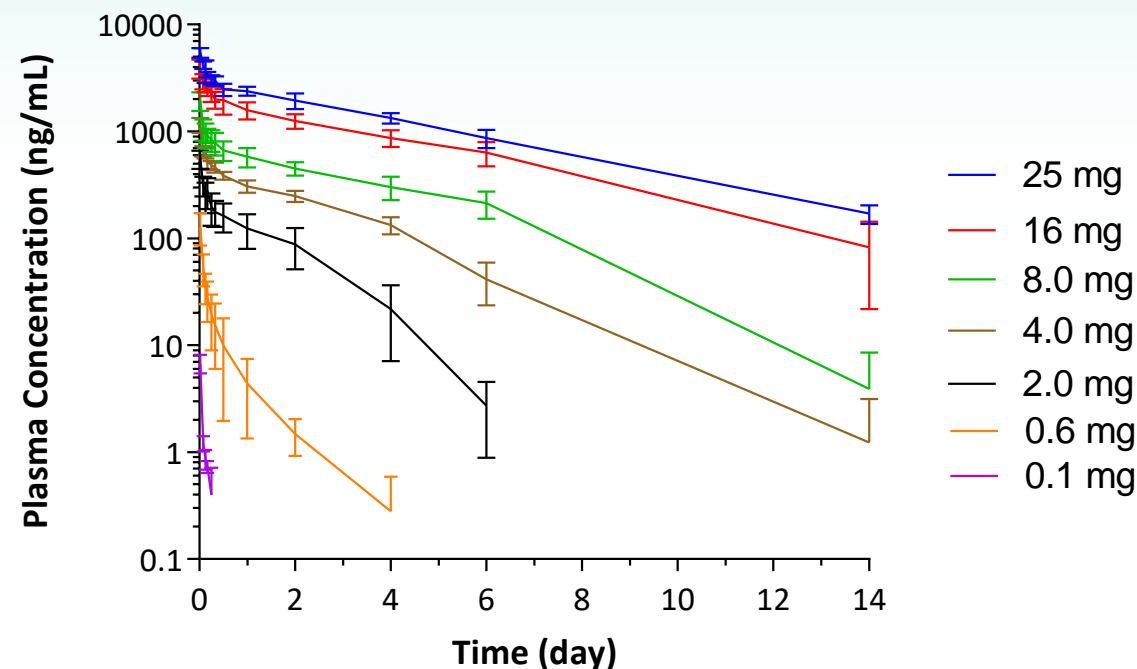
- ✓ First small-molecule inhibitor of CD73 to enter the clinic
- ✓ **Extremely potent and selective against both tumor and soluble CD73** and orders of magnitude more potent than CD73 antibodies
- ✓ Established safety profile as a single agent in healthy volunteers and in combination with chemo/anti-PD-1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

AB680 Has Displayed Excellent Pharmacological Properties

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



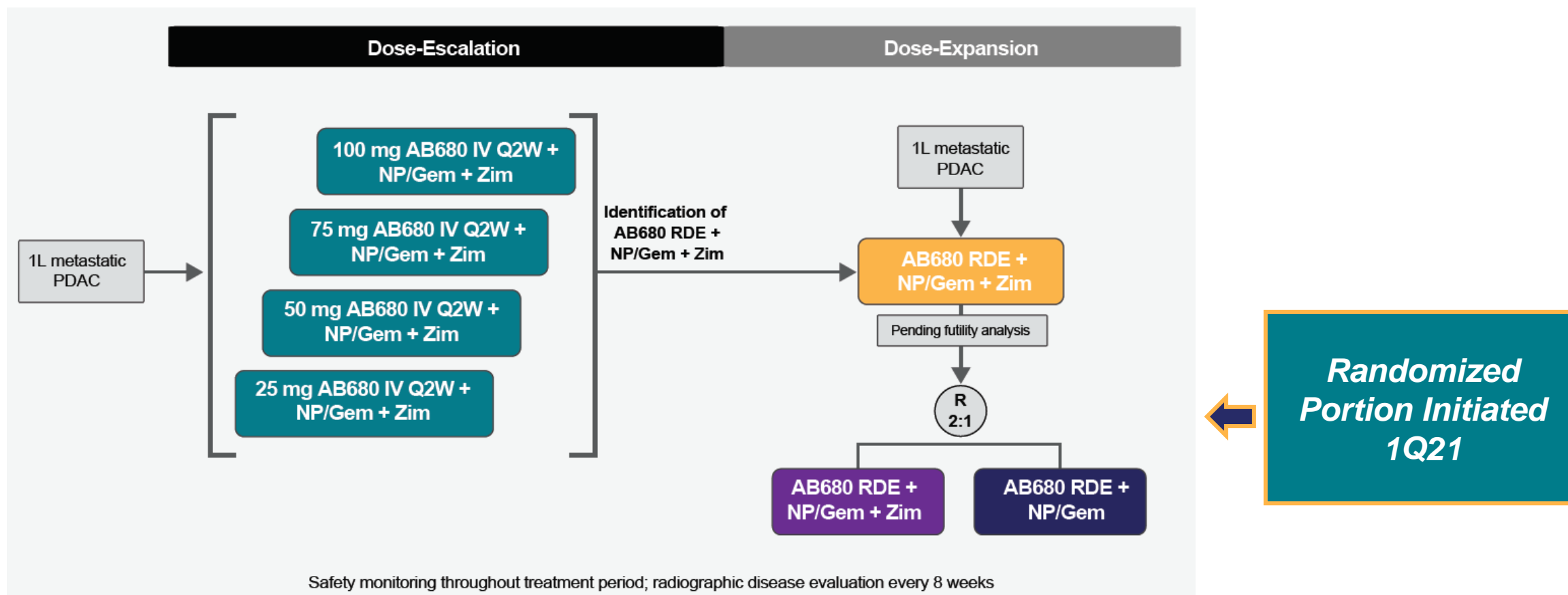
AB680 Displays Excellent PK Profile in Healthy Human Volunteers Consistent with q2w Dosing



^a MED19447 synthesized by Arcus based on the following publication and patent application: Hay et al., *Oncolimmunology* (2016) 5, e1208875; Patent Appl. US 2016/0129108.

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

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



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

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)

¹Of 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

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

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

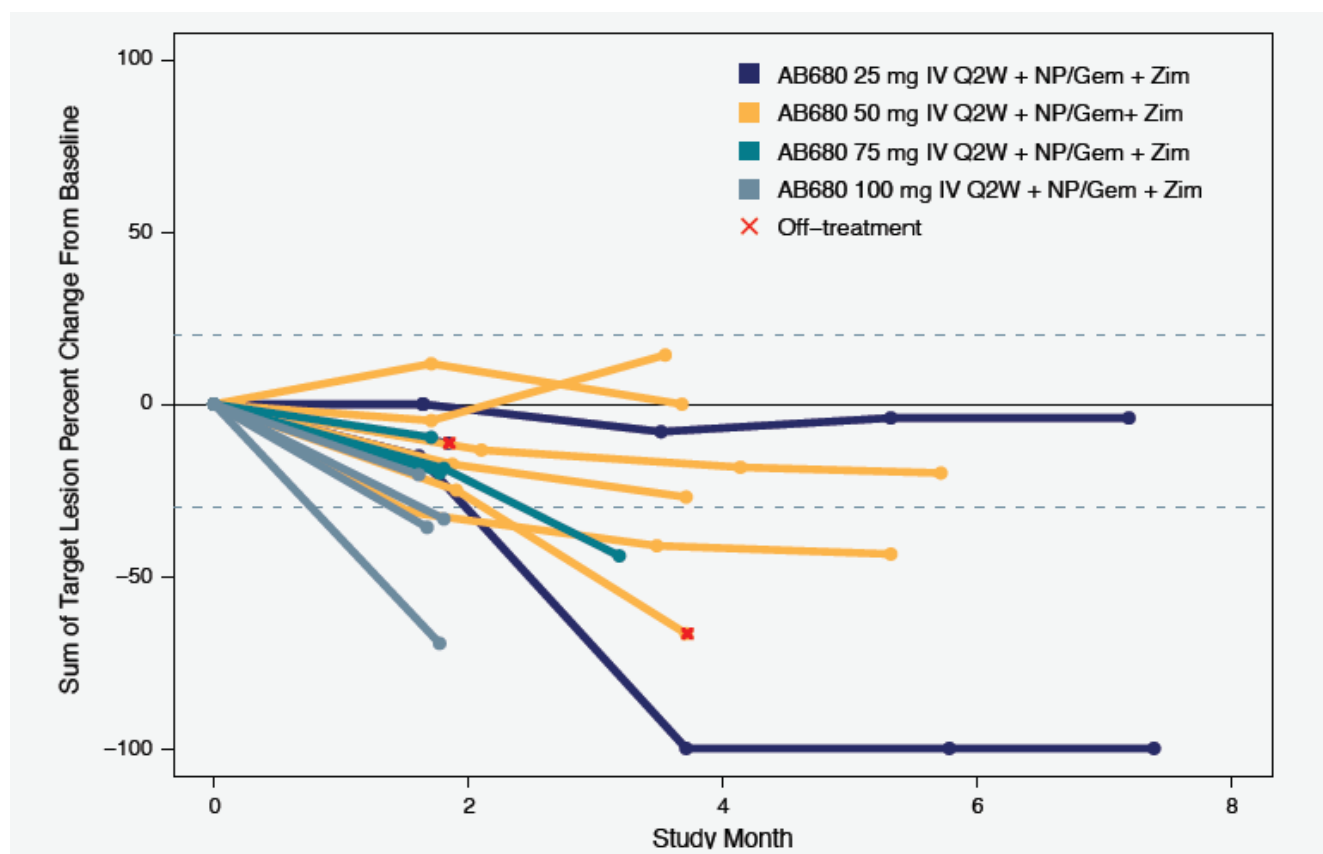


IV, intravenously; NP/Gem, nab-paclitaxel/gemcitabine; Q2W, every 2 weeks; Zim, zimberelimab.

* Confirmed Response

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.

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

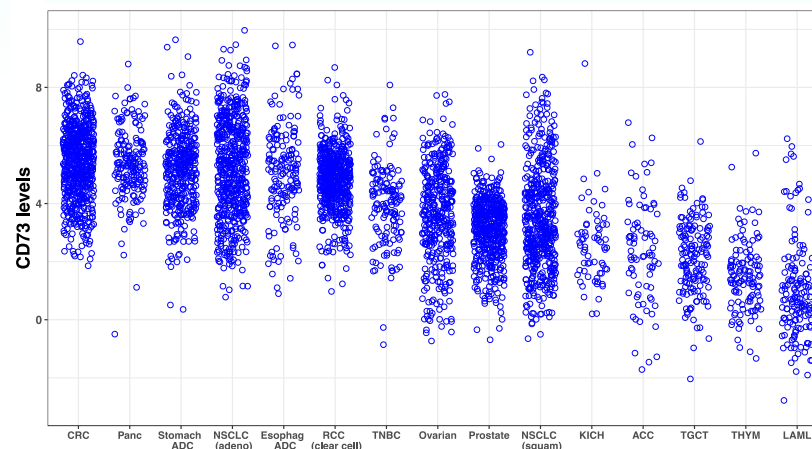
AB680 + Etruma +/-
Zimberelimab arm

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	<ul style="list-style-type: none"> Etruma Zim Dom Others
SOC	<ul style="list-style-type: none"> Chemotherapy Radiation

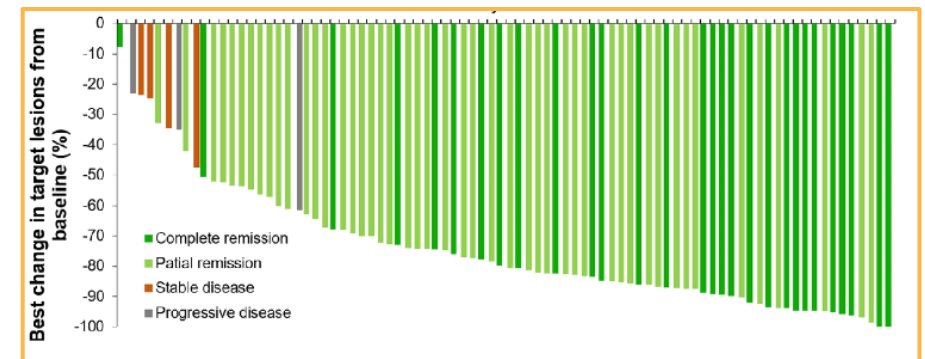
ZIMBERELIMAB

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

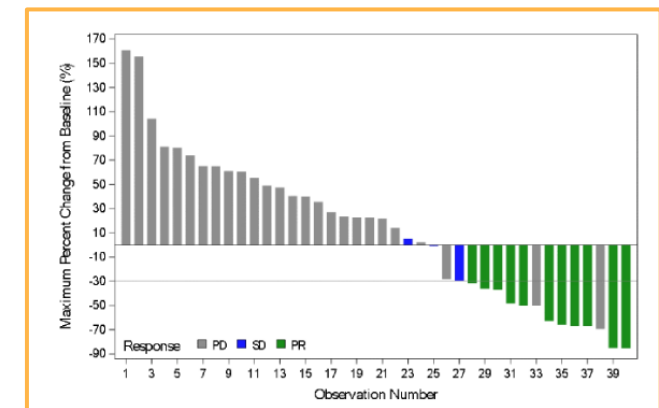
- Zim was in-licensed by Arcus to fully enable portfolio combinations
- Zim partnerships with Gilead and Taiho facilitate global development and enable additional opportunities to broaden potential therapeutic combinations
- Demonstrated ORR similar to other checkpoint inhibitors¹
 - >90% ORR in late-line 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



PROGRAMS ADVANCING TOWARDS CLINICAL DEVELOPMENT

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

HIF-2 α Inhibitor

Transcription factor



HIF-2 α 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

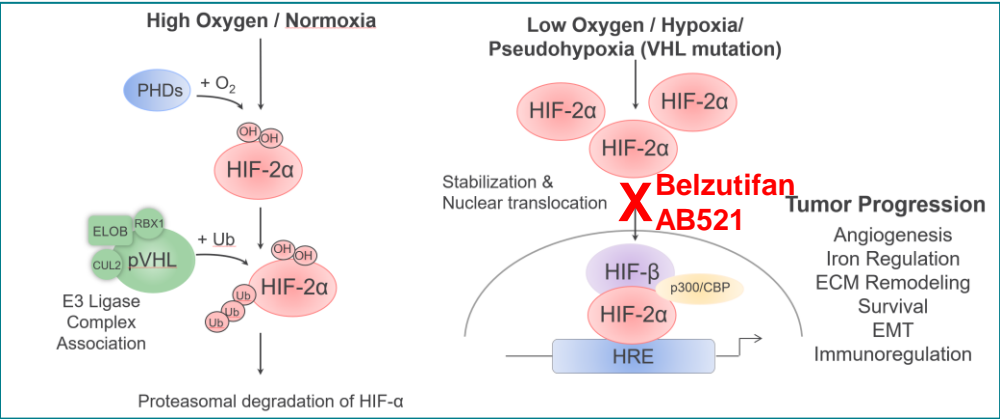


PAK4 overexpression is responsible for T-cell exclusion from immune desert tumors

Cancer cell intrinsic target

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

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

