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# COMBINING TO CURE

Arcus is at the forefront of designing precision combinations in the pursuit of cures for patients living with cancer.

**3Q22 CORPORATE PRESENTATION**

**NOVEMBER 28, 2022**

# 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, and expectations, including regarding our productivity and competitiveness; expectation that our cash and investments are sufficient to fund operations into 2026; potential of our investigational products and portfolio; anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca; expected timing of our clinical and developmental milestones, including clinical trial initiation and clinical readouts; expected timing for our investigational products to be commercially available and possible first to market advantage for any of our investigational products. 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: risks associated with preliminary or interim clinical data or preclinical data not being guarantees that future data will be similar; the unexpected emergence of adverse events or other undesirable side effects; difficulties or delays in initiating, conducting or completing our clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials, all of which may be exacerbated by unfavorable global economic, political and trade conditions; risks associated with our collaboration arrangement with Gilead including our dependence on Gilead for the successful development and commercialization of our investigational products; changes in the competitive landscape; our limited operating history and our ability to manage our growth; risks regarding our license and collaboration agreements and our ability to obtain and maintain intellectual property protection for our product candidates; and the inherent uncertainty associated with pharmaceutical product development and clinical trials.

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.

You should not rely upon forward-looking statements as predictions of future events. Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations.

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# Highlights

## $1.2B
in cash, cash equivalents & marketable securities

Funding into 2026

## Global, late-stage company
6 clinical-stage molecules

## 4 Phase 3 studies in GI and Lung Cancer
ARC-10

PACIFIC-8

STAR-121

STAR-221

## 2022 milestones

Dom (TIGIT)
- ✓ Phase 3 PACIFIC-8 study initiated
- ✓ Initiate two new Phase 3 studies
- ✓ Complete enrollment of ARC-7
- ✓ ARC-7 topline data (2H), presentation (2023)

Etruma / Quemli (A2R / CD73)
- ○ Initiate two Phase 2 platform studies in NSCLC

AB521 (HIF-2α)
- ✓ AB521 data in healthy volunteers
- ✓ Initiate Phase 1/1b in cancer patients

## Top tier partners
GILEAD

AstraZeneca

TAIHO PHARMA

## Productive research organization
1-2 new development candidates a year

At least 2 new FIH in 2022/2023:
- AB598 (CD39)
- AB801 (Axl)
- 1st inflammation candidate


FIH: first in human



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# Arcus Has a Broad Portfolio of Molecules with Best-in-Class Potential, Enabling Differentiated Combination Therapies

## DIFFERENTIATED SMALL MOLECULES

**etrumadenant (AB928)**: First-in-class dual $A_{2a}R$ / $A_{2b}R$ antagonist; generated early evidence of clinical activity in colorectal, prostate and lung cancers

**quemliclustat (AB680)**: First-in-class small-molecule CD73 inhibitor; generated early evidence of clinical activity in pancreatic cancer

**AB521:** Highly potent and selective HIF-2α inhibitor; first study in healthy volunteers and a Phase 1/1b in cancer patients are ongoing

## ENABLING ANTIBODIES

**domvanalimab (AB154)**: Anti-TIGIT monoclonal antibody (mAb; Fc silent) – ongoing randomized Phase 2 study ARC-7 in 1L NSCLC; four ongoing, Phase 3 studies in lung and GI cancers

**AB308:** Anti-TIGIT mAb (Fc enabled); Phase 1/1b expansion enrolling

**zimberelimab (AB122)**: anti-PD-1 mAb; approved in China for classical Hodgkin Lymphoma (cHL)*

## NEXT GENERATION PROGRAMS

**AB598:** Anti-CD39 mAb

**AB801:** small molecule Axl inhibitor

**Undisclosed:** Small molecule inhibitor of target involved in inflammation

**WORLD-CLASS DRUG DISCOVERY**

*Gloria Biosciences secured China approval; it holds commercial rights to zim in China and conducts its activities independently from Arcus





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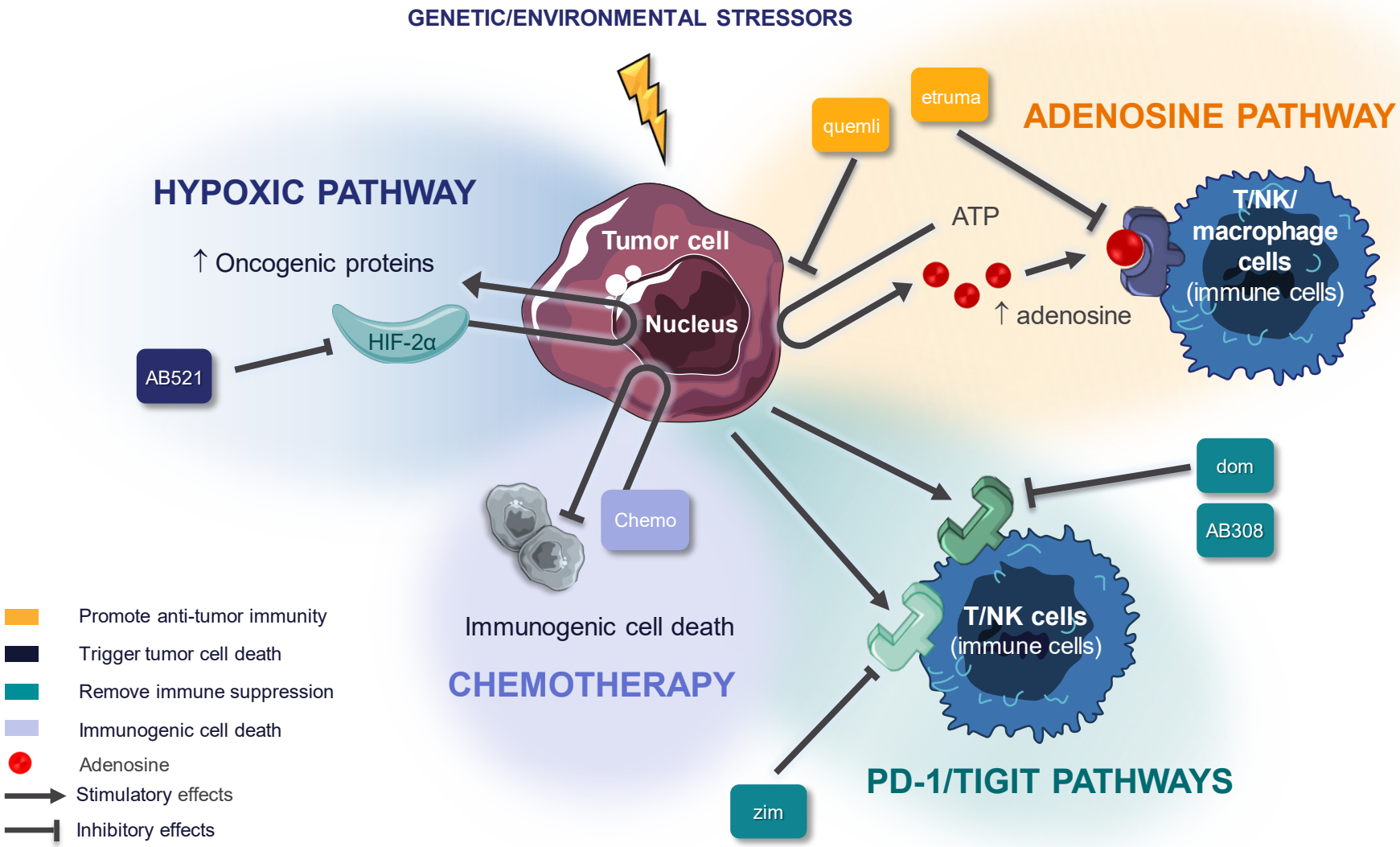
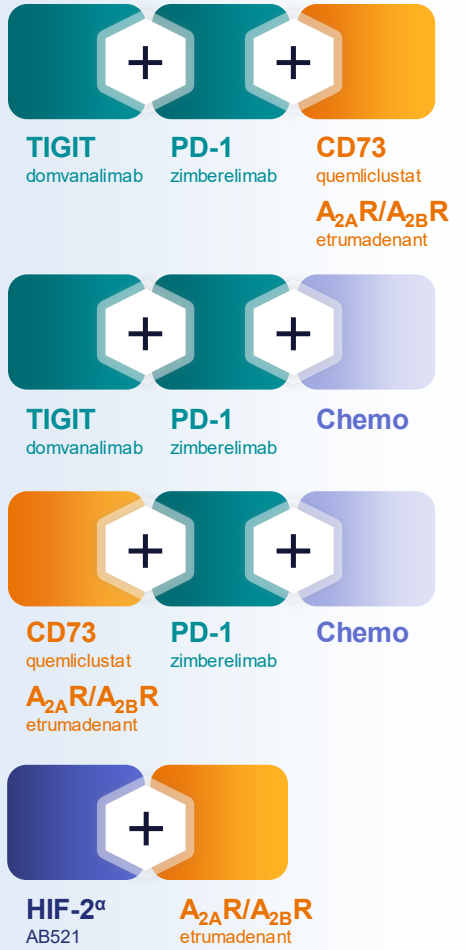
# Biology-Driven Combination Strategy to Enhance Anti-Cancer Activity




## NEW INTRA-PORTFOLIO COMBINATIONS



# Arcus Portfolio Evolution

## Today

TIGIT-based doublet combinations

Key molecule(s): domvanalimab

### Two Phase 2 Studies

ARC-7 ARC-21

### Four Phase 3 studies ongoing

ARC-10 STAR-121

PACIFIC-8 STAR-221

## 1-2 Years to Randomized Data

Adenosine-based combinations & triplets

Key molecule(s): etrumadenant, quemliclustat

### Five Phase 2 Studies

ARC-6 ARC-8 ARC-9

EDGE-Lung* Velocity-Lung* Gilead Platform

## 2+ Years to Randomized Data

Next generation small molecules

Key molecule(s): AB521 (HIF-2α), AB801 (Axl), AB598 (CD39), inflammation program

### Phase 1 Studies

ARC-20

**Advancement of next set of molecules into the clinic**

**1-2 new development candidates per year**



*To be initiated by year-end 2022



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# Four Phase 3 Studies Initiated in Lung and GI Cancers

| | PHASE 1/1b | PHASE 2 | PHASE 3 |
|---|---|---|---|
| DOMVANALIMAB (DOM) | | **1L / 2L Upper GI Malignancies (ARC-21)**<br>**dom** + **zim** + FOLFOX | **1L NSCLC, PD-L1 ≥50% (ARC-10)**<br>**dom** + **zim** vs. pembro |
| | | **1L / 2L NSCLC (Velocity-Lung)** ★<br>**dom** +/- **zim** +/- **etruma** +/- sacituzumab govitecan | **Stage III, unresectable, PD-L1≥1% NSCLC (PACIFIC-8)** ★<br>**dom** + durvalumab vs. durvalumab |
| | | **1L / 2L NSCLC, All Comers (EDGE-Lung)**<br>**dom** +/- **zim** +/- **quemli** +/- chemo | **1L NSCLC, PD-L1 All Comers (STAR-121)** ★<br>**dom** + **zim** + chemo vs. pembro + chemo vs. **zim** + chemo |
| | | **1L NSCLC, PD-L1 ≥50% (ARC-7)**<br>**zim** vs **dom** + **zim** vs **dom** + **zim** + **etruma** | **1L Upper GI Malignancies (STAR-221)**<br>**dom** + **zim** + chemo vs. nivo + chemo |
| AB308 | **Expansion Cohort (ARC-12)**<br>**AB308** + **zim** | | |
| QUEMLICLUSTAT (QUEMLI) | | **1L, 2L Pancreatic Cancer (ARC-8)**<br>**quemli** + **zim** + gem/nab-pac vs. **quemli** + gem/nab-pac | |
| ETRUMADENANT (ETRUMA) | | **2L CRPC (ARC-6)**<br>**etruma** + **zim** + docetaxel vs. docetaxel<br>**etruma** + **zim** + sacituzumab govitecan | |
| | | **2L / 3L+ mCRC (ARC-9)**<br>**etruma** + **zim** + FOLFOX/bev vs. FOLFOX/bev<br>**etruma** + **zim** + FOLFOX/bev vs. regorafenib | |
| AB521 | **HV Study (ARC-14)** | | |
| | **2L+, inc. ccRCC (ARC-20)**<br>**AB521 monotherapy** | | |

★ PACIFIC-8 is being operationalized by AstraZeneca. STAR-121 and Velocity-Lung will be operationalized by Gilead Sciences.

bev: bevacizumab, dom: domvanalimab, etruma: etrumadenant, gem/nab-pac: gemcitabine/nab-paclitaxel, nivo: nivolumab, pembro: pembrolizumab, quemli: quemliclustat, zim: zimberelimab

CRC: colorectal cancer, ccRCC: clear cell renal cell carcinoma, GI: gastrointestinal cancers (gastric, gastroesophageal junction, and esophageal adenocarcinoma), NSCLC: non-small cell lung cancer, PDAC: pancreatic ductal adenocarcinoma

Planned — NSCLC — Advanced Malignancies — PDAC — CRPC — CRC — Healthy Participants — GI

# Key Updates from Q3 2022

| | |
|---|---|
| **Late-Stage Anti-TIGIT Program in Lung Cancer** | • Pursuing broad TIGIT lung strategy which includes three ongoing registrational Phase 3 trials (ARC-10, STAR-121 and PACIFIC-8) in multiple NSCLC settings.<br>– A strategic amendment to the registrational Phase 3 study, ARC-10, in first-line PD-L1≥50% NSCLC now compares dom+zim vs SOC pembro, enabling site activation in the U.S. and Western Europe.<br>– Initiated the Phase 3 study, STAR-121, comparing dom+zim+chemo vs pembro+chemo in first-line, metastatic, PD-L1 all-comer NSCLC.<br>• Topline data disclosure for Phase 2 ARC-7 study on track for Q4, with anticipated presentation at a medical conference in 2023. |
| **Late-Stage Anti-TIGIT Program in GI Cancers** | • Arcus initiated two new studies in GI cancers:<br>– ARC-21 a Phase 2 study of dom+zim-based combinations, including with quemliclustat, in upper GI cancers<br>– STAR-221, a registrational Phase 3 study comparing dom+zim+chemo vs. nivo+chemo in first-line locally advanced unresectable or metastatic gastric, esophageal and gastro-esophageal junction adenocarcinomas |
| **Continued progress of AB521, HIF2α inhibitor** | • ARC-20, a Phase 1/1b study to evaluate AB521 in cancer patients was initiated<br>• Data from HV study enabled Arcus to start dose escalation in patients at 25mg, a pharmacologically active dose |
| **Advancement of early discovery pipeline** | • Phase 1 studies of AB598 (anti-CD39 antibody) and AB801 (small molecule Axl inhibitor) are expected to initiate in 2023<br>• First IND for the treatment of inflammatory disease expected to be filed in 2023 |
| **Corporate Updates** | • Arcus is well positioned to advance its expanding portfolio, with $1.2 billion in cash, cash equivalents and marketable securities; funding into 2026 |

dom: domvanalimab, nivo: nivolumab, ,pembro: pembrolizumab, zim: zimberelimab
GI: gastrointestinal, HV: healthy volunteers, NSCLC: non-small cell lung cancer, SOC: standard-of-care

# Gilead is Co-Developing Four Optioned Programs with Arcus

GILEAD

- Currently has rights to five of our clinical-stage candidates through its exercised options:
  - domvanalimab and AB308: anti-TIGIT antibodies
  - etrumadenant: A2a/A2b receptor antagonist
  - quemliclustat: small-molecule CD73 inhibitor
  - zimberelimab: anti-PD-1 antibody
- Arcus and Gilead share expenses for all these programs
- Arcus and Gilead will co-commercialize and equally share profits in the U.S. on approved products
- Gilead holds exclusive rights outside the U.S., subject to any rights of Arcus's existing collaboration partners, with tiered royalties payable to Arcus that range from mid-teens to low-twenties
- Expanded research collaboration to focus on two jointly-selected, novel targets in oncology

## WHAT THIS MEANS FOR ARCUS AND THE COLLABORATION

- ✓ $725 million payment and cost sharing puts Arcus in a strong position to invest in its programs
- ✓ Accelerates and expands our collaboration activities
- ✓ Brings operational expertise with global reach
- ✓ Enables earlier alignment on clinical studies and priorities to move fast
- ✓ Accelerates the exploration of new cross-portfolio combinations, with first-in-class potential



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

## 10-YEAR "ALL-IN" COLLABORATION

- **Nearly $1.4b in non-dilutive payments and equity investments from Gilead**
  - Includes $725mm in option payments in 1Q22
  - Gilead holds ~19% equity stake
- Opted in to nearly all of Arcus's clinical-stage portfolio
- Gilead equally shares co-development costs for the global joint development program
- Gilead has option rights to future molecules from current and future programs
- Arcus retains U.S. co-commercial rights

## COLLABORATION FOR JAPAN AND OTHER TERRITORIES IN ASIA (EX-CHINA)

- Facilitates global development & commercialization of Arcus molecules
- Up to $275mm in development, regulatory and commercial milestones per program
- Tiered royalties from high-single digit to mid-teens on net sales
- Option rights to programs arising during first 5 years; option rights exercised for majority of Arcus's clinical-stage portfolio— domvanalimab, zimberelimab, etrumadenant, and AB308

## CLINICAL COLLABORATION FOR DOMVANALIMAB PLUS DURVALUMAB

- Companies collaborating on PACIFIC-8, a Phase 3 registrational trial sponsored by AstraZeneca
- 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
- Trial initiated in 1Q22

**~$1.2B IN CASH AND INVESTMENTS AS OF 9/30/22 AND FUNDING INTO 2026**

# Multiple Clinical Readouts and Initiations in 2022 / 2023

| | COMBINATION / ARMS | SETTING | ANTICIPATED TIMING |
|---|---|---|---|
| ARC-6 | **etruma** + **zim** + SOC *vs.* SOC | Randomized Phase 2 Trial in 2L/3L mCRPC | • Data in-house by year-end<br>• Data presentation 2023 |
| ARC-7 | **dom** + **zim** + *vs.* **zim** *vs.* **etruma** + **dom** + **zim** | Randomized Phase 2 Trial in 1L mNSCLC (PD-L1 ≥ 50%) | • Enrollment completed 3Q22<br>• Topline data 2H22<br>• Data presentation Dec. 20, 2022 |
| ARC-8 | **quemli** + **zim** + gem/nab-pac | Phase 1/1b Trial in 1L mPDAC | • PFS and OS data expected 1H23 |
| ARC-9 | **etruma** + **zim** + FOLFOX *vs.* SOC | Randomized 2L/3L+ mCRC | • Data expected 1H 2023 |
| ARC-20 | **AB521** (HIF-2α) | Phase 1/1b in cancer patients | • Initiated in 3Q22 |
| ARC-21 | **dom** + **zim** + FOLFOX | Phase 2 in 1L/2L upper GI cancers | • Initiated in 3Q22 |
| STAR-121 | **dom** + **zim** + chemo vs pembro + chemo *vs.* **zim** + chemo | Phase 3 in 1L NSCLC, all comers | • Initiated in 3Q22 |
| STAR-221 | **dom** + **zim** + chemo *vs.* nivo + chemo | Phase 3 in 1L Upper GI malignancies | • Initiated in 4Q22 |
| EDGE-Lung | **dom** +/- **zim** +/- **quemli** +/- chemo | Phase 2 platform in NSCLC | • Initiation expected by YE 2022 |
| **Velocity-Lung** | **dom** +/- **zim** +/- **etruma** +/- sacituzumab govitecan (Trodelvy) or other combos | Phase 2 platform in NSCLC | • Initiation expected by YE 2022 |

dom: domvanalimab; etruma: etrumadenant; gem/nab-pac: gemcitabine/nab-paclitaxel; quemli: quemliclustat; SOC: standard of care; zim: zimberelimab; CRPC: castrate-resistant prostate cancer; m: metastatic; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; PFS: progression-free survival; OS: overall survival; GI: gastrointestinal

# ANTI-TIGIT PROGRAM

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

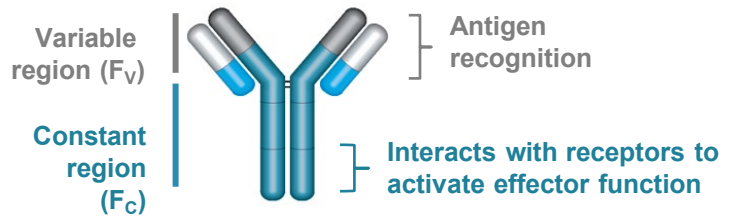
**Domvanalimab's advancement into four registrational studies coupled with AB308's rapid advancement into expansion cohorts reinforces Arcus as a leader in the development of anti-TIGIT therapies**

## DOMVANALIMAB (FC-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
- Four phase 3 studies ongoing: **ARC-10** (1L, PD-L1 high NSCLC), **PACIFIC-8** (Stage 3 NSCLC), **STAR-121** (1L PD-L1 all-comer NSCLC), **STAR-221** (1L upper GI)

## AB308 (FC-ENABLED)

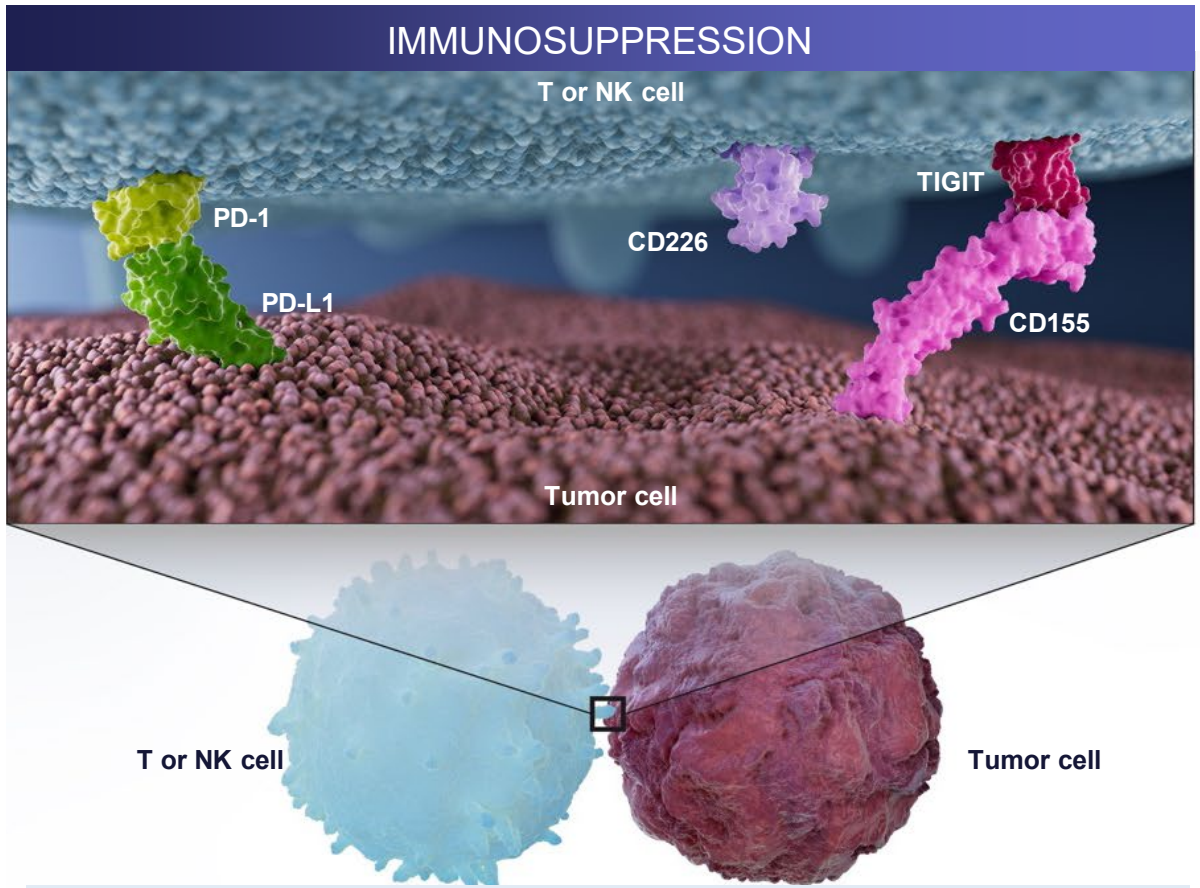
- Also blocks the CD155 interaction with TIGIT, critical for T cell activation
- Potential to deplete TIGIT-bearing cancer cells (e.g., myeloma, NHL)
- Phase 1/1b ARC-12 study evaluating AB308 plus zimberelimab in advanced malignancies is ongoing

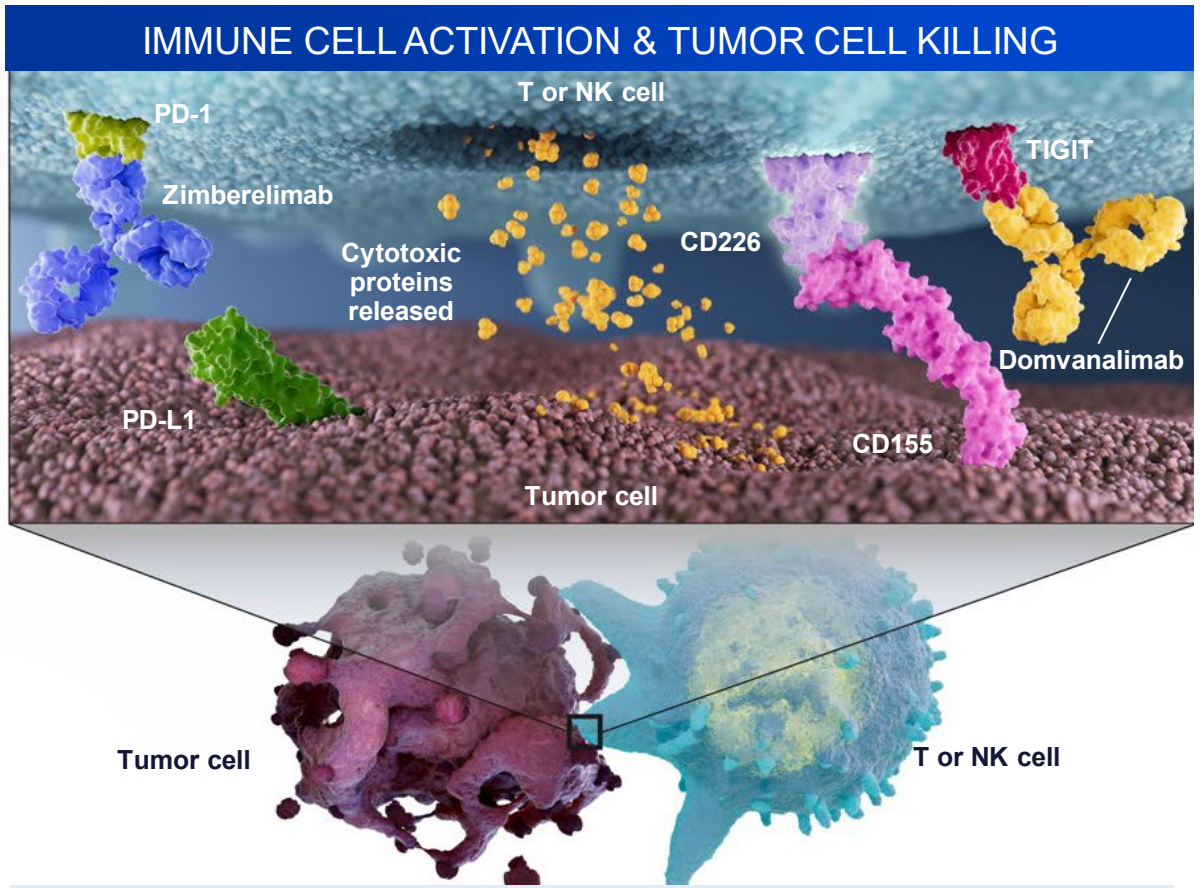



**NO DEPLETION OF T-CELLS OR PERIPHERAL T-REGS**

**POTENTIAL FOR ACTIVITY IN HEME MALIGNANCIES**

# Anti-TIGIT Mechanism of Action: domvanalimab (dom)



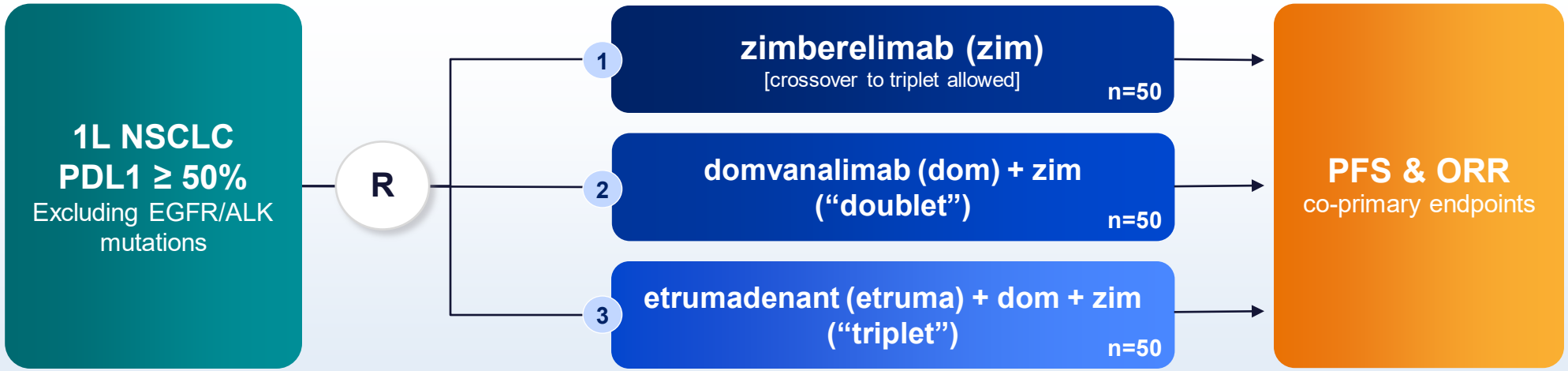




TIGIT is another checkpoint receptor expressed on immune cells that binds CD155 on tumor cells, leading to further evasion of anti-tumor immunity

Dom blocks TIGIT, enabling CD155:CD226 interaction and immune cell activation

Combined inhibition of TIGIT and PD1 may have a synergistic effect, unleashing immune activity against certain tumor cells

# ARC-7 Randomized Phase 2 in 1L NSCLC (PD-L1 ≥ 50%): zim vs. dom + zim vs. etruma + dom + zim




| | |
|---|---|
| **STUDY DESIGN** | Phase 2, multicenter, 3-arm randomized, open-label study |
| **PATIENT POPULATION** | 1L NSCLC, Stage IV, PD-L1 TPS ≥ 50% without EGFR/ALK mutation |
| **STRATIFICATION FACTORS** | ECOG PS: 0 vs 1; male vs female |
| **CROSSOVER** | Subjects in Arm 1 have the option to cross over to Arm 3 at the time of confirmed progression |

ENROLLMENT COMPLETED IN 3Q22


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

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# 4th Interim Analysis (IA4)

## SUMMARY OF EFFICACY OBSERVATIONS FROM IA4:

- In this interim analysis, both domvanalimab-containing arms continued to show clinically meaningful differentiation compared to zimberelimab monotherapy across multiple efficacy measures, including objective response rates (ORR), progression-free survival (PFS) and six-month landmark PFS.
- The protocol-specified fourth interim analysis was conducted when the trial reached full enrollment, with a clinical data cutoff date of August 31, 2022. A total of 150 patients have been randomized across the three study arms.
- For the current interim analysis, efficacy was evaluated in study patients who had at least 13 weeks of potential follow-up and were eligible for at least two imaging scans (n=133).
- Detailed results from this fourth interim analysis and an exploratory analysis on 12 patients who crossed over from zimberelimab monotherapy arm to triplet therapy will be presented in an upcoming medical meeting.

## SUMMARY OF SAFETY OBSERVATIONS FROM IA3:

- At time of data cutoff, no unexpected safety signals were observed across the three study arms. Both domvanalimab-containing arms were generally well tolerated and showed an overall safety profile consistent with the known safety profiles for each individual molecule to date.

## NEXT STEPS:

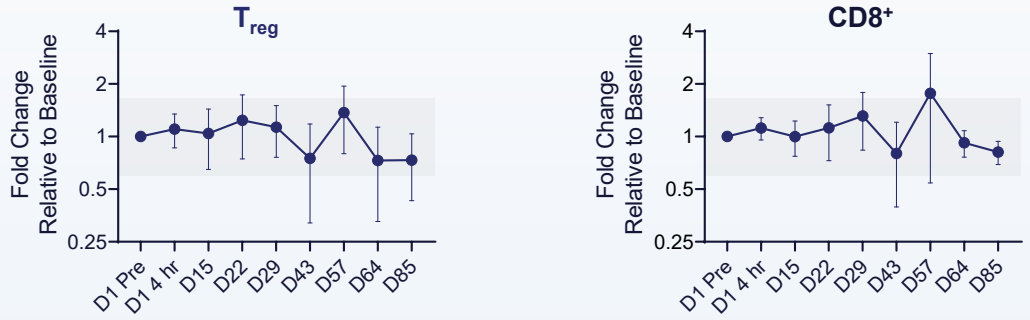
- **Data will be presented Dec. 20, 2022,** at the ASCO Monthly Plenary Series by Melissa L. Johnson, M.D., Director Lung Cancer Research, Sarah Cannon Research Institute at Tennessee Oncology, and Lead Investigator for the ARC-7 study.

# Anti-tumor Activity and Lower Frequency of irAEs Observed with domvanalimab (dom) in the Absence of $T_{reg}$ Depletion

### Important differences between dom (phase 1 in combination with zim) and Fc enabled anti-TIGIT competitors

- Peripheral $T_{reg}$ numbers do not decrease with dom + zim, but they do with Fc-enabled anti-TIGIT competitors
- Lower frequency of various irAEs reported with dom + zim, compared to values reported for Fc-enabled anti-TIGIT competitors
- Several clinical responses seen in Phase 1 study, without any effects in blood T cell populations

### Peripheral T cell numbers did not change in Phase 1 patients treated with Dom + Zim




### Immune-related AEs for Dom+Zim ongoing phase 1 (n=56)

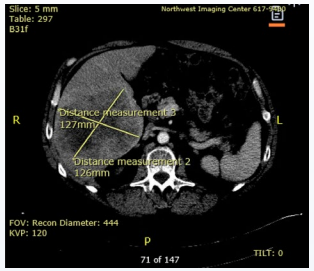
| | Dom + zim n (%) |
|---|---|
| **Hypothyroidism** | 5 (8.9%) |
| **Pruritus** | 4 (7.1%) |
| **Rash** | 4 (7.1%) |
| **Maculopapular rash** | 3 (5.4%) |
| **Infusion-related reaction** | 3 (5.4%) |

**irAEs (n>2) in the ongoing Phase 1 trial of domvanalimab (NCT03628677) as of 01Apr2022.** Regimens containing Fc-enabled anti-TIGIT monoclonal antibodies, including those reported to deplete peripheral $T_{reg}$,[1,2,3] have reported incidences in the following ranges: pruritus (~20-38%), rash (~21-40%), maculopapular rash (~0-9%), and infusion-related reactions (~10-31%)[2,3,4,5].

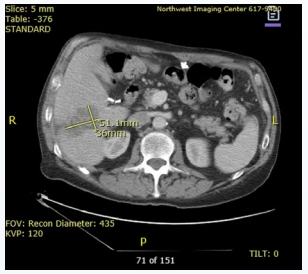
## PHASE 1 CASE STUDY

- Stage IV esophageal adenocarcinoma; PD-L1 (CPS) ~2%
- Prior treatment: (1) FOLFOX; (2) Carbo/Pac; (3) pembro
- Study regimen: 10 mg/kg dom Q3W + 360 mg zim Q3W

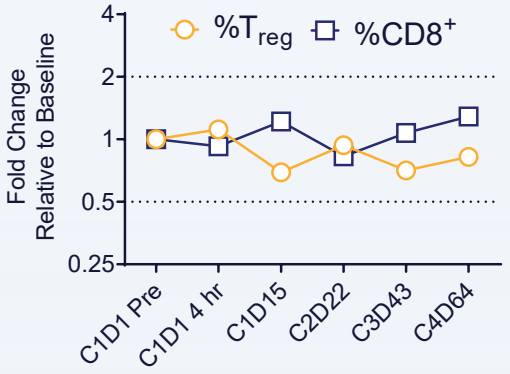
**BASELINE SCAN**
Target lesion #1: **127 mm long axis**



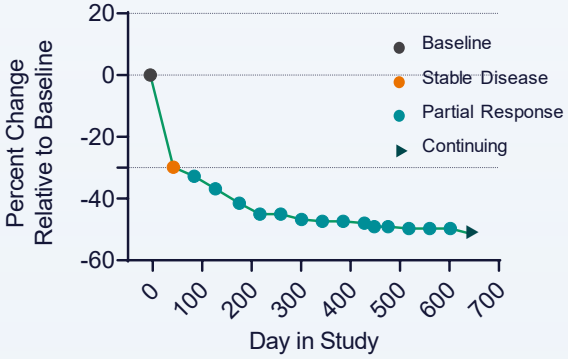

**POST-CYCLE 30 SCAN**
Target lesion #1: **62 mm long axis**



### Peripheral Blood




### Measurable Target Lesions





Gauthier, K. et al; Immunology 2022 (#2719): Anti-TIGIT Antibodies Promote Immune Activation Relevant to Targeting Stem-like and Tumor-specific T Cells in Combination With Anti-PD-1

[1]Mettu *et al.* 2022 Clin Cancer Res DOI:10.1158/1078-0432.CCR-21-2780 (etigilimab); [2]Van den Mooter *et al.* 2021 Cancer Res DOI:10.1158/1538-7445.AM2021-CT118 (EOS-448). [3]Cuende *et al.* 2022 AACR #LB189 (EOS-448); [4]Niu *et al.* 2022 Ann Oncol DOI:10.1016/j.annonc.2021.11.002 (vibostolimab); [5]Cho *et al.* 2021 Ann Oncol DOI:10.1016/j.annonc.2021.10.217 (tiragolumab)

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# Phase 3 Program for domvanalimab in NSCLC

## Arcus is operationalizing only one of the three initiated registrational studies in NSCLC for dom, preserving our financial and clinical resources

| STUDY | LEAD SPONSOR | SETTING | PATIENT POPULATION[1] |
|---|---|---|---|
| ARC-10 | ARCUS BIOSCIENCES | 1L NSCLC, PD-L1>50% | 33k patients |
| STAR-121 | GILEAD | 1L NSCLC, PD-L1 All comers | 119k patients |
| PACIFIC-8 | AstraZeneca | Stage 3 NSCLC | 21k patients |

**Multi-billion revenue opportunities for Arcus / Gilead**

**$10B+ addressable market**

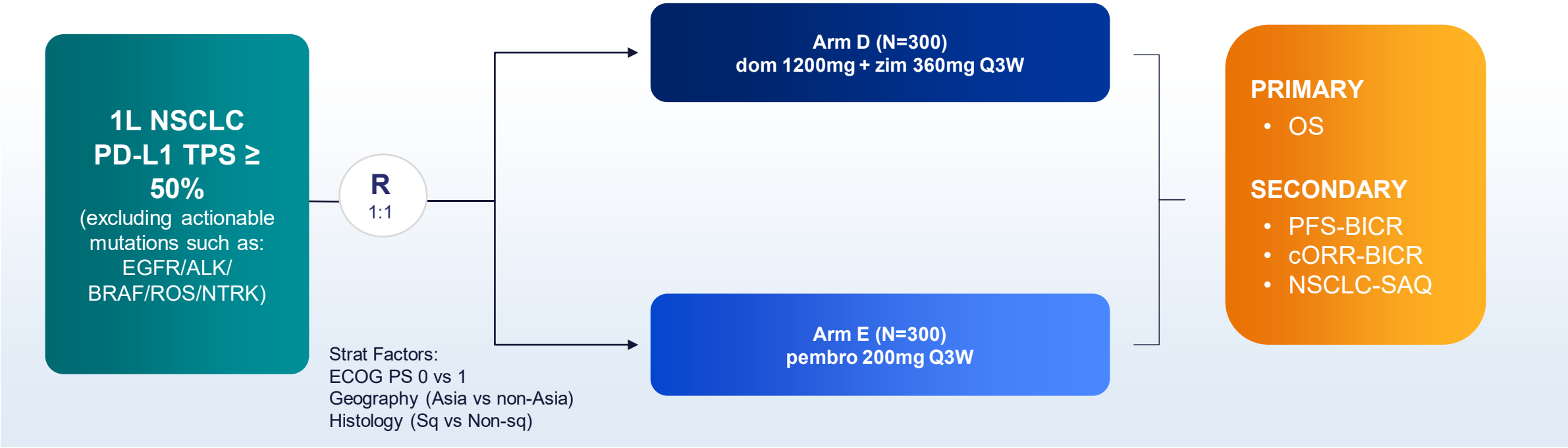
[1]Based on drug treatable US patient population. Excludes patients with actionable mutations. Source: Decision Resources Group.



ARCUS BIOSCIENCES

# ARC-10 | Phase 3 Trial to Evaluate dom + zim vs. pembro in 1L NSCLC (PD-L1 ≥ 50%)

- We aim to establish dom + zim as a standard of care IO-IO backbone to enable novel combinations with portfolio assets
- Objective is to facilitate approval of dom + zim as chemo-free regimen in this setting, and potentially contribute to a broad spectrum of NSCLC indications being evaluated across our other ongoing Phase 3 studies (STAR-121 and PACIFIC-8)
- Strategic amendment for ARC-10 to drop chemo arm and compare dom + zim vs. pembro
- Inclusion of pembro as the active comparator enables site activation in the United States and Western Europe




domvanalimab: dom; pembrolizumab: pembro; zimberelimab: zim


NCT#: NCT04736173

ARCUS BIOSCIENCES

# Phase 3 1L NSCLC All Comer Study evaluating dom + zim + chemo vs. pembro + chemo vs. zim + chemo

**ELIGIBILITY CRITERIA**

- Metastatic NSCLC without actionable mutations
- No prior systemic treatment for metastatic NSCLC
- PD-L1 all-comers
- ECOG 0-1
- No interstitial lung disease
- No untreated brain metastases

→

**COHORT A**
**dom + zim + platinum doublet**

**COHORT B**
**pembro + platinum doublet**

**COHORT C**
**zim + platinum doublet**

→

**ENDPOINTS**

**Primary**
- PFS by BICR
- OS

**Secondary**
- ORR and DOR
- Safety and QoL

New **Initiated in 3Q22**

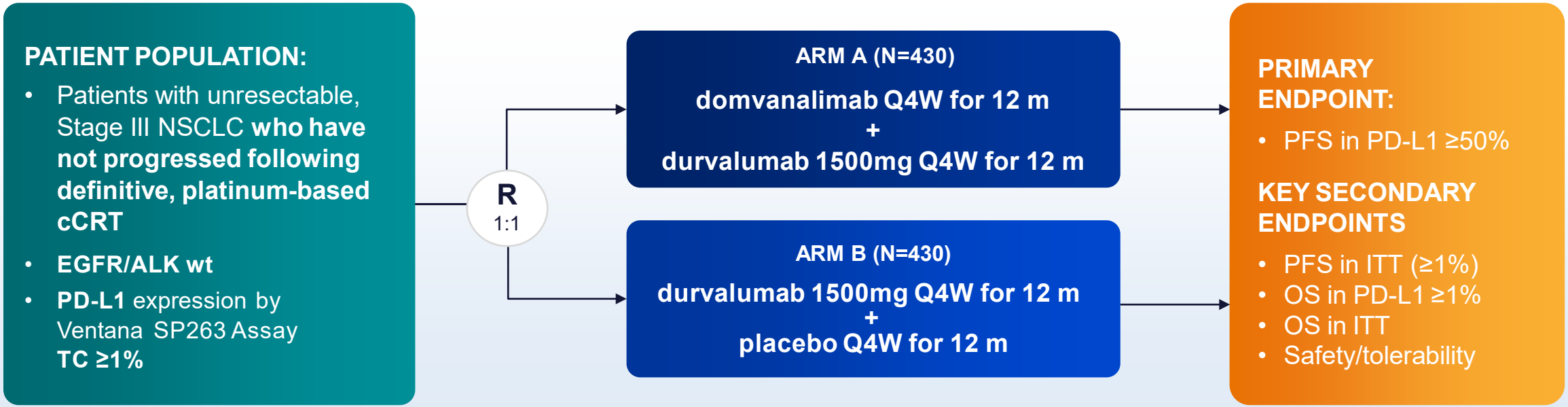
domvanalimab: dom; pembrolizumab: pembro; zimberelimab: zim

ORR: objective response rate; DOR: duration of response; OS: overall survival; PFS: progression-free survival; ECOG: Eastern Clinical Oncology Group; QoL: quality of life; BICR: blinded independent central review


Gilead Sciences is operationalizing STAR-121

# Phase 3 Trial to Evaluate dom + durva vs durva + placebo in Unresectable, Stage III NSCLC

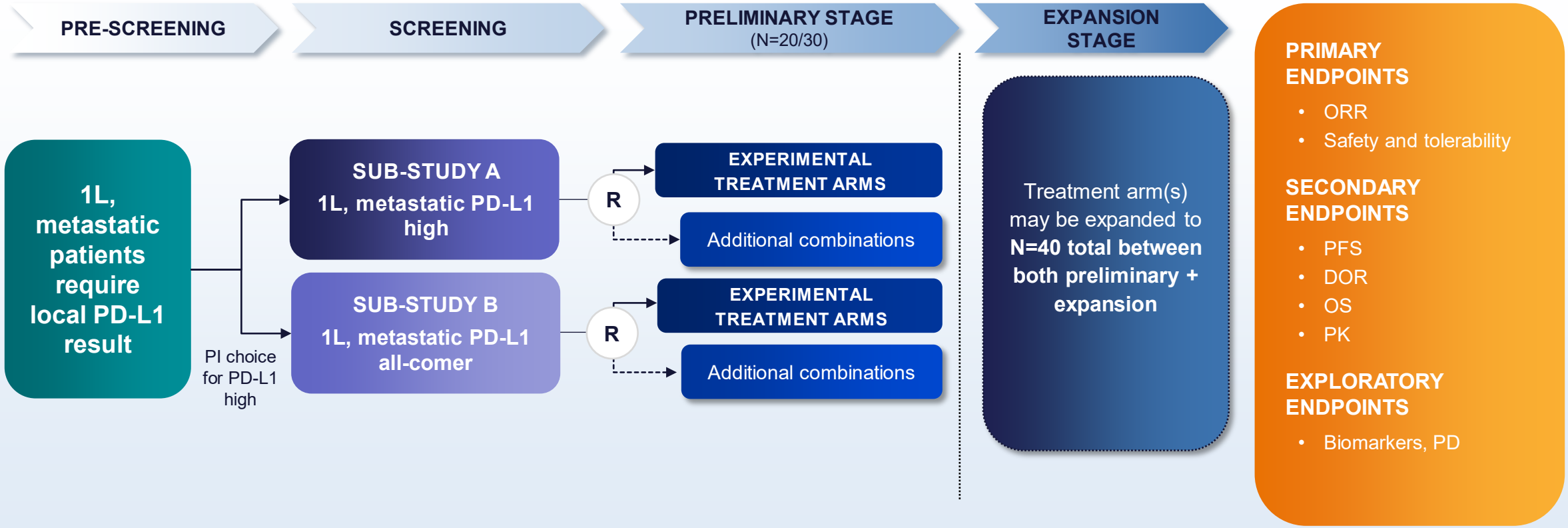
- Combines domvanalimab (dom) with standard-of-care in Stage III NSCLC
- Potential to be first anti-TIGIT combination in this curative intent setting
- Initiated in 1Q22





domvanalimab: dom; durvalumab: durva

# Platform Design to Rapidly Evaluate Novel Combinations for NSCLC, Including quemli and dom-based Regimens




1L, first line; AC, all comer; DOR: duration of response; IO, immuno-oncology; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PD, pharmacodynamics; PD-L1,ORR programmed death-ligand 1; PK, pharmacokinetics; PI, principal investigator; R, randomized.

# Strategy for dom in Upper GI Malignancies

## RATIONALE FOR ANTI-TIGIT IN GI CANCERS

- PD-L1 is overexpressed in esophageal squamous cell carcinoma (ESCC) and adenocarcinoma (EAC) histologies[1,2]
  - PD-1 inhibitors have become SOC in 1L ESCC and EAC/GEJ/Gastric[3]
- TIGIT is often co-expressed with PD-1 on tumor-infiltrating T cells, resulting in reduced anti-tumor immune response
- Combined blockade of TIGIT and PD-1 with tiragolumab and atezolizumab has shown activity in both ESCC and EAC[4]

1. Ohigashi et al. Clin Cancer Res 2005; 2. Derk et al. Cancer Immunol Res 2015; 3. NCCN Clinical Practice Guidelines in Oncology. Esophageal and Esophagogastric Junction Cancers v2.2021; 4. Wainberg et al. ESMO World Congress on GI Cancer 2021: LBA 5

ARC-21

- **Phase 2 study** evaluating dom + zim + chemo in 1L GE cancers and dom + zim in 2L+ GE cancers
- Initiated 3Q22

STAR-221

- **Registrational phase 3 study** in gastric, gastroesophageal junction, and esophageal adenocarcinoma
- Initiated in 3Q22



ARCUS BIOSCIENCES

# Tiragolumab + Atezo Demonstrated Anti-tumor Activity in Heavily Pretreated Esophageal Cancer Patients (ESMO IO 2021)

## EXPANSION COHORT OBJECTIVE:

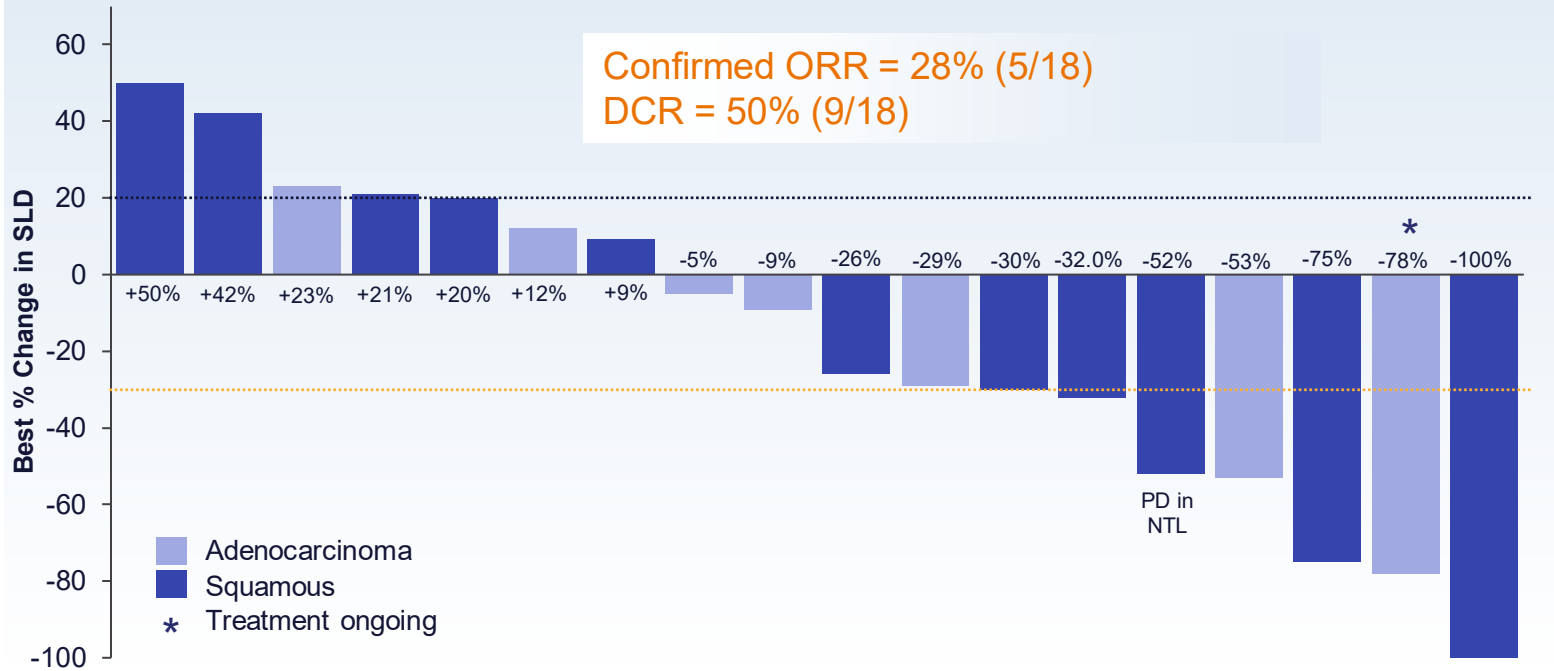
To determine the preliminary safety, tolerability, and anti-tumor activity of tiragolumab 600 mg IV Q3W and atezolizumab 1200 mg IV Q3W in metastatic esophageal cancer

## ELIGIBILITY:

- Metastatic esophageal cancer of any histology
- Any line of therapy
- Any PD-L1 status
- No prior treatment with immunotherapy

**Tiragolumab + Atezo Esophageal Cohort** (n=18)

| | |
|---|---|
| **Median PFS, months (95% CI)** | 3.5 (1.2-5.6) |
| **Median (DoR, months (95% CI)** | 15.3 (7.0–NR) |




| Prior lines of systemic therapy | 2 | 2 | 2 | 3 | 2 | 1 | 3 | 4 | 3 | 1 | 8 | 2 | 1 | 2 | 2 | 4 | 2 | 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PD-L1 negative/low (TC or IC <5%) | ■ | | | | ■ | ■ | ■ | ■ | ■ | | ■ | n/e | | ■ | ■ | ■ | | |
| PD-L1 positive (TC or IC ≥5%) | | ■ | ■ | ■ | | | | | | ■ | | n/e | ■ | | | | ■ | ■ |

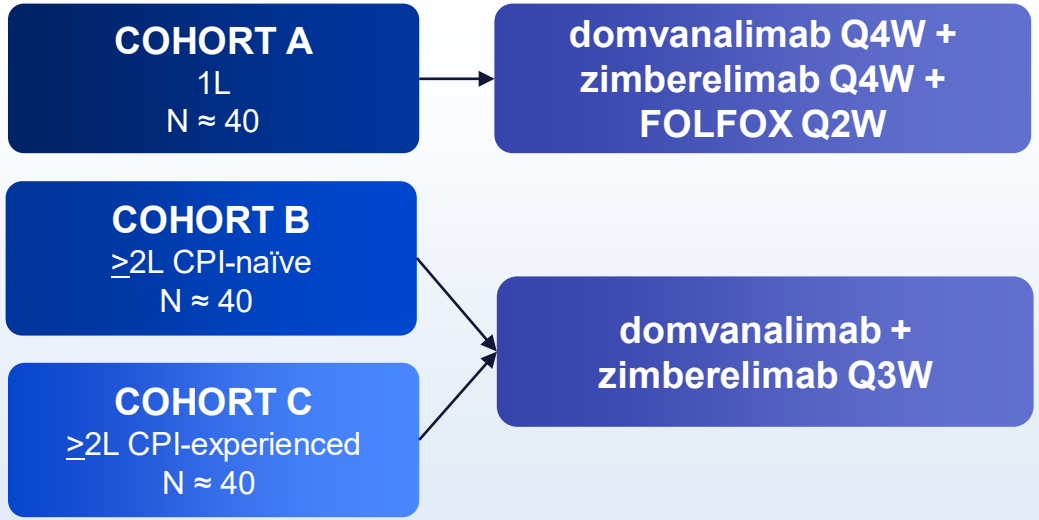

Wainberg et al. ESMO World Congress on GI Cancer 2021: LBA 5

ARCUS BIOSCIENCES

# ARC-21 | Phase 2 Trial to Evaluate dom + zim + chemo vs dom + zim in Advanced Upper Gastrointestinal Tract Malignancies

**KEY ELIGIBILITY CRITERIA**

- EAC/GEJ/Gastric
- Locally advanced unresectable or metastatic disease w/o prior systemic treatment
- Measurable disease per RECIST 1.1




**PRIMARY ENDPOINTS**

- Safety
- ORR per Investigator

New **Initiated in 3Q22**


domvanalimab: dom; zimberelimab: zim

# STAR-221 Phase 3 Trial of dom + zim + chemo vs nivo + chemo in Gastric, GEJ and Esophageal Adenocarcinoma

## KEY ELIGIBILITY CRITERIA

- 1L locally advanced unresectable or metastatic w/o prior systemic treatment
- Measurable disease (RECIST 1.1)
- PD-L1 all comers
- Known HER-2 positive tumors excluded

N=970

R 1:1

- **domvanalimab + zimberelimab + PI Choice of Chemo***
- **nivolumab + PI Choice of Chemo***

No crossover or change of chemotherapy allowed

## DUAL PRIMARY ENDPOINTS:

- OS ITT
- OS in TAP ≥5%

## KEY SECONDARY ENDPOINTS:

- PFS ITT
- PFS in TAP ≥5%

New **Initiated in 3Q22**

**Stratification Factors:**

- PD-L1 expression (TAP ≥5% or TAP <5%)
- ECOG PS (0 or 1)
- Region (US/Canada/EU5 vs. Asia vs. rest of world)

*PI choice of chemo: FOLFOX or CAPOX.
TAP: tumor area positivity (revised nomenclature for vCPS [visually-estimated composite positive score])


domvanalimab: dom; nivolumab; nivo; zimberelimab: zim

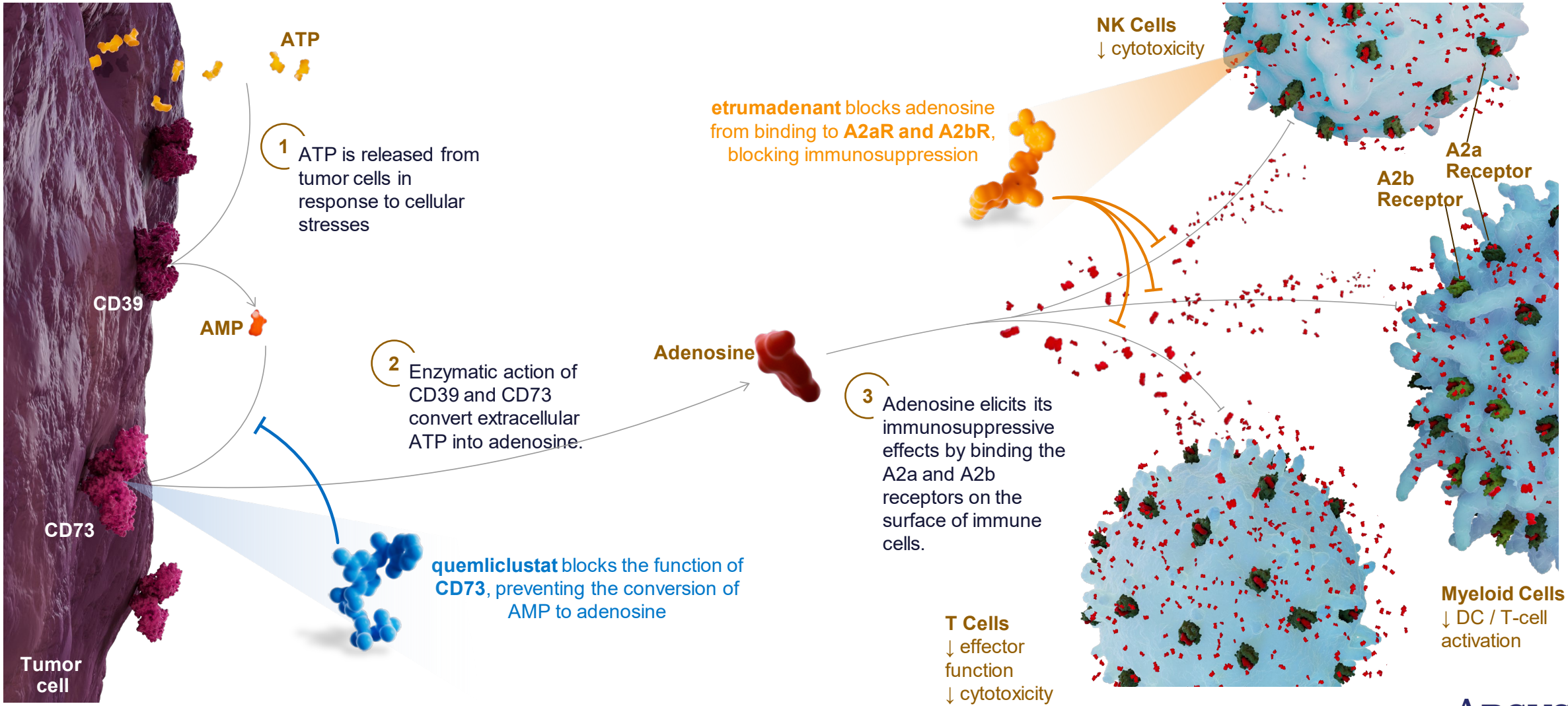
# Domvanalimab: Compelling Advantages as the First Fc-Silent TIGIT Program that Support Best-in-Class Potential

| | Roche | Arcus Biosciences / Gilead | BeiGene / Novartis | Merck |
|---|---|---|---|---|
| **Potential First-to-Market Opportunity (in U.S.)[1]** | • 1L NSCLC, PD-L1 high<br>• Stage 3 NSCLC<br>• LA ESCC | • 1L NSCLC, all-comers<br>• 1L EAC/GEJ/Gastric | | • 1L NSCLC, all-comers<br>• ES-SCLC |
| **Potential Advantages** | • First mover advantage | • Fc-silent, potentially yielding safety/combinability benefits<br>• In Stage 3 NSCLC, with the current SOC durva (and enriching for PD-L1 ≥1%)<br>• Flexibility in pricing Dom+Zim combinations | • Strong presence in China<br>• China data generation with Ph1b/2 studies | • Pembro is an entrenched SOC in 1L NSCLC (not SOC in Stage III) |
| **Potential Liabilities** | • Evidence of ADA's w/ Atezo<br>• High incidence of IRRs; moderate incidence of certain irAEs (rash, pruritus)<br>• Limited Atezo use in NSCLC | • Newcomer to IO market<br>• Zim is not yet approved | • Certain studies are China-centric<br>• Tisle approvals will be limited in US & EU | • Co-form is unattractive to clinicians & payers<br>• Large 1L Lung Ph3 study with 1200 patients extends timeline to first approval |
| **Ph3 Studies** (initiated/ongoing) | • 1L NSCLC (PD-L1 ≥50%)<br>• 1L NSCLC, non-squamous<br>• Stage 3 NSCLC<br>• LA ESCC<br>• 1L ESCC (China only) | • 1L NSCLC (PD-L1 ≥50%)<br>• 1L NSCLC (all comer)<br>• Stage 3 NSCLC<br>• 1L EAC/GEJ/Gastric | • 1L NSCLC (PD-L1 ≥50%)<br>• Stage 3 NSCLC | • 1L NSCLC (PD-L1 ≥1%)<br>• 1L NSCLC (all comer)<br>• Stage 3 NSCLC<br>• ES-SCLC |

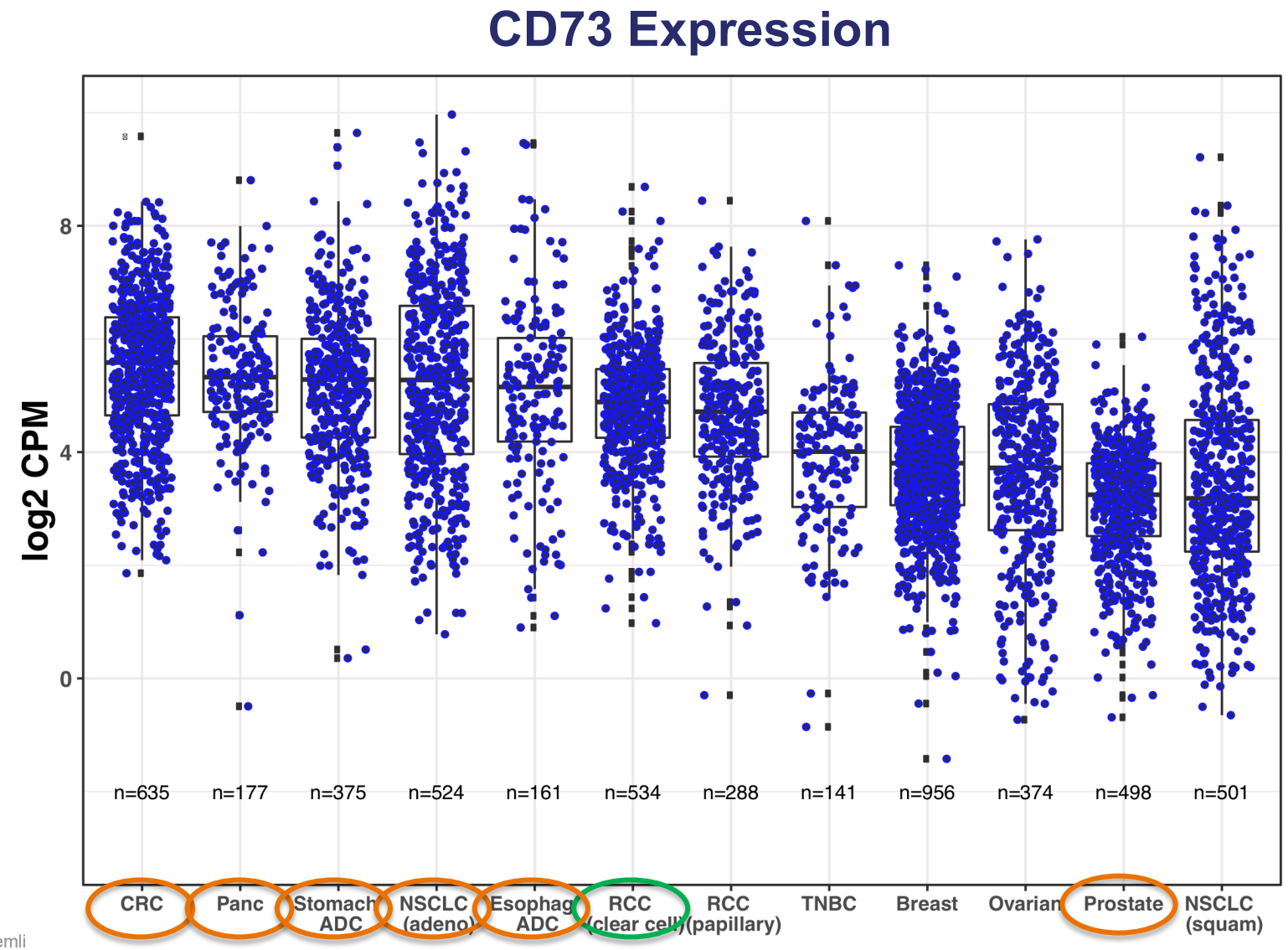

[1]Includes indications relevant to current Arcus/Gilead development program

# CD73-Adenosine Axis Programs

# The CD73-Adenosine Axis Plays a Well-Established and Critical Role in Suppression of the Immune Response



# Ongoing Development with etruma and quemli is Directed to Tumor Types with Potential for High Adenosine




etrumadenant: etruma; quemliclustat: quemli

Arcus Analysis of Tumor Cancer Genome Atlas (TCGA)

# High CD73 is a Negative Prognostic Factor

| TUMOR TYPE | CD73$^{HI}$ PROGNOSTIC FOR | REFERENCE | SAMPLE TYPE, # | CD73 METHOD | COMMENT |
|---|---|---|---|---|---|
| **PDAC** | Negative outcome | **Sciarra, A** et al. CD73 expression in normal and pathological human hepatobiliopancreatic tissues. Cancer Immuno, immunother (**2019**) slide #3 | PDAC (n=42), PDAC metastasis (n=12) | D7F9A, IHC | • CD73 data from additional surgical samples in hepatobiliopancreatic samples |
| | Negative for OS and DSS | **Tahkola, K**., et al. Prognostic impact of CD73 expression and its relationship to PD-L1 in patients with radically treated pancreatic cancer. Virchows Arch (**2021**) slide #4 | TMA of radically treated stage 1-IV PDAC, N=110 | D7F9A, IHC | • Cut off selected by ROC vs 3 yr mortality |
| | Negative for OS and RFS | **Zhao, J** et al. Overexpression of CD73 in PDAC is associated with immunosuppressive TME and poor survival. Pancreatology (**2021**) slide #5 | MDA cohort, n=138 with upfront surgery | D7F9A, IHC | • Cut off at TPS ≥ 75%<br>• CD73 expression correlates with low TILs and shorter OS |
| **CRC** | Negative for TTR and DSS | **Messaoudi, N** et al. Prognostic value of CD73 expression in resected colorectal cancer liver metastasis. Oncoimmunology (**2020**) slide #6, 7 | TMA of n=215 who underwent resection | Ab91084, multiplex IF | • Cut off set at upper tertile tCD73 (tumoral + stromal expression) |
| **NSCLC** | Negative for OS and PFS | **Inoue,** Y et. al. Prognostic impact of CD73 and A2aAR expression in NSCLC. Oncotarget (**2017**) 8:8738-8751 slide #8, 9 | TMA of resected NSCLC; n=642 | D7F9A, IHC *SA654* | • ~10% of subjects were CD73 high |
| | *CD73 is predictive for ICI response* | Ishii, H et al. Predictive value of CD73 expression for the efficacy of ICI in NSCLC. Thoracic Cancer (2020) 11:950 | Pre-treatment biopsy; n=91 | D7F9A, IHC | • Not prognostic but predictive for the immune checkpoint inhibitor |
| **RCC** | Negative for OS and DFS | **Tripathi A** et al. Prognostic significance and immune correlates of CD73 expression in RCC. J Immunother Cancer (**2020**) slide #11 | TMA of nephrectomy samples with RCC(n=138) | D7F9A, IHC | • Cut-off at median by combined score (% positive cells x intensity)<br>• *Includes TCGA RNAseq data mining* |



DSS: Disease-specific survival, RFS: Recurrence free survival, TTR: Time to recurrence

# etrumadenant (etruma): Represents a Potentially Best-in-Class Adenosine Receptor Antagonist

- First $A_2R$ antagonist to enter clinical development that:
  - Was specifically designed for the oncology setting
  - Inhibits both $A_{2a}R$ and $A_{2b}R$ receptors
- Multiple advantages over other A2aR antagonists in clinical development:
  - Minimal shift in potency due to decreased non-specific protein binding
  - Excellent penetration of tumor tissue
  - Excellent drug properties (PK, etc.)
- Differentiated, highly efficient clinical development plan ongoing:
  - First clinical program to evaluate an $A_2R$ antagonist with chemo

## High potency against both the A2aR and A2bR receptors allows for potentially broader activity

| Compound | A2aR Blood (IC50, nM)c | A2aR (KB, nM)d | A2bR (KB, nM)d |
|---|---|---|---|
| **AB928** *(Arcus)* | **80** | **1.3** | **2.0** |
| CPI-444 [a,b] *(Corvus)* | ~10,000 | 5.4 | 493 |
| AZD 4635 [a,b] *(AstraZeneca)* | 2,600 | 5 | 46 |
| NIR178 [a,b] *(Novartis)* | ~10,000 | 58 | 189 |
| Preladenant [a,b] *(Merck)* | 785 | 3.3 | 3,121 |

## AB928 has ideal pharmacological properties for an oncology drug

| Attribute | AB928 Value |
|---|---|
| Retains potency in physiologically relevant conditions | **$IC_{50}$ = 87 nM** |
| High tumor penetration | **Tumor : Plasma ratio: >60%** |
| Low CNS permeability (in mouse model) | **~ 1% of the concentration found in blood** |
| Full engagement of target across dosing time period in humans | **≥90% target inhibition at trough** |

[a] Arcus data generated with compound samples synthesized or purchased by Arcus.

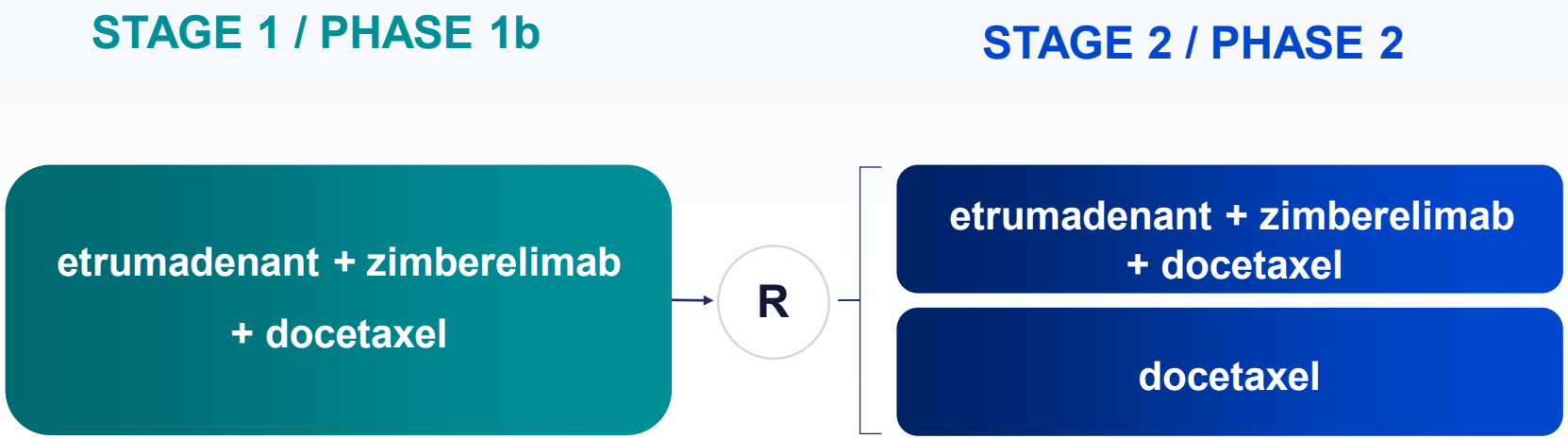
[b] CPI-444: Structure from AACR, April 2017 (#CT119), synthesized by Arcus; AZD4635: Structure from AACR, April 2017 (#2641), synthesized by Arcus; NIR178: Structure from WHO Drug Information, Vol. 32, No. 4, 2018; https://www.who.int/medicines/publications/druginformation/innlists/PL120.pdf?ua=1), synthesized by Arcus. Preladenant: Purchased from Ark Pharma (AK-43905).

[c] Measured in human blood CD8+ T cells; CREB is a transcription factor that becomes phosphorylated when A2aR is activated; thus, the level of pCREB inhibition is a measure of the ability of an A2aR antagonist to inhibit A2aR.

[d] $K_B$ is a measure of a compound's thermodynamic ability to bind/block its target receptor; lower $K_B$ values reflect greater potency for a given receptor.

# Phase 1b/2 Platform Study is Evaluating etruma in second-line mCRPC

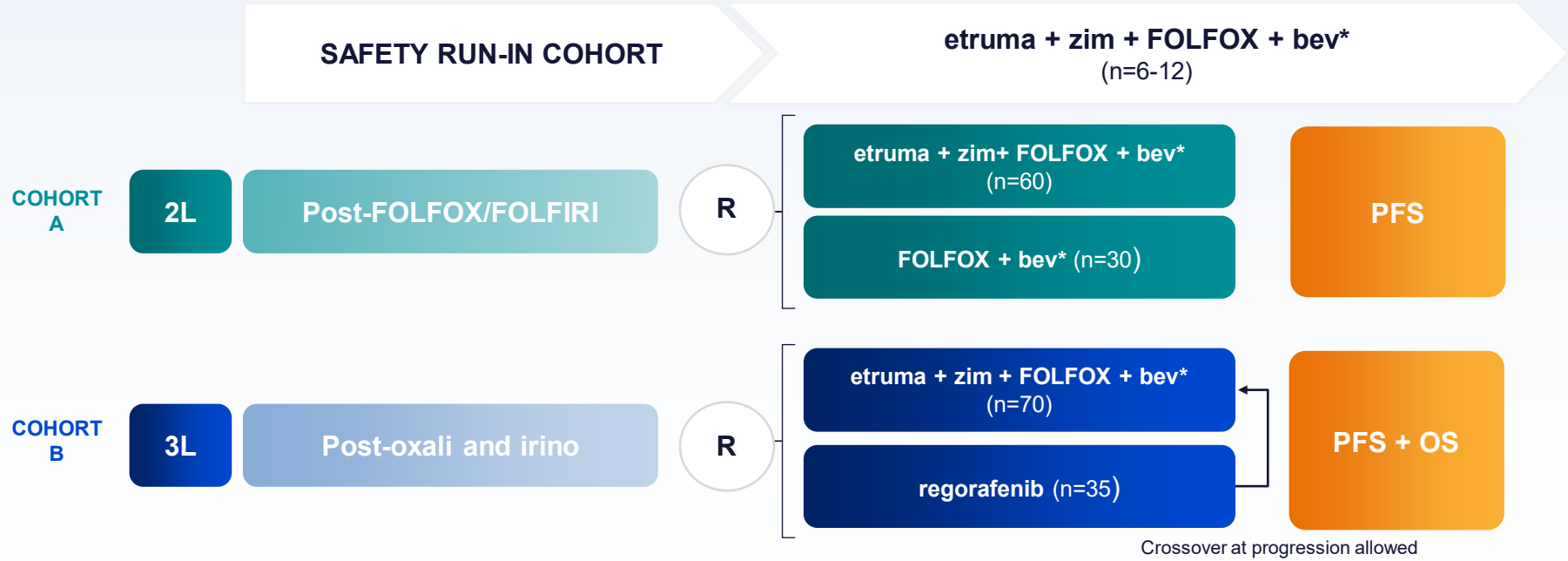
- Randomized Phase 2 study evaluating etruma + zim combined with docetaxel vs. docetaxel alone in 2L mCRPC (following treatment with a novel hormonal therapy)
- Data expected in-house by year-end; data presentation in 2023




mCRPC: metastatic castrate-resistant prostate cancer; 2L: second-line; ORR: overall response rate; PFS: progression-free survival

# Randomized Phase 2 Study to Evaluate etruma Combinations in 3L+ mCRC

- Randomized Phase 2 study evaluating etruma + zim + chemo combinations vs. SOC in 2L/3L mCRC
- Data expected in 1H 2023




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

Bevacizumab: bev; etrumadenant: **etruma;** irinotecan: irino; oxaliplatin: oxali; zimberelimab: zim:

# quemliclustat (quemli): A Unique, Highly Potent and Selective Small Molecule CD73 Inhibitor with Several Key Advantages

**HIGHLY POTENT**

- Target coverage achieved at doses as low as 25 mg every two weeks
- Extremely long (~4 days) half-life, enabling dosing every two weeks
- Oral formulation also in development

**POTENTIAL ADVANTAGES OVER CD73 ANTIBODIES**

- Extremely potent and selective against both tumor and soluble CD73
- Orders of magnitude more potent than CD73 antibodies
- Greater permeability of tumor tissue

**LIMITED ADDITIVE TOXICITY**

- High selectivity limits potential for "off-target" effects
- AE profile of quemli + gem/nab-pac appears similar to that of gem/nab-pac alone

**INCREASINGLY VALIDATED TARGET**

- COAST data supports potential of CD73 inhibition in Stage 3 NSCLC
- Rapidly growing number of CD73 antibodies in clinical development

-Manji, GA et al; ASCO GI 2021 (Abstract 404): ARC-8: Phase 1/1b Study to Evaluate Safety and Tolerability of AB680 + Chemotherapy + Zimberelimab (AB122) in Patients with Treatment-Naive Metastatic Pancreatic Adenocarcinoma

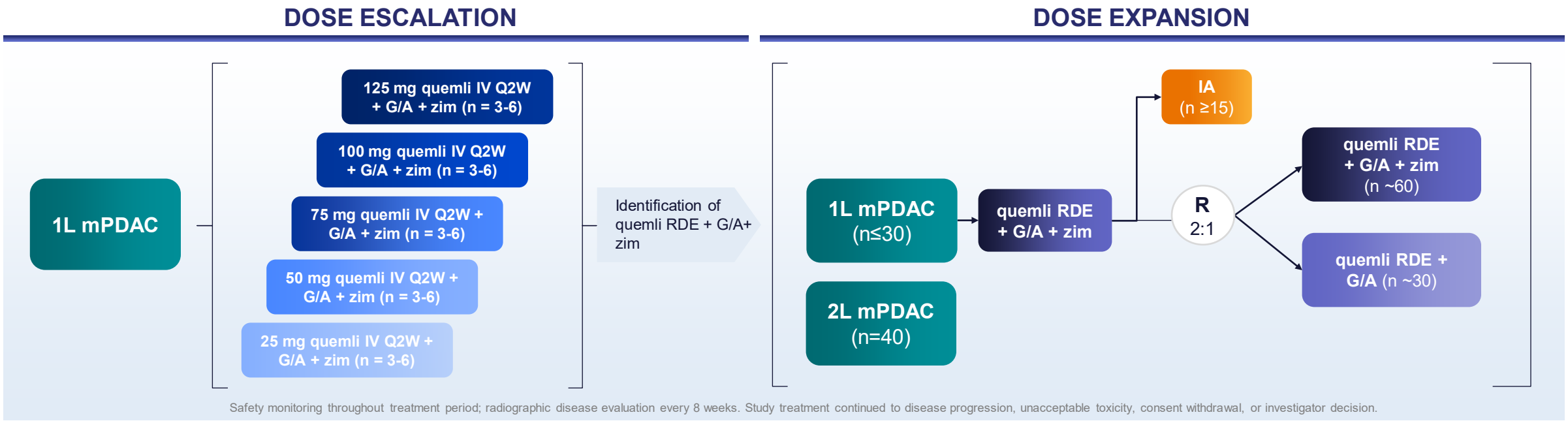
-Martinez-Marti, A et al; ESMO 2021 (LBA42): COAST: An open-label, randomised, phase II platform study of durvalumab alone or in combination with novel agents in patients with locally advanced, unresectable, stage III NSCLC





ARCUS BIOSCIENCES

# ARC-8 | A Phase 1/1b, Open-Label, Dose-Escalation and Dose-Expansion Study




Safety monitoring throughout treatment period; radiographic disease evaluation every 8 weeks. Study treatment continued to disease progression, unacceptable toxicity, consent withdrawal, or investigator decision.

## KEY ELIGIBILITY CRITERIA

- Histologically- or cytologically-confirmed mPDAC
- ≥1 measurable lesion per RECIST v1.1
- ECOG PS 0-1
- No prior treatment for M1 disease
- Prior (neo)adjuvant treatment for PDAC (chemotherapy G/A and/or radiotherapy) allowed if completed ≥6 months prior to enrollment

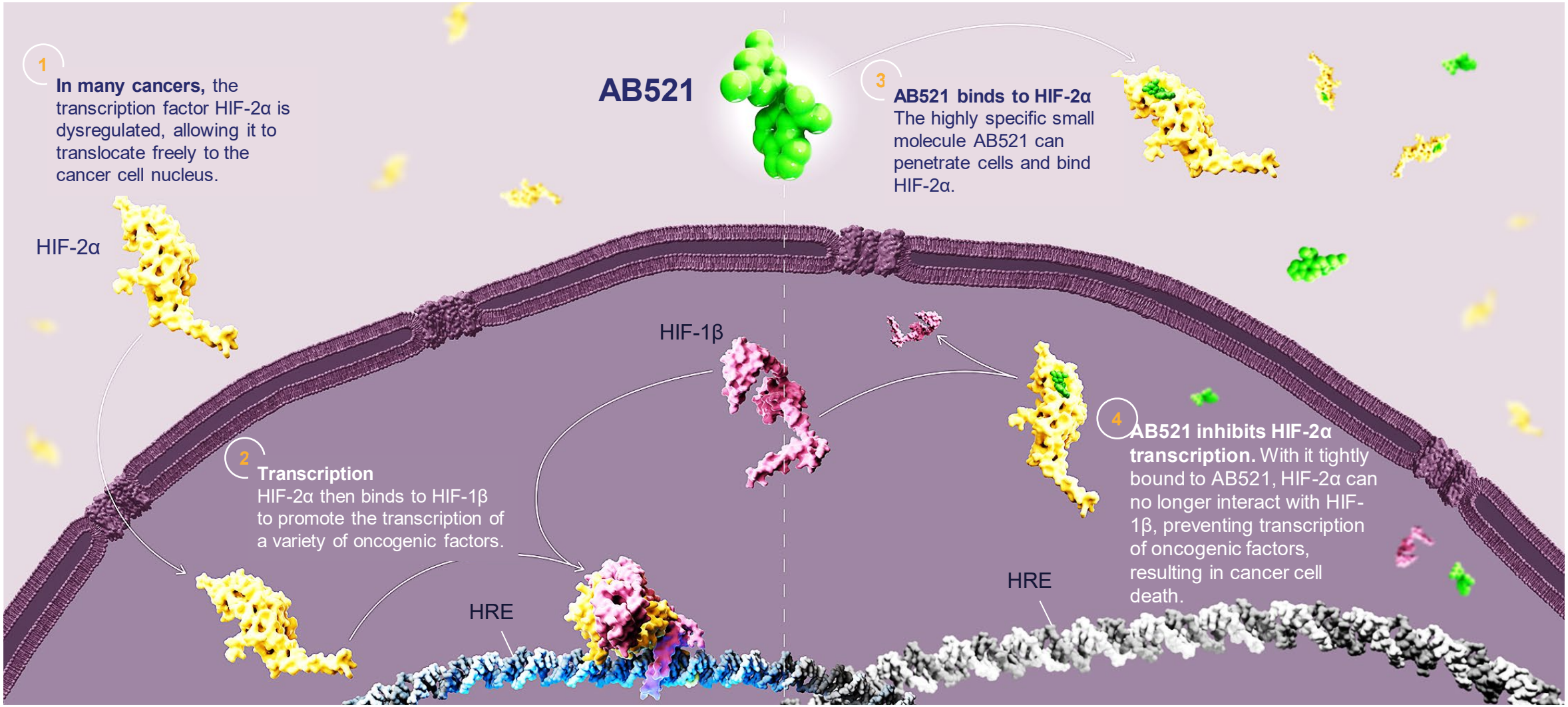
## STUDY OBJECTIVES

- **Primary:** Safety and tolerability
- **Secondary:** PK and clinical activity

1L, first-line; IV, intravenously; G/A, gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; Q2W, every 2 weeks; R, randomization; RDE, recommended dose for expansion; quemliclustat: quemli; zimberelimab:zim

# HIF-2α Program

# AB521 in the Tumor Cell Nucleus






HRE, Hypoxia Response Element.

# 2-Prong Value Proposition for an Arcus HIF-2α Inhibitor

## Opportunity to reach greater intra-tumoral HIF-2α inhibition compared to 120-mg dose of belzutifan

- Potentially without increased toxicity, which appears to be driven by peripheral effects that saturate at lower doses
- Requires a compound with greater potency and/or a better PK profile

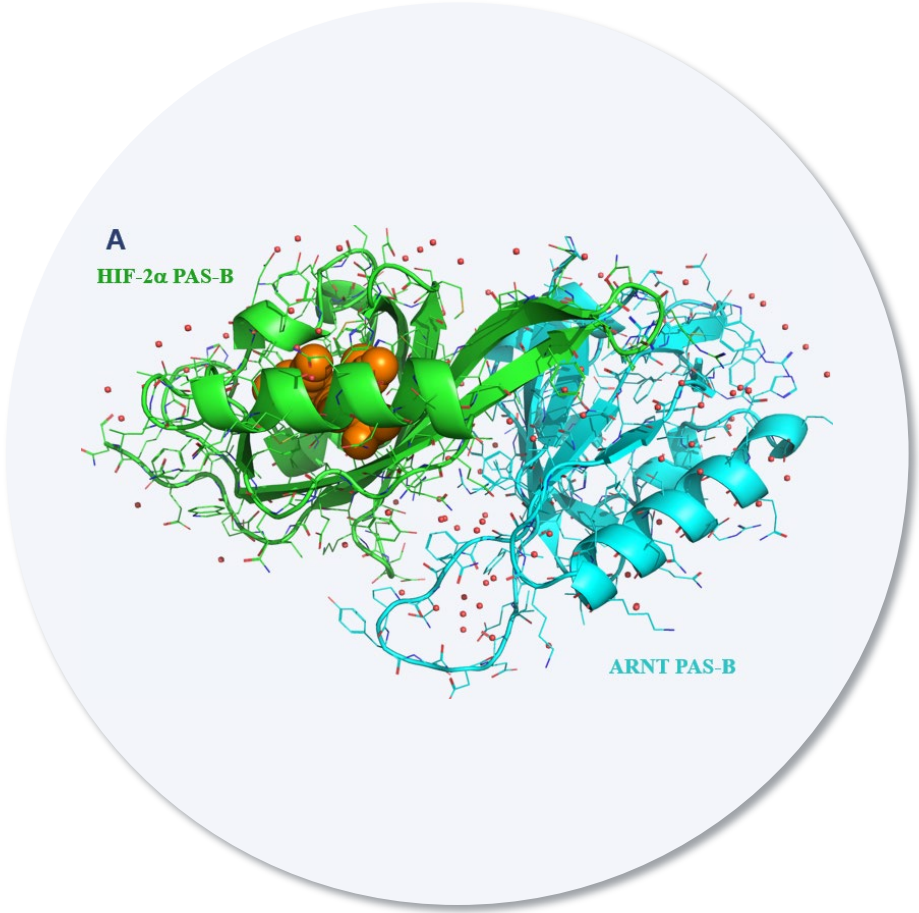
## Evaluation of unique combinations and/or unique tumor types

- Possible combinations with quemli/etruma, potentially in combination with SOC and other agents


Etrumadenant: etruma; quemliclustat: quemli

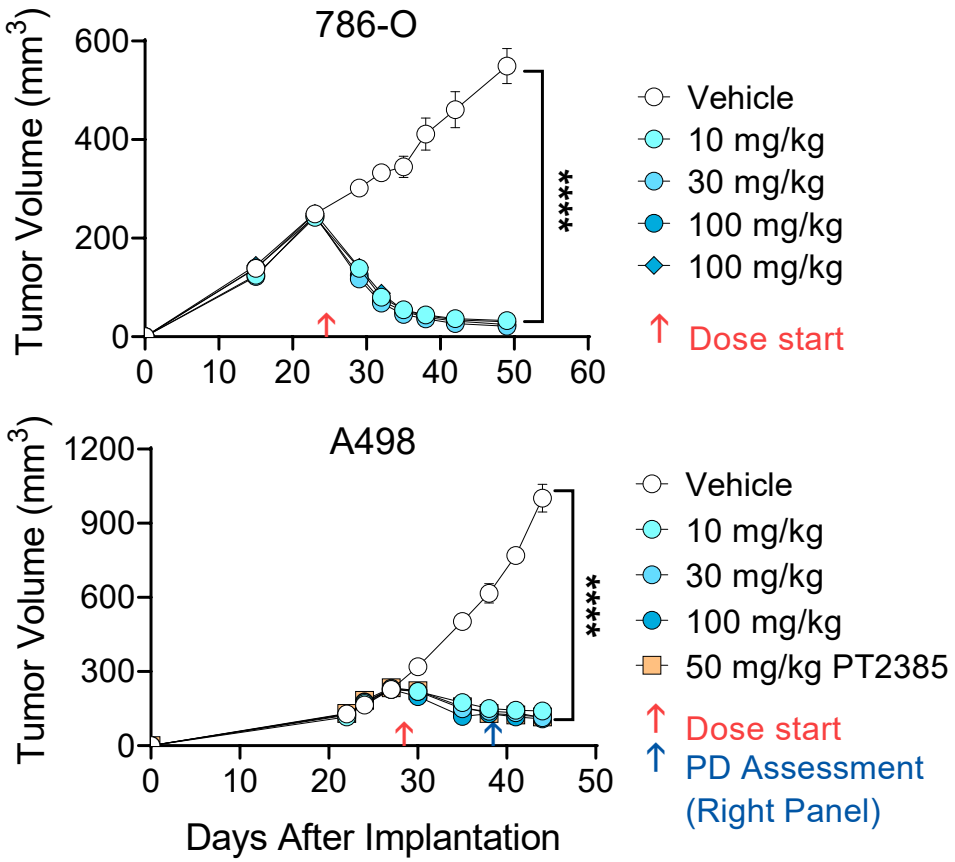
# Extensive Characterization Confirms Greater Potency of AB521 Relative to belzutifan (MK-6482)

| | ASSAY | AB521 | MK-6482[a] |
|---|---|---|---|
| CELLULAR | HIF-2α 786-O Luc Reporter $IC_{50}$ (nM) | 8.2 ± 2.5 (n=24) | 16.9 ± 10.1 (n=8) |
| | Control 786-O Luc Reporter $IC_{50}$ (nM) | > 10,000 (n=6) | > 10,000 (n=7) |
| | HIF-2α 786-O Luc Reporter $IC_{50}$ (nM) [in 100% Serum] | 46.5 ± 14.2 (n=24) | 61.8 ± 6.6 (n=4) |
| | 786-O VEGF AlphaLISA $IC_{50}$ (nM) | 28.9 ± 3.6 (n=11) | 47.7 ± 30.8 (n=4) |
| BIOCHEMICAL | HIF-2α $TSAT_m\Delta$ (°C) | 14.7 ± 0.6 (n=14) | 12.1 ± 0.3 (n=4) |
| | HIF-2α MST $K_D$ (nM) | 2.4 ± 0.8 (n=3) | 15.4 ± 2.7 (n=3) |
| | HIF-2α ITC $K_D$ (nM) | 53.6 ± 17.9 (n=3) | 53.8 ± 19.3 (n=3) |
| | HIF-2α SPA $IC_{50}$ (nM) | 16.6 ± 5.0 (n=8) | 22.3 ± 5.6 (n=5) |



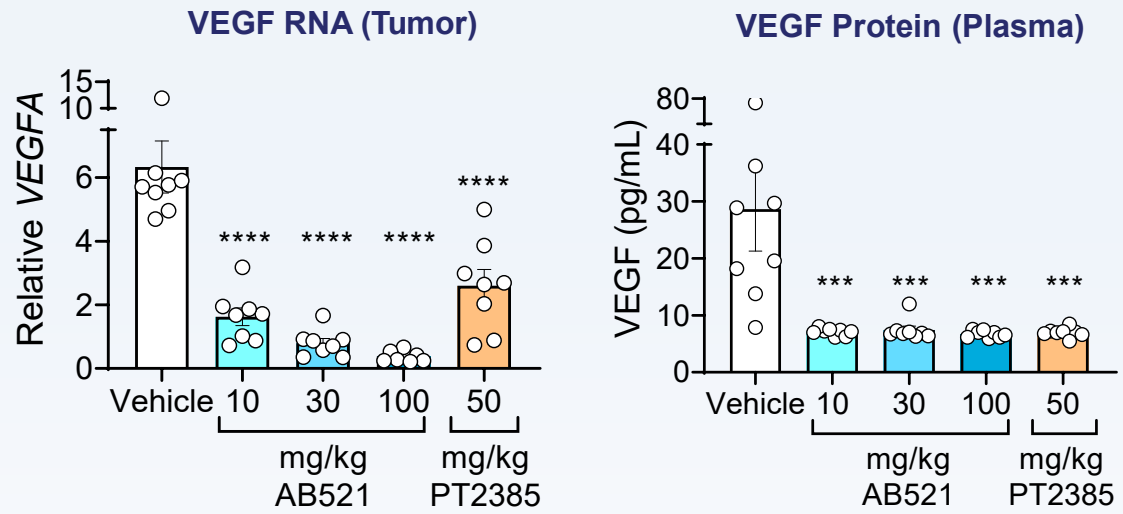

[a] MK-6482 was synthesized according to Xu *et al.* 2019 J Med Chem; DOI: 10.1021/acs.jmedchem.9b00719

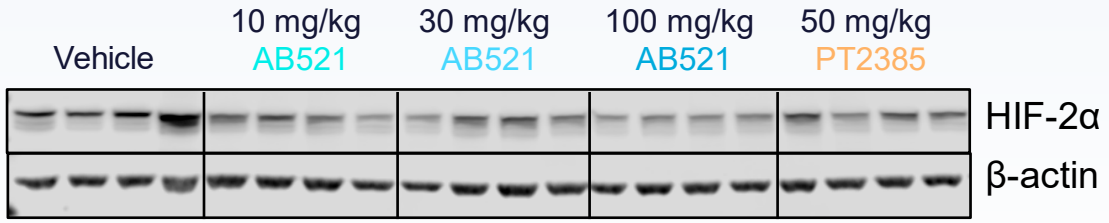
# AB521 Inhibits Tumor Growth and HIF-2α Activity in ccRCC Tumor-Bearing Mice




- **Circles**, Vehicle or AB521 given orally twice-daily; **Diamond**, AB521 given orally once-daily; **Square**, PT2385 (synthesized by Arcus using methodology published in Wehn *et al.* DOI: 10.1021/acs.jmedchem.8b01196) given orally once-daily
- Efficacy (n=10) and PD data representative of two independent experiments; Stats, ANOVA with multiple comparisons test for each group vs Vehicle

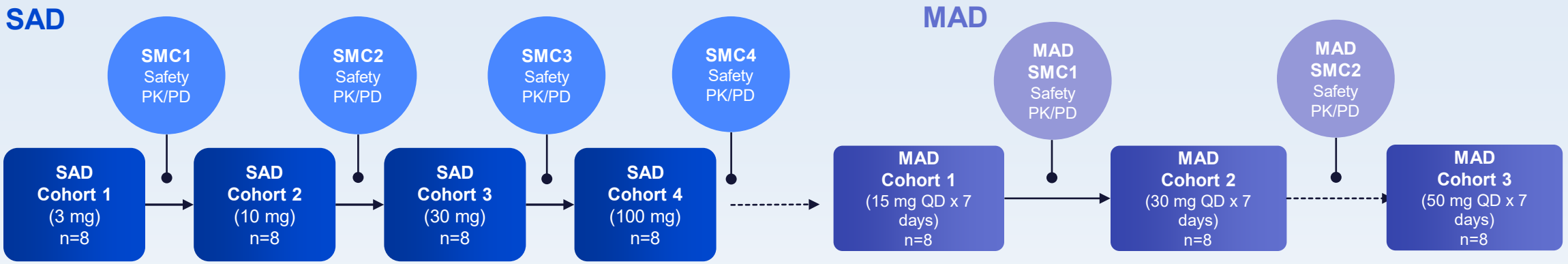
## 10 DAYS AFTER TREATMENT PD ASSESSMENT IN A498 MODEL




- **TOP:** each symbol represents an individual mouse
- **BOTTOM:** Western blot; Each lane contains tumor lysate from an individual mouse

# ARC-14 | Phase 1 Study of AB521 in Healthy Volunteers

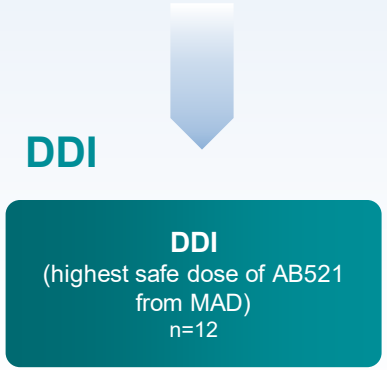



## SAD and MAD

- Cohorts of 8 subjects, randomized 3:1 AB521:placebo
- Evaluate safety and PK for single/multiple ascending doses of AB521
- PK/PD modeling based on exposure and changes in erythropoietin, Hgb levels

## DDI

- Single cohort of 12 subjects, no randomization
- Evaluate the impact of AB521 dosing on PK of midazolam



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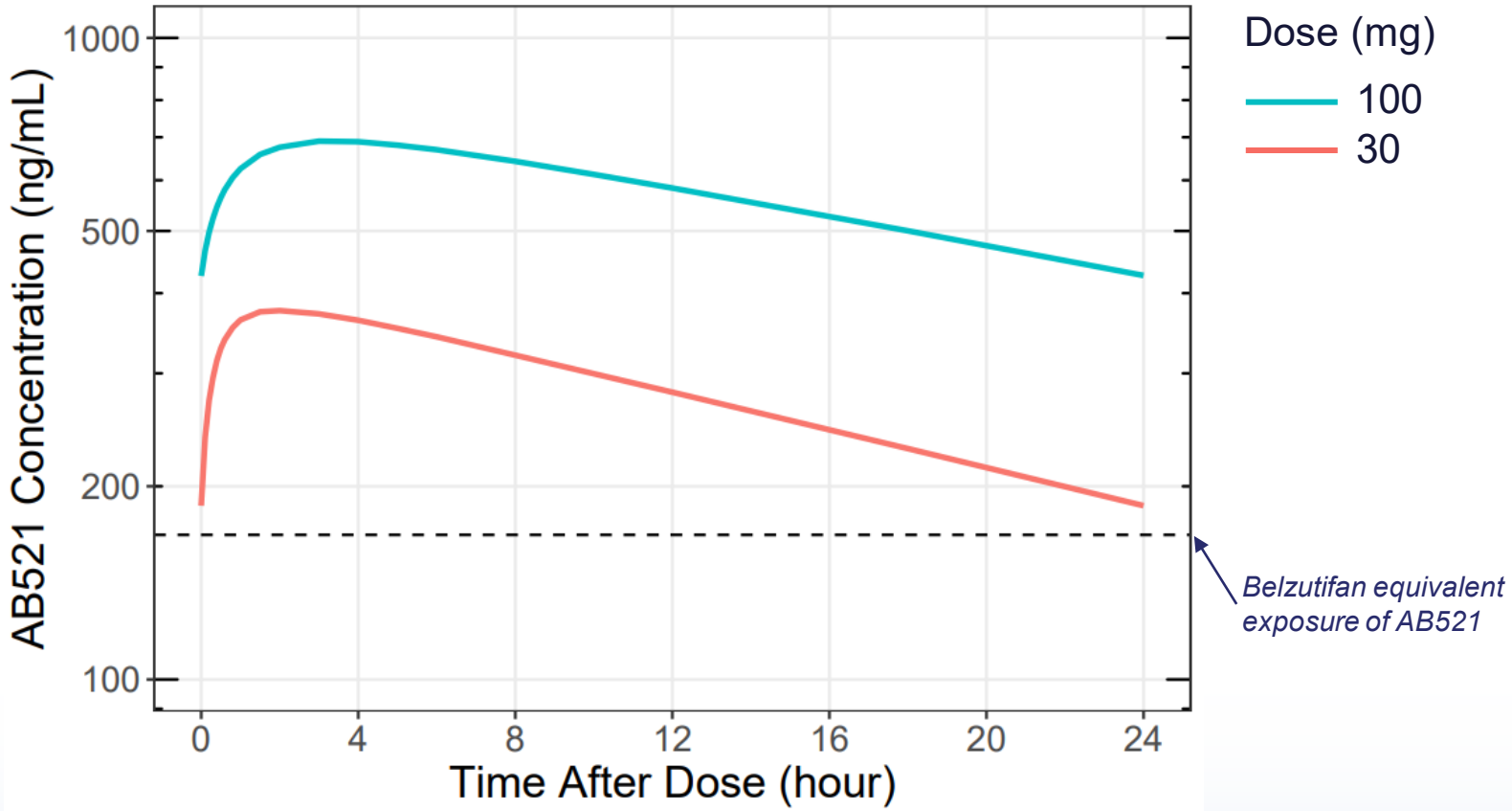
# Modeled Steady-State Exposure of AB521 Based on SAD (3, 10, 30 and 100 mg) and MAD (15 and 30 mg) Arms




AB521 doses ≥ 30 mg QD would yield potency-corrected concentrations that are similar to belzutifan 120 mg with lower peak-trough concentration ratios

# Phase 1 Study of AB521 in Advanced Solid Tumors and Clear Cell Renal Cell Carcinoma (ccRCC)

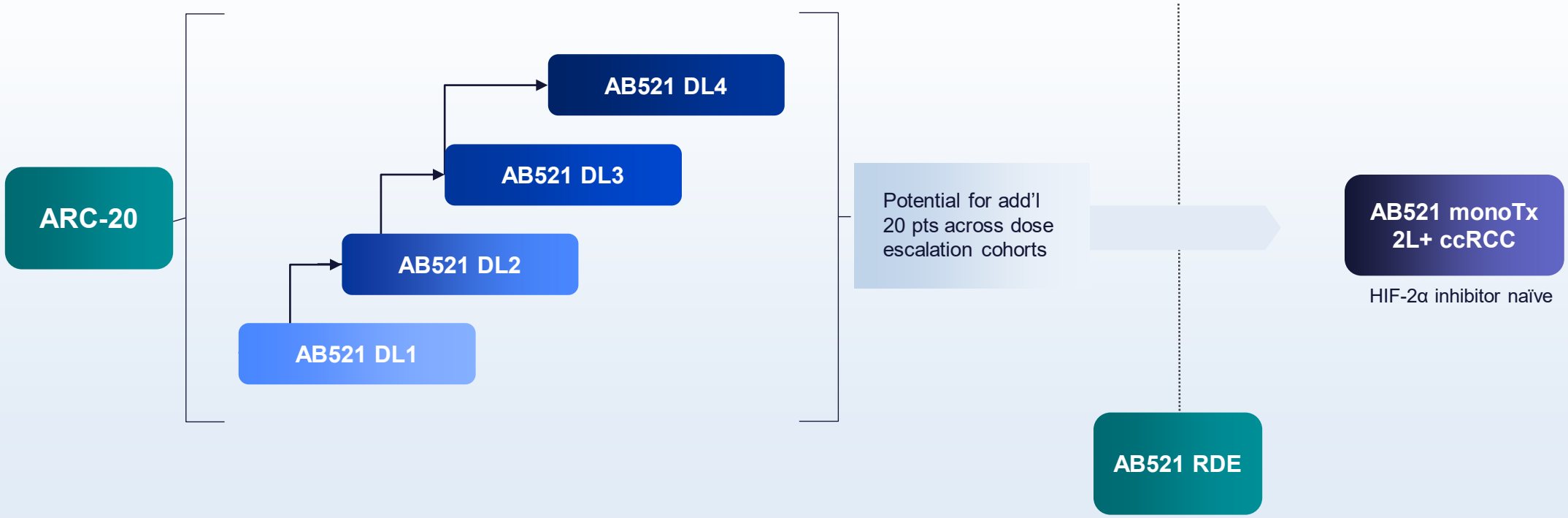
## PH 1 DOSE ESCALATION

3+3 design with 21-day DLT window

**Solid-tumor pts w/o SOC**

## PH 1B DOSE EXPANSION

(n=30/cohort)






DL: dose level; RDE: recommended dose for expansion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