# COMBINING TO CURE®

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

1Q23 EARNINGS | CORPORATE PRESENTATION

**May 2023**

ARCUS BIOSCIENCES

# 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; possible first to market advantage for any of our investigational products; anticipated marketing or packaging strategies 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.

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**All of Arcus's molecules are investigational and Arcus (and Gilead for all of the molecules in each optioned program) has not received approval from any regulatory authority for any use globally, nor established the safety and efficacy of these investigational molecules.**

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# Arcus Has Created a Late-stage Portfolio of Differentiated Assets, Fueled by a Highly Productive R&D Engine

## ~$1B

in cash, cash equivalents & marketable securities

**FUNDING INTO 2026**

## GLOBAL, LATE-STAGE COMPANY

6 clinical-stage molecules

## 4 PHASE 3 STUDIES IN LUNG (3) & UPPER GI (1)

ARC-10 · STAR-121 · PACIFIC-8 · STAR-221

## 2023 MILESTONES

**Dom (TIGIT)**

- ARC-7 ASCO oral presentation, all 150 pts
- ARC-21 initial ORR data 2H23

**AB521 (HIF-2α)**

- ARC-20 initial dose escalation data late 2023-early 2024
- Initiate Phase 2 kidney cancer study in 2H

**Quemli (CD73)**

- ARC-8 mature OS data 2H23

**Etruma (A2R)**

- ARC-6 data 2H23
- ARC-9 data 2H23

**AB598 (CD39)**

- Initiate Phase 1 2Q23

**AB801 (Axl)**

- Initiate Phase 1 2H23

## TOP TIER PARTNERS

GILEAD

AstraZeneca

TAIHO PHARMA

## PRODUCTIVE RESEARCH ORGANIZATION

1-2 new development candidates a year

**At least 2 new FIH expected in 2023:**

| | | |
|---|---|---|
| ✓ AB598 oncology | AB801 oncology | AB375 inflammation |

✓ = IND Cleared by FDA



FIH: first in human; GI: gastrointestinal

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# Arcus Has a Broad Portfolio of Investigational 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; enrolling new cohorts in lung and GI cancers

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

## DIFFERENTIATED ANTI-TIGIT + ANTI-PD-1 BACKBONE

**domvanalimab (AB154)**: Potential best in class anti-TIGIT monoclonal antibody (mAb; **Fc silent**) – multiple ongoing Phase 2 and 3 studies enrolling

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

## NEXT-GENERATION PROGRAMS

**AB598:** Anti-CD39 mAb (oncology)

**AB801:** small molecule Axl inhibitor (oncology)

**AB375:** Small molecule KIT inhibitor (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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# ARC-7 Key Highlights from ASCO Plenary Dec. 2022 – Updated Data to be Presented at ASCO, June 3, 2023

## SELECT PFS TAKEAWAYS:

- **Interim mPFS 12.0 months for the doublet (DZ) and 10.9 months for triplet (EDZ)** vs. 5.4 months for zim mono (median follow-up: 12 months)
- **Doublet PFS HR=0.55; triplet HR=0.65**
- DZ PFS curve showed early and sustained separation from zim monotherapy

## PRIMARY PROGRESSIVE DISEASE TAKEAWAYS:

- Dom-containing arms resulted in reduction of early primary progressive disease (patients who progress at first scan)
- 5% and 13% for the doublet and triplet, respectively, vs. 25% for zim mono
- Demonstrates potential for an anti-TIGIT + anti-PD-1 combo to displace the use of anti-PD-1 in patients with aggressive disease

## SUMMARY:

- Largest and first prospective randomized dataset to date for an anti-TIGIT combination in 1L PD-L1-high NSCLC
- Both dom-containing arms demonstrated clinically meaningful differentiation compared to zim monotherapy across all efficacy measures evaluated
- No unexpected safety signals were observed in both dom-containing arms
- Low rates of immune-related adverse events and infusion-related reactions observed; potential differentiator for domvanalimab

Analysis reflects data as of August 31, 2022 - the data cut-off used for the December 2022 ASCO Plenary Session.

dom: domvanalimab; zim: zimberelimab; doublet: dom + zim; triplet: dom + zim + etrumadenant; cORR: confirmed overall response rate; mPFS: median progression-free survival



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# Four Phase 3 Studies Initiated in Lung and GI Cancers

| | PHASE 1/1b | PHASE 2 | PHASE 3 |
|---|---|---|---|
| **DOMVANALIMAB (DOM) (Fc-silent anti-TIGIT)** | | **1L / 2L Upper GI Malignancies (EDGE-Gastric)**<br>**dom +/- zim +/- quemli** +/- 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>**dom** + **zim** +/- **etruma** vs **zim** | **1L Upper GI Malignancies (STAR-221)**<br>**dom** + **zim** + chemo vs. nivo + chemo |
| **QUEMLICLUSTAT (QUEMLI) (CD73)** | | **1L, 2L Pancreatic Cancer (ARC-8)**<br>**quemli** + **zim** + gem/nab-pac vs. **quemli** + gem/nab-pac | |
| **ETRUMADENANT (ETRUMA) (A2a/A2b)** | | **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 (HIF-2a)** | **2L+, inc. ccRCC (ARC-20)**<br>**AB521 monotherapy** | | |

★ PACIFIC-8 is being operationalized by AstraZeneca. STAR-121 and Velocity-Lung are being 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

NSCLC · Advanced Malignancies · PDAC · CRPC · CRC · Healthy Participants · GI



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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 in Arcus
- Opted in to 5 of 6 of Arcus's clinical-stage molecules
- Gilead equally shares co-development costs for the global joint development program
- Gilead has option rights to 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**
  - Eligible for milestones, expected in late 2023
- Tiered royalties from high-single digit to mid-teens on net sales
- Option rights exercised for majority of Arcus's clinical portfolio — dom, zim, etruma 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
- Financial terms enable efficient utilization of capital

**~$1B IN CASH AND INVESTMENTS AS OF 3/31/2023 AND FUNDING INTO 2026**


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# Multiple Readouts Expected in 2023

| | COMBINATION / ARMS | SETTING | ANTICIPATED MILESTONE |
|---|---|---|---|
| ARC-6 | **etruma** + **zim** + SOC *vs.* SOC | Randomized Phase 2 in mCRPC | • **Data expected in 2H23** |
| ARC-7 | **dom** + **zim** + *vs.* **zim** *vs.* **etruma** + **dom** + **zim** | Randomized Phase 2 in 1L mNSCLC (PD-L1 ≥ 50%) | • **ASCO presentation on all 150 patients** |
| ARC-8 | **quemli** + **zim** + gem/nab-pac | Phase 1/1b in 1L mPDAC | • **Mature OS data expected 2H23** |
| ARC-9 | **etruma** + **zim** + FOLFOX *vs.* SOC | Randomized Phase 2 in 2L/3L+ mCRC | • **Data expected in 2H23** |
| ARC-20 | **AB521** (HIF-2α) | Phase 1/1b in cancer patients | • **Initial dose escalation data late 2023 / early 2024** |
| ARC-21 | **dom** + **zim** + FOLFOX | Phase 2 in 1L/2L upper GI cancers | • **Initial ORR data 2H23** |

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; ORR: objective response rate; OS: overall survival; GI: gastrointestinal


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# ARC-7 Results and Domvanalimab Clinical Program

Data presented at ASCO Monthly Plenary Series Dec. 20, 2022, based on data cut off of Aug. 31, 2022

Updated data will be presented at ASCO Annual Meeting June 3, 2023



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# ARC-7 Evaluates dom, zim and etruma in 1L, PD-L1-High NSCLC

## DOMVANALIMAB (FC-SILENT TIGIT)

- **Most clinically advanced Fc-silent TIGIT antibody in development**
- Blocks TIGIT on T-cells to prevent binding of CD155; **does NOT deplete TIGIT-bearing immune cells**
  - **Depletion of TIGIT-bearing T-REGs can result in immune-related AEs**
- **Low incidence of ADAs** (which can impact clinical efficacy)

## ZIMBERELIMAB (PD-1 ANTIBODY)

- Discovered by WuXi using Ligand's OmniAb discovery platform
- In *in vitro* studies, binds to PD-1 with similar affinity to pembrolizumab
- **6th PD-1 antibody approved in China** (Gloria Bio has commercial rights in China)

## ETRUMADENANT ($A_2R$ ANTAGONIST)

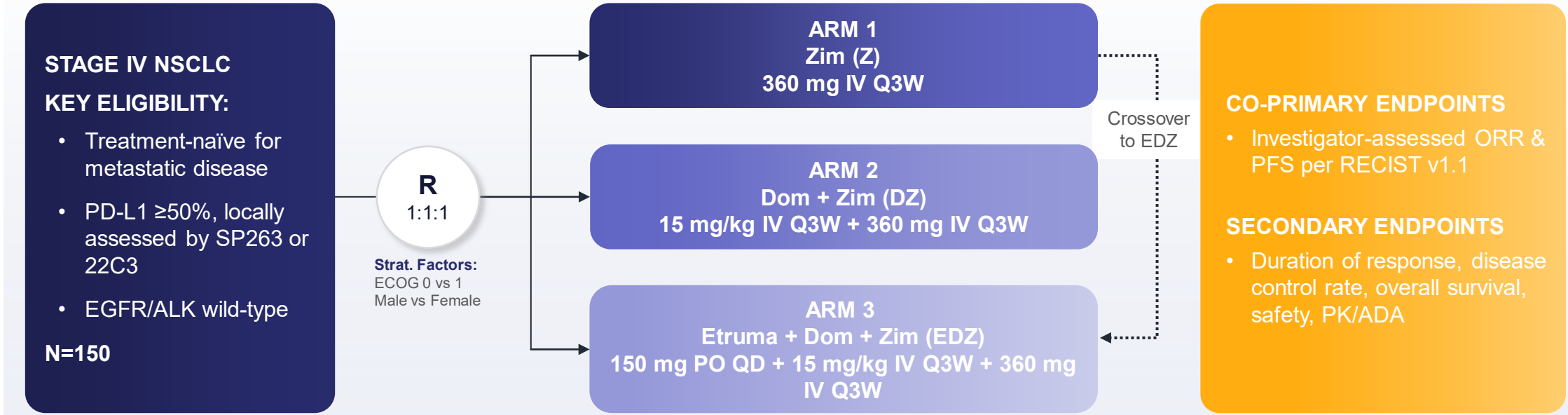
- **First A2R antagonist to enter clinical development specifically designed for oncology**
- Blocks both $A_{2a}R$ and $A_{2b}R$ receptors
- Multiple advantages over other $A_{2a}R$ antagonists in clinical development:
  - Minimal shift in potency
  - Excellent penetration of tumor tissue
  - Excellent drug properties, e.g. Pharmacokinetics/ pharmacodynamics

ADA: anti-drug antibody, dom: domvanalimab, etruma: etrumadenant, NSCLC: non-small cell lung cancer; zim: zimberelimab



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# ARC-7: Randomized, Open-label, Ph2 Study in First-Line, Metastatic, PD-L1-High NSCLC




Participants randomized to Arm 1 have the option to crossover to EDZ upon radiographically confirmed disease progression (PD)

- As of the clinical cut-off date (31 August 2022), a total of 150 patients were randomized, with a median follow-up of 11.8 months (range: 0.03 – 23.5)

ADA: anti-drug antibody, Dom: domvanalimab, Etruma: etrumadenant, NSCLC: non-small cell lung cancer; ORR: overall response rate, PFS: progression-free survival, PK: pharmacokinetics; R: randomized; Zim: zimberelimab



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# Study Population for ARC-7 and IA4 Provide Confidence as a Surrogate for Phase 3 Population

| POPULATION, n (%) | ARM 1 (Z) | ARM 2 (DZ) | ARM 3 (EDZ) | TOTAL |
|---|---|---|---|---|
| **Intent-to-treat (ITT)** | **50** | **50*** | **50** | **150** |
| **Safety-Evaluable** | 50 (100) | 49 (98) | 50 (100) | 149 (99) |
| **ITT-13** | 44 (88) | 44 (88)* | 45 (90) | 133 (89) |
| **Ongoing first-line treatment** | 14 (28) | 25 (50) | 24 (48) | 63 (42) |

***Includes one patient who was discontinued before dosing, due to being deemed ineligible for the study after randomization**
**ITT:** all participants who are randomized and assigned investigational product; data cut-off of August 31, 2022
**Safety-evaluable:** all participants who are treated with at least one dose of any study drug
**ITT-13:** all participants randomized at least 13 weeks prior to data cut-off (potential for at least two post-baseline scans)

- Enrolled from May 2020 – Aug 2022, **in 7 countries in APAC (61%) and N. America (39%), primarily in non-academic centers**
- Efficacy for all IAs has been analyzed in ITT-13, which includes participants randomized at least 13 weeks prior to data cut-off, allowing for the opportunity of ≥2 post-baseline scans for potential response confirmation
  - **ITT-13 population includes both efficacy-evaluable patients and any non-evaluable** patients who discontinued prior to first scan for any reason
- At the time of the data cut-off for IA4, **approx. half of patients in dom-containing arms remain on study treatment compared to only 28% of patients with zim mono**


Johnson et al. ASCO Plenary Series, Dec. 2022
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# Baseline Characteristics Were Relatively Well-Balanced with a Few Factors *Slightly* Favoring the zim Arm Over the Other Arms

| ITT, n (%) | | ARM 1 (Z) (N=50) | ARM 2 (DZ) (N=50) | ARM 3 (EDZ) (N=50) |
|---|---|---|---|---|
| **Median Age, years (range)** | | 66 (43, 84) | 69 (45, 92) | 69 (49, 83) |
| **≥ 65 years** | | 28 (56) | 34 (68) | 35 (70) |
| **Sex*: Male** | | 34 (68) | 33 (66) | 34 (68) |
| **Race** | Asian | 25 (50) | 23 (46) | 27 (54) |
| | White | 20 (40) | 24 (48) | 21 (42) |
| **Never Smokers** | | 7 (14) | 5 (10) | 5 (10) |
| **ECOG Status: 1** | | 37 (74) | 35 (70) | 35 (70) |
| **Squamous cell carcinoma** | | 9 (18) | 16 (32) | 16 (32) |
| **Brain mets at baseline** | | 7 (14) | 7 (14) | 8 (16) |
| **Liver mets at baseline** | | 9 (18) | 11 (22) | 4 (8) |
| **Local PD-L1 scoring, %TPS median (range)** | | 80 (50, 100) | 70 (50, 100) | 78 (50, 100) |
| **PD-L1: ≥ 75%** | | 30 (60) | 23 (46) | 29 (58) |

- **A few factors favored the zim mono arm over the dom-containing arms:** younger age and lower percentage of patients with squamous histology

Johnson et al. ASCO Plenary Series, Dec. 2022
dom: domvanalimab; mets: metastasis; zim: zimberelimab



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# Confirmed Objective Response Rate (cORR): RECIST v1.1 – ITT-13

| ITT-13, n (%) | ARM 1 (Z) (N=44) | ARM 2 (DZ) (N=44) | ARM 3 (EDZ) (N=45) |
|---|---|---|---|
| **ORR, Confirmed** [95% CI] | **12 (27)** [15.0, 42.8] | **18 (41)** [26.3, 56.8] | **18 (40)** [25.7, 55.7] |
| Complete Response (CR) | 0 (0) | 0 (0) | 0 (0) |
| Partial Response (PR) | 12 (27) | 18 (41) | 18 (40) |
| Stable Disease (SD) | 14 (32) | 15 (34) | 16 (36) |
| Progressive Disease (PD) | **11 (25)** | **2 (5)** | **6 (13)** |
| Not evaluable | 7 (16) | 9 (21) | 5 (11) |

CI: Confidence Interval; ORR: Objective Response Rate

- **Improved response rate was seen in dom-containing arms across multiple subgroup analyses, including PD-L1 status, tobacco history, disease histology, race, etc. (data not shown)**
- **30% of responders in dom-containing arms did not respond until the third scan or later**
- Subjects ongoing treatment with stable disease have potential to contribute to ORR with further data maturity; as of the data cutoff date, there were 2, 6 and 2 patients in Arm 1, Arm 2 and Arm 3, respectively, ongoing treatment with stable disease – every new or confirmed response increases the ORR by approx. 2.3%

Johnson et al. ASCO Plenary Series, Dec. 2022
dom: domvanalimab


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# Best Overall Response by RECIST v1.1 Showed High ORRs for All Treatment Arms – ITT-13

| | RESPONSE PER RECIST V1.1 | | |
|---|---|---|---|
| **ITT-13, n (%)** | **ARM 1 (Z) (N=44)** | **ARM 2 (D+Z) (N=44)*** | **ARM 3 (E+D+Z) (N=45)** |
| **ORR, (95% CI)** | **15 (34)** (20.5, 49.9) | **19 (43)** (28.3, 59.0) | **22 (49)** (33.7, 64.2) |
| Confirmed ORR (95% CI) | **12 (27)** (15.0, 42.8) | **18 (41)** (26.3, 56.8) | **18 (40)** (25.7, 55.7) |
| Pending confirmation | 0 | 0 | 3 (7) |
| Cannot be confirmed | 3 (7) | 1 (2) | 1 (2) |

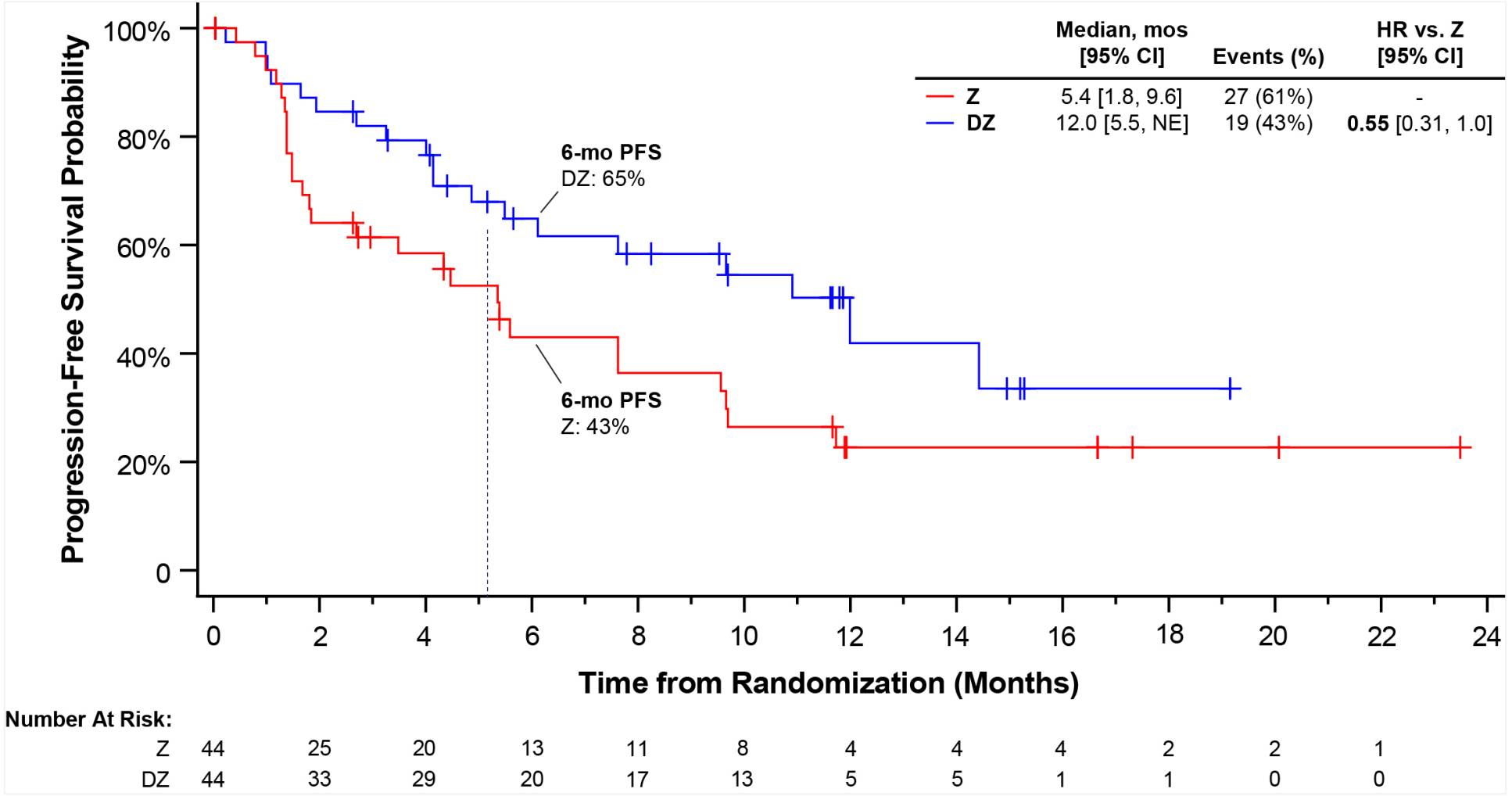
**Pending confirmation**: subject ongoing study with potential to have confirmed response.
**Cannot be confirmed**: subject discontinued study without potential to have confirmatory scan.
* Includes subject randomized improperly; not treated.

- Primary reasons for lack of confirmatory scan were adverse event leading to withdrawal/death or progressive disease (one patient in each arm did not confirm due to progressive disease)

Johnson et al. ASCO Plenary Series, Dec. 2022
AE: adverse event; CI: confidence interval; ITT: intent to treat; ORR: overall response rate; PD: progressive disease; PR: partial response


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# Kaplan Meier Curves for PFS (ITT-13) Showed Early and Sustained Separation for the Doublet



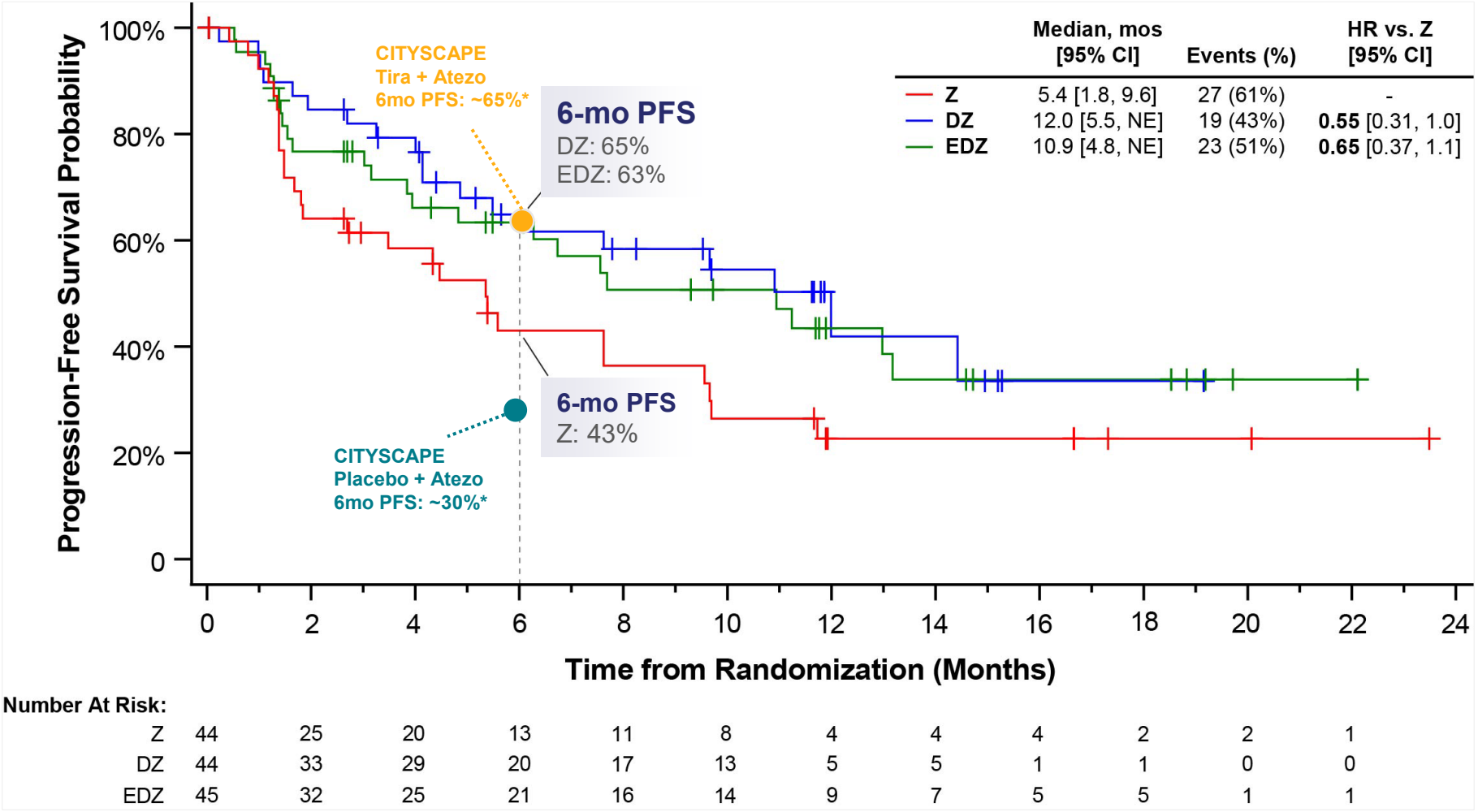

Note: Median follow-up of 12 months

Johnson et al. ASCO Plenary Series, Dec. 2022
D/Dom: domvanaimab; E: etrumadenant; ITT: intent to treat; mo: month; PFS: progression free survival; Z: zimberelimab



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# Kaplan Meier Curves for PFS (ITT-13) Were Similar for Both dom-Containing Arms




**Number At Risk:**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Z | 44 | 25 | 20 | 13 | 11 | 8 | 4 | 4 | 4 | 2 | 2 | 1 |
| DZ | 44 | 33 | 29 | 20 | 17 | 13 | 5 | 5 | 1 | 1 | 0 | 0 |
| EDZ | 45 | 32 | 25 | 21 | 16 | 14 | 9 | 7 | 5 | 5 | 1 | 1 |

Median follow-up of 12 months; Mos: Months; HR: Hazard Ratio; CI: Confidence Interval; *Cho et al. *Lancet* 2022

Johnson et al. ASCO Plenary Series, Dec. 2022
atezo: atezolizumab; D/dom: domvanaimab; E: etrumadenant; ITT: intent to treat; mo: month; PFS: progression free survival; tira: tiragolumab' Z: zimberelimab



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# Median PFS for dom-containing Arms Exceeds Pembro Mono and Pembro/Chemo Combo Phase 3 Results in PD-L1>50 Patients

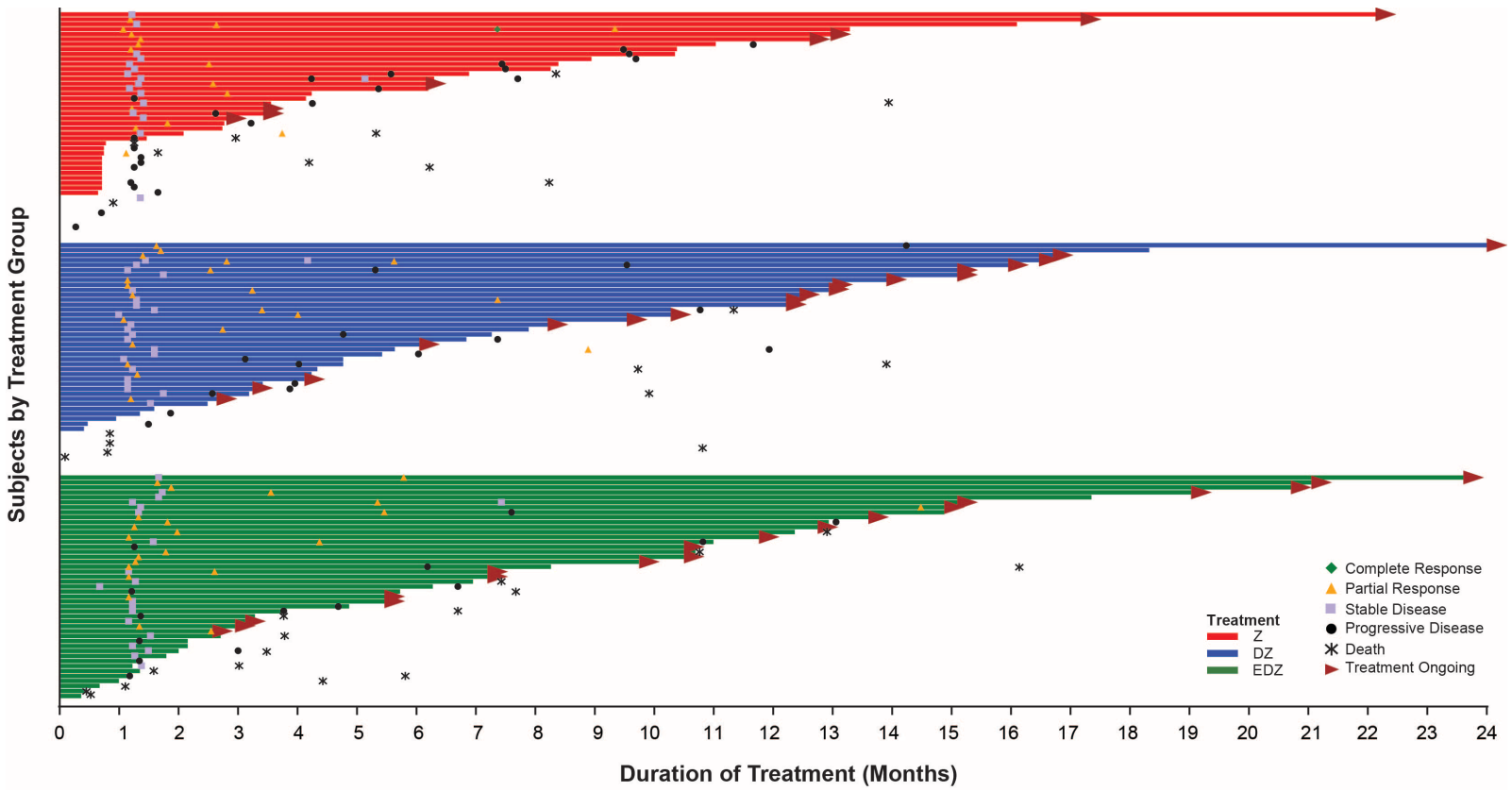
- Earlier PD-1 monotherapy studies likely benefited from 1) long turnaround times for central testing (may have limited rapidly progressing patients) and 2) chemo comparator arm resulting in enrollment of a “fitter” patient population
- Keynote studies conducted scans every 9 weeks which could have benefitted PFS

| STUDY | REGIMEN | MEDIAN PFS (MONTHS) | ENROLLMENT PERIOD |
|---|---|---|---|
| **ARC-7[1]** | | | |
| TIGIT + PD-1 | **Dom + Zim** | **12.0 (doublet), 10.9 (triplet)** | **March 2020 – August 2022** |
| **PD-1 Combination Studies:** | | | |
| RWD – Waterhouse et al[2] | Pembro + chemo | 7.8 (non-squams), 6.5 (squams) | January 2011 – March 2022 |
| Keynote-407[3] | Pembro + chemo | 8.0 | August 2016 – December 2017 |
| Keynote-189[4] | Pembro + chemo | 9.0 (10 mos follow-up)<br>11.1 (23.1 mos follow-up) | February 2016 – March 2017 |
| **PD-1 Monotherapy Studies:** | | | |
| RWD – Waterhouse et al[2] | Pembro | 5.4 (non-squams), 4.9 (squams) | January 2011 – March 2022 |
| RWD – Peters et al[5] | Pembro | 5.8 (ECOG 0-1) | November 2016 – May 2021 |
| Keynote-042[6] | Pembro (vs. chemo) | 6.5 | December 2014 – March 2017 |
| Keynote-024[7] | Pembro (vs. chemo) | 10.3 (11.2 mos follow-up)<br>7.7 (5 year follow-up) | September 2014 – October 2015 |

(1) Johnson et al. ASCO Plenary Series, Dec. 2022
(2) “Real-world overall and progression-free survival for first-line immunotherapy-based regimens in metastatic non-small cell lung cancer”; ESMO IO 2022; n=11,445 patients sourced from Flatiron database; included ECOG 2-3
(3) "A Randomized, Placebo-Controlled Trial of Pembrolizumab Plus Chemotherapy in Patients With Metastatic Squamous NSCLC: Protocol-Specified Final Analysis of KEYNOTE-407" Paz-Ares et al, J Thoracic Oncol 2020
(4) "Pemetrexed plus platinum with or without pembrolizumab in patients with previously untreated metastatic nonsquamous NSCLC: protocol-specified final analysis from KEYNOTE-189" Rodriguez-Abreu et al. Ann Oncol 2021
(5) “Outcomes of patients with metastatic non-small-cell-lung cancer receiving first-line immunotherapy with or without chemotherapy; real world evidence versus clinical trial results (CORRELATE); ESMO IO 2022; sourced from Flatiron database.
(6) "Five-Year Outcomes With Pembrolizumab Versus Chemotherapy as First-Line Therapy in Patients With Non-Small-Cell Lung Cancer and Programmed Death Ligand-1 Tumor Proportion Score ≥ 1% in the KEYNOTE-042 Study" de Castro Jr et al. J Clin Oncol 2022.
(7) "Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer" Reck et al. N Engl J Med 2015. “Five-Year Outcomes With Pembrolizumab Versus Chemotherapy for Metastatic Non–Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ‡ 50%” Reck et al. J Clin Oncol 2021
dom: domvanalimab; mos: months; pembro: pembrolizumab; PFS: progression free survival; zim: zimberelimab


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# Swim Lanes Demonstrated Highly Durable Responses Observed in the Doublet and Triplet Arms – ITT-13 Population



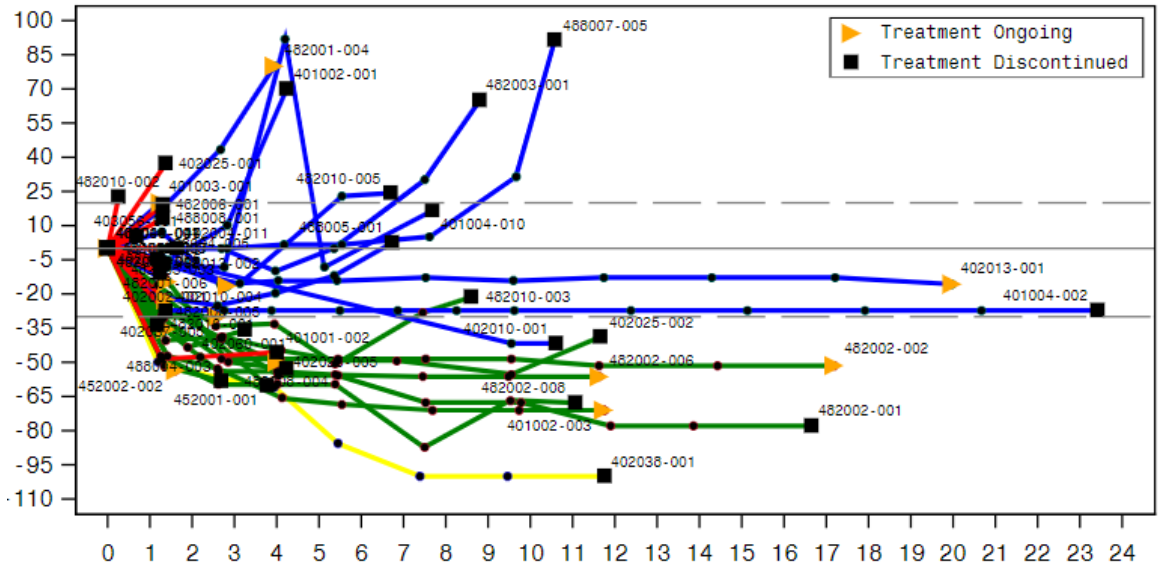

- At the DCO, 31 patients with PRs remain on treatment:
  - **With PRs: Arm 1 (n=5), Arm 2 (n=13), Arm 3 (n=13)**
  - **With SD: Arm 1 (n=3), Arm 2 (n=6), Arm 3 (n=5)**
- Time to initial response ranged from 1.2 – 14.6 months across all arms
- **Median duration of response was not yet reached in any arm** (range in months: 1.3+, 17.8+)

Johnson et al. ASCO Plenary Series, Dec. 2022
DCO: data cut off; ITT: intent to treat; PRs: partial responses; SD: stable disease

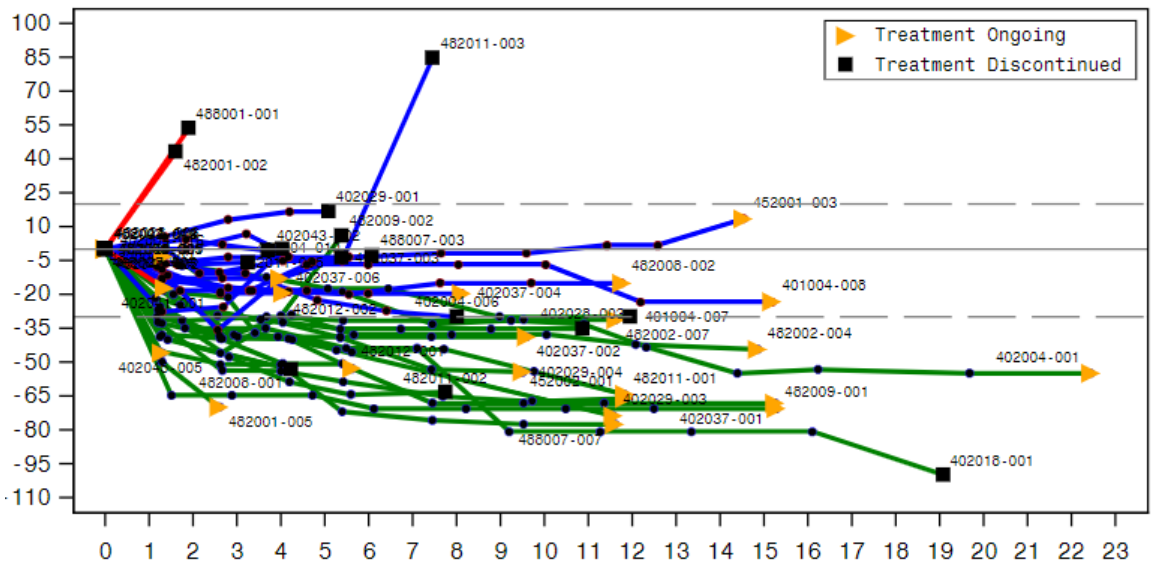

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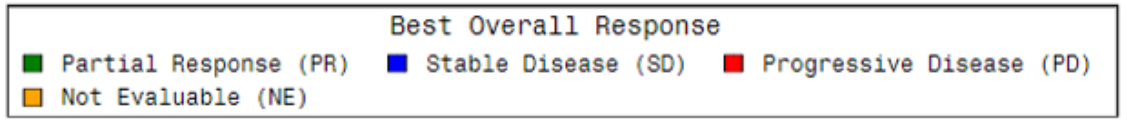
# Fewer Rapid Progressors and More Durable Responses are Observed with the Doublet

## ZIM MONOTHERAPY




## DOM + ZIM



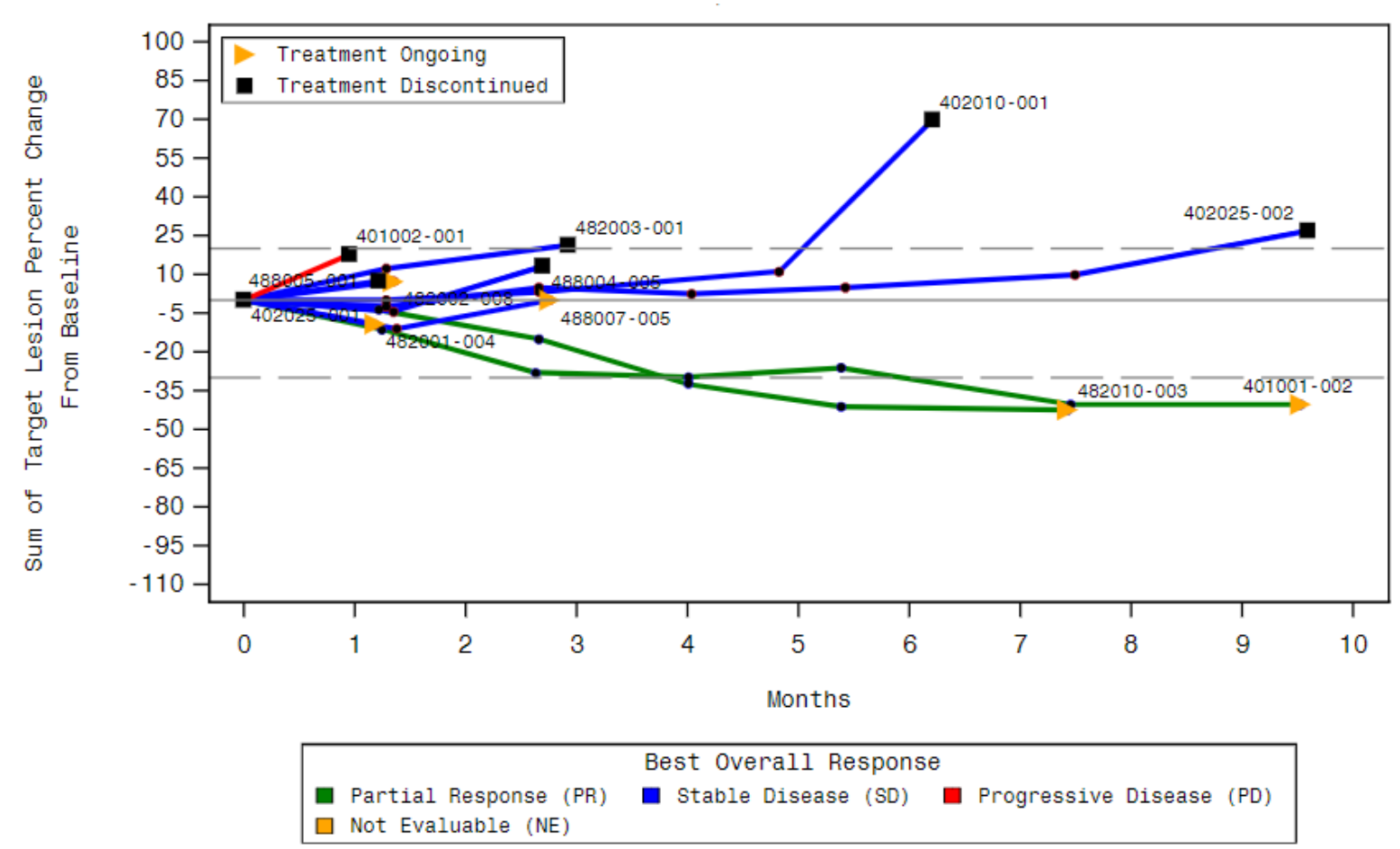

CCOD: 31Aug22, Snapshot: 14Oct22



dom: domvanalimab; zim: zimberelimab

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# Intriguing Responses Observed in Patients Crossing over from zim Mono to the Triplet Arm




- **To cross-over from zim mono to the triplet arm, <u>patients required documented progression on 2 consecutive scans</u>**
- **Three subjects ongoing crossover treatment beyond 6 months:** stable disease, partial response (after progressive disease on zim mono due to new lesion), partial response (after progressive disease on zim mono due to increase in SLD + new lesion)

**CCOD: 31Aug22, Snapshot: 14Oct22**

SLD: sum of the longest diameter; zim: zimberelimab



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# Overall Safety Profile

| SAFETY EVALUABLE POPULATION, n (%) | ARM 1 (Z) (N=50) | ARM 2 (DZ) (N=49) | ARM 3 (EDZ) (N=50) |
|---|---|---|---|
| **Any TEAEs** | 50 (100) | 47 (96) | 48 (96) |
| **Grade ≥3 TEAE** | 29 (58) | 23 (47) | 26 (52) |
| **Grade 5, Related to Study Treatment*** | 1 (2) | 1 (2) | 2 (4) |
| **Serious TEAE** | 27 (54) | 16 (33) | 26 (52) |
| **TEAEs leading to study drug discontinuation** | 14 (28) | 8 (16) | 10 (20) |
| **Immune-related TEAE** | 24 (48) | 23 (47) | 30 (60) |
| **Infusion-related Reactions** | 2 (4) | 2 (4) | 5 (10) |
| **Median Treatment Duration, weeks (range)** | 9.8 (0, 97) | 21.0 (0, 105) | 24.3 (2, 107) |

Designation of immune-related TEAEs based on basket of Preferred Terms. TEAE: Treatment-Emergent Adverse Event; *Per Physician assessment

- Most common TEAEs (≥15% overall) were fatigue, nausea, constipation, dyspnea, decreased appetite and pneumonia. Grade ≥3 events occurring in ≥5% of patients were pneumonia (8.7%) and anaemia (5.4%)
- Related Grade 5 TEAEs: interstitial lung disease (Arm 1), myocarditis (Arm 2), pneumonitis (Arm 3), and congestive heart failure (Arm 3)



Johnson et al. ASCO Plenary Series, Dec. 2022
TEAEs: treatment emergent adverse events

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# Immune-related TEAEs (≥ 10% Overall)

| SAFETY EVALUABLE POPULATION, n (%) | ARM 1 (Z) (N=50) | ARM 2 (DZ) (N=49) | ARM 3 (EDZ) (N=50) |
|---|---|---|---|
| **Any Immune-related TEAE*** | 24 (48) | 23 (47) | 30 (60) |
| **Pneumonitis** | 7 (14) | 4 (8) | 5 (10) |
| **Grade ≥3** | 3 (6) | 1 (2) | 2 (4) |
| **Pruritus** | 8 (16) | 3 (6) | 5 (10) |
| **Rash** | 6 (12) | 5 (10) | 9 (18) |

*Designation of immune-related TEAEs based on basket of Preferred Terms.

- Majority of pneumonitis events reported were primarily Grade 1 – 2. No clear increase in rates of pneumonitis in Dom-containing arms compared to Zim alone
- Rash was reported with greater frequency in Arm 3 and were all Grade 1 – 2
  - Rash is a known side effect of etruma
  - Majority of subjects received treatment with topical corticosteroids and reported resolution of symptoms
  - No cases of rash led to study treatment discontinuation



Johnson et al. ASCO Plenary Series, Dec. 2022
etruma: etrumadenant; TEAEs: treatment emergent adverse events; zim: zimberlimab

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# ARC-7 Key Highlights from ASCO Plenary Dec. 2022 – Updated Data to be Presented at ASCO, June 3, 2023

## SELECT PFS TAKEAWAYS:

- **Interim mPFS 12.0 months for the doublet (DZ) and 10.9 months for triplet (EDZ)** vs. 5.4 months for zim mono (median follow-up: 12 months)
- **Doublet PFS HR=0.55; triplet HR=0.65**
- DZ PFS curve showed early and sustained separation from zim monotherapy

## PRIMARY PROGRESSIVE DISEASE TAKEAWAYS:

- Dom-containing arms resulted in reduction of early primary progressive disease (patients who progress at first scan)
- 5% and 13% for the doublet and triplet, respectively, vs. 25% for zim mono
- Demonstrates potential for an anti-TIGIT + anti-PD-1 combo to displace the use of anti-PD-1 in patients with aggressive disease

## SUMMARY:

- Largest and first prospective randomized dataset to date for an anti-TIGIT combination in 1L PD-L1-high NSCLC
- Both dom-containing arms demonstrated clinically meaningful differentiation compared to zim monotherapy across all efficacy measures evaluated
- No unexpected safety signals were observed in both dom-containing arms
- Low rates of immune-related adverse events and infusion-related reactions observed; potential differentiator for domvanalimab

Analysis reflects data as of August 31, 2022 - the data cut-off used for the December 2022 ASCO Plenary Session.

dom: domvanalimab; zim: zimberelimab; doublet: dom + zim; triplet: dom + zim + etrumadenant; cORR: confirmed overall response rate; mPFS: median progression-free survival



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# Phase 3 Program for dom is Targeting Large Market Opportunities

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

| STUDY | LEAD SPONSOR | SETTING | US 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 |
| STAR-221 | ARCUS BIOSCIENCES | 1L Gastric/GEJ/Esoph, Adenos | 30k patients |

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

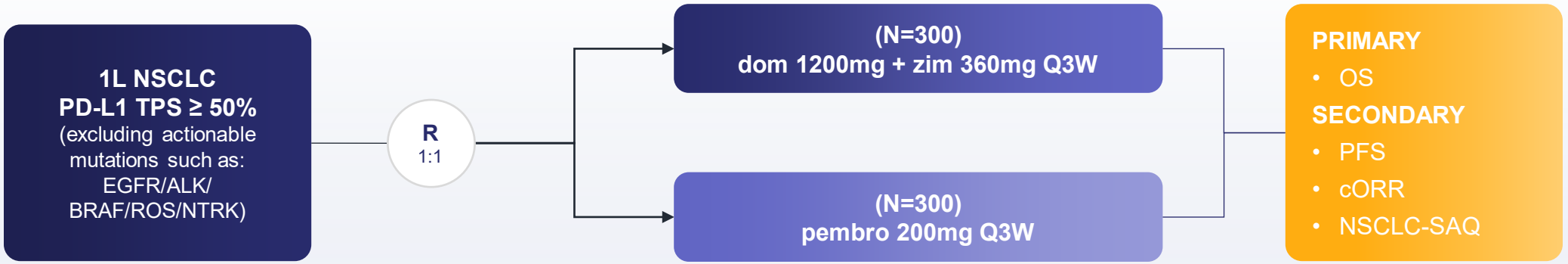
**$10B+ addressable market[1]**

[1]Based on drug treatable US patient population. Excludes patients with actionable mutations. Source: Decision Resources Group.
Adenos: adenocarcinoma; Dom: domvanalimab; GEJ: gastroesophageal junction; GE: gastroesophageal; NSCLC: non-small cell lung cancer


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# ARC-10 Phase 3 Evaluating Dom + Zim vs. Pembro, 1L NSCLC (PD-L1 ≥ 50%)

- Uses standard of care, pembrolizumab, in the comparator arm:
- Several similarities to Phase 2 design:
  - Almost identical inclusion criteria / patient population
  - Open label
  - Same dosing regimen and scanning interval
- Larger study (with stratification) to minimize imbalances between arms
  - Three stratification factors including ECOG status (also used in ARC-7), geography and histology
  - Centralized PD-L1 testing

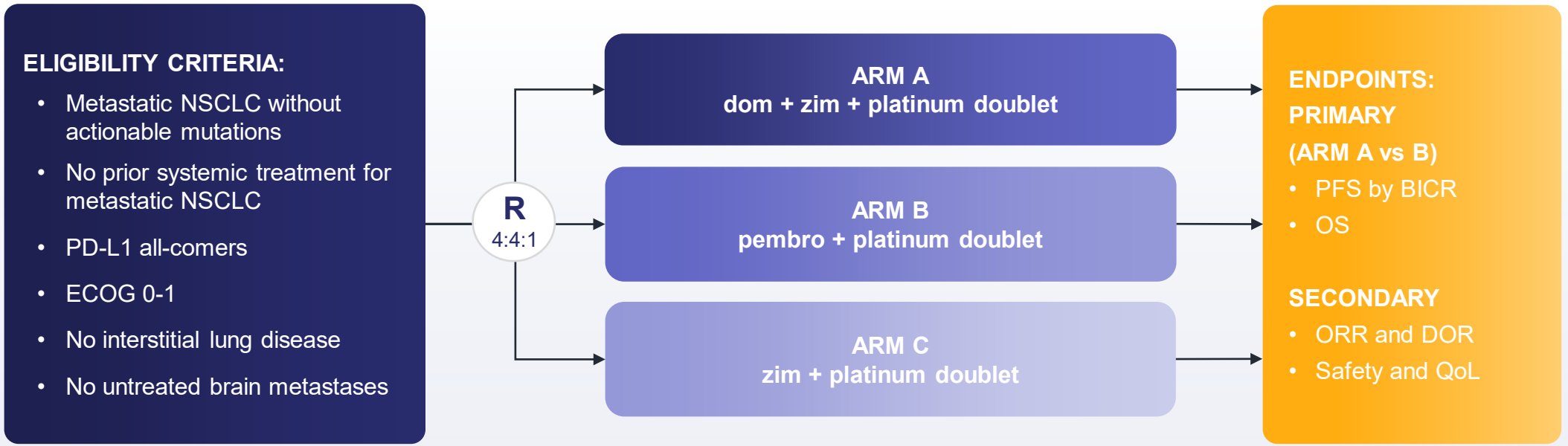



**Strat Factors**:
- ECOG PS 0 vs 1
- Geography (Asia vs non-Asia)
- Histology (Sq vs Non-sq)

cORR: confirmed overall response rate; Dom: domvanalimab; NSCLC: non-small cell lung cancer; OS: overall survival pembro: pembrolizumab; PFS: progression free survival; zim: zimberelimab
NCT#: NCT04736173


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# Phase 3 Evaluating Dom + Zim + Chemo vs. Pembro + Chemo in 1L NSCLC (All PD-L1 Subgroups)




**Strat Factors:**
- Baseline PDL1 PD-L1 status (≥50% vs. 1-49%)
- Geography (east Asia vs non-east Asia)
- Histology (Sq vs Non-sq)

New **Initiated in 3Q22**

dom: domvanalimab; pembro: pembrolizumab; zim: zimberelimab

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

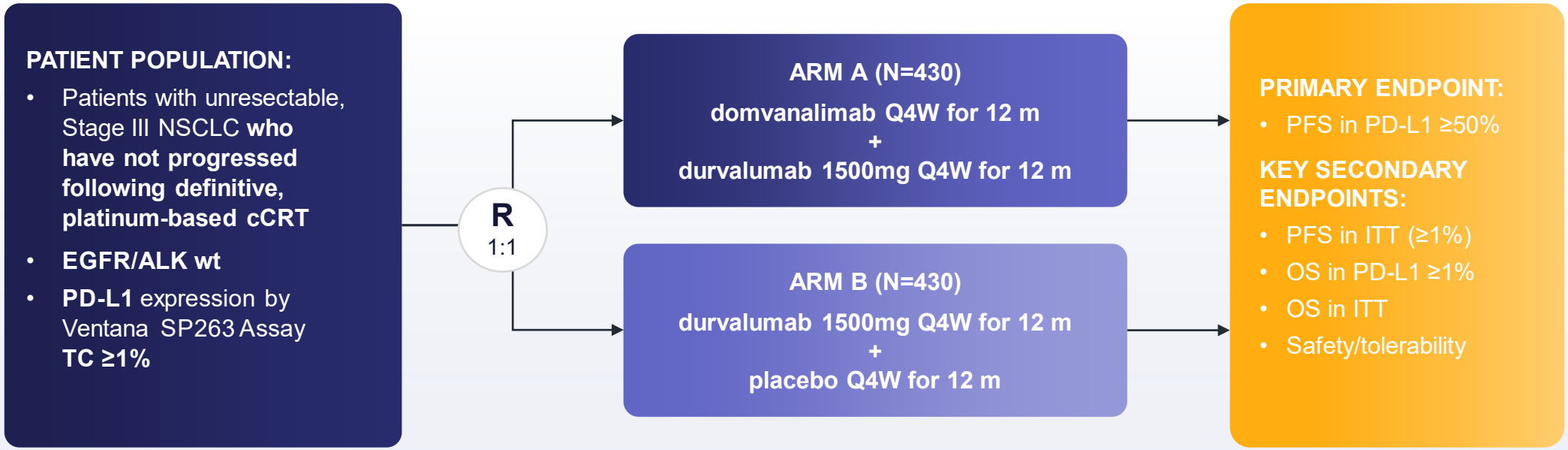
Gilead Sciences is operationalizing STAR-121



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# Phase 3 Evaluating Dom + Durva vs Placebo + Durva in Unresectable, Stage III NSCLC

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




**Strat Factors:**

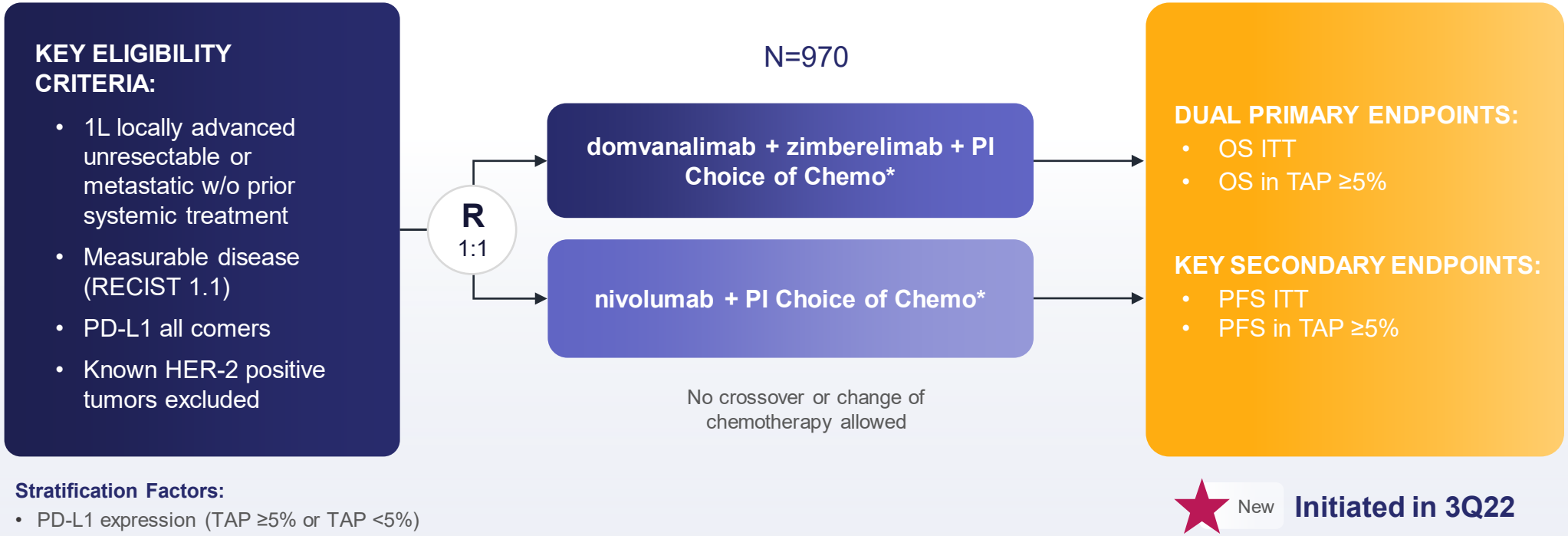
- Disease stage prior to cCRT (IIIA vs. IIIB/IIIC)
- PD-L1 status (TC ≥ 50% vs. TC 1-49%), as assessed by a central reference laboratory using the VENTANA PD-L1 (SP263) IHC assay
- Histology (Sq vs Non-sq)



domvanalimab: dom; durvalumab: durva: ITT: intent to treat; OS: overall survival; PFS: progression free survival

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# Phase 3 Evaluating Dom + Zim + Chemo vs Nivo + Chemo in 1L Gastric, GEJ and Esophageal Adenocarcinoma




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

domvanalimab: dom; GEJ: gastroesophageal junction; nivolumab; nivo; ITT: intent to treat; OS: overall survival; PFS: progression free survival; PI: principal investigator; zimberelimab: zim


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# Potential Advantages Support Best-in-Class Potential for Dom

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- Fc-silent antibody, **potentially resulting in safety/combinability benefits and low incidence of immune related AEs**
- To be packaged initially as individual agents, providing clinicians with **full control over administration**
  - Potentially enables dom to be **used in combination with other agents and regimens**
- **Optimally designed, broad Phase 3 program, all versus current SOC, and** operationalized by multiple companies
  - ARC-10: pembro comparator; enrolling only PD-L1≥50% patients
  - STAR-121: includes both pembro + chemo (active comparator) and zim + chemo arms
  - PACIFIC-8: durva (current SOC) is the PD-x in both the experimental and comparator arm; only enrolling PD-L1>1%
  - STAR-221: first phase 3 study to be initiated for a TIGIT antibody in the 1L gastric/GEJ/esophageal adenocarcinoma setting; nivo (current SOC) is comparator

AEs: adverse events; dom: domvanalimab; durva: durvalumab; GEJ: gastroesophageal junction nivo: nivolumab; pembro: pembrolizumab; SOC: standard of care

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



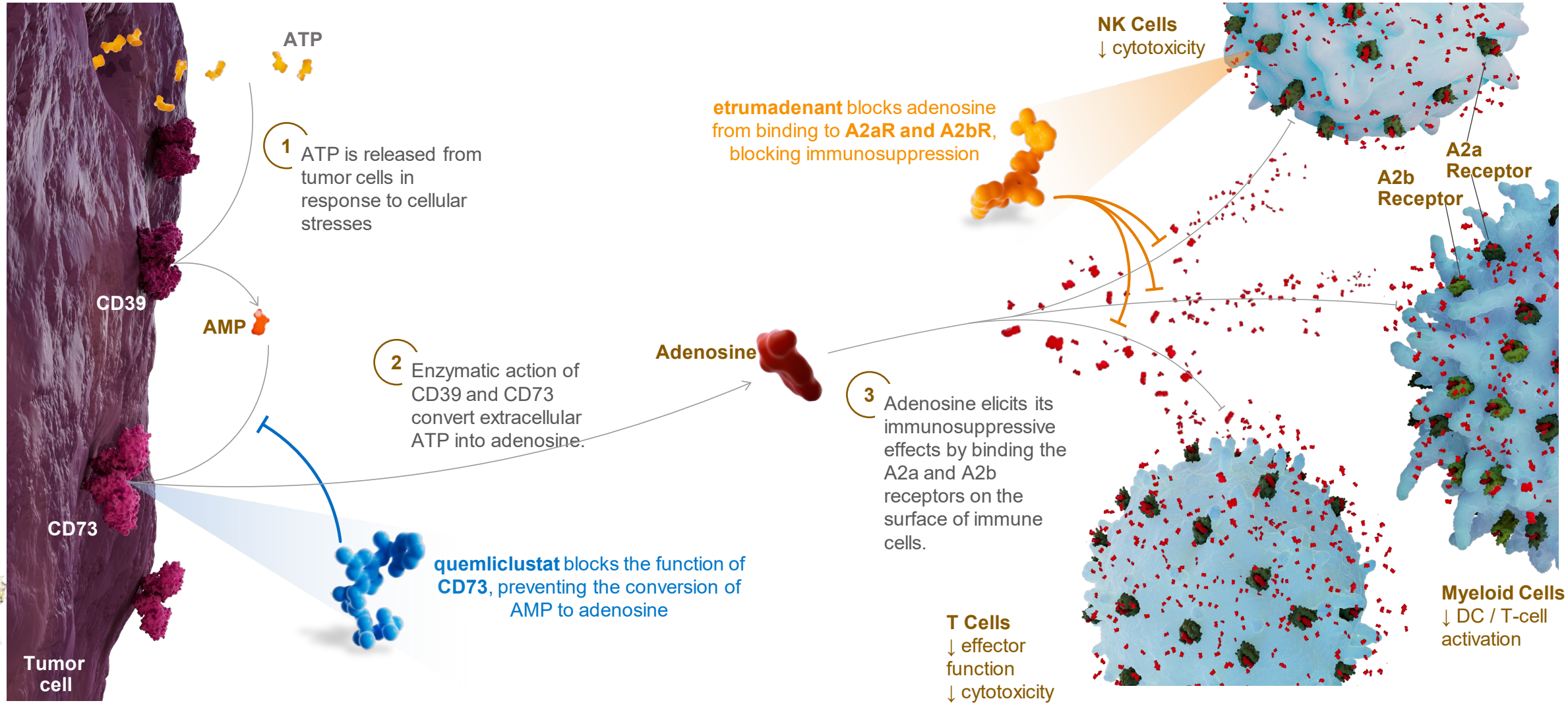
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# CD73-Adenosine Axis Programs



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






Arcus and Gilead have not received regulatory approval from any regulatory authority for etrumadenant and quemliclustat and their uses are investigational only.

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# 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 $A_{2a}R$ 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 | $A_{2a}R$ BLOOD (IC50, nM)c | $A_{2a}R$ (KB, nM)d | $A_{2b}R$ (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.

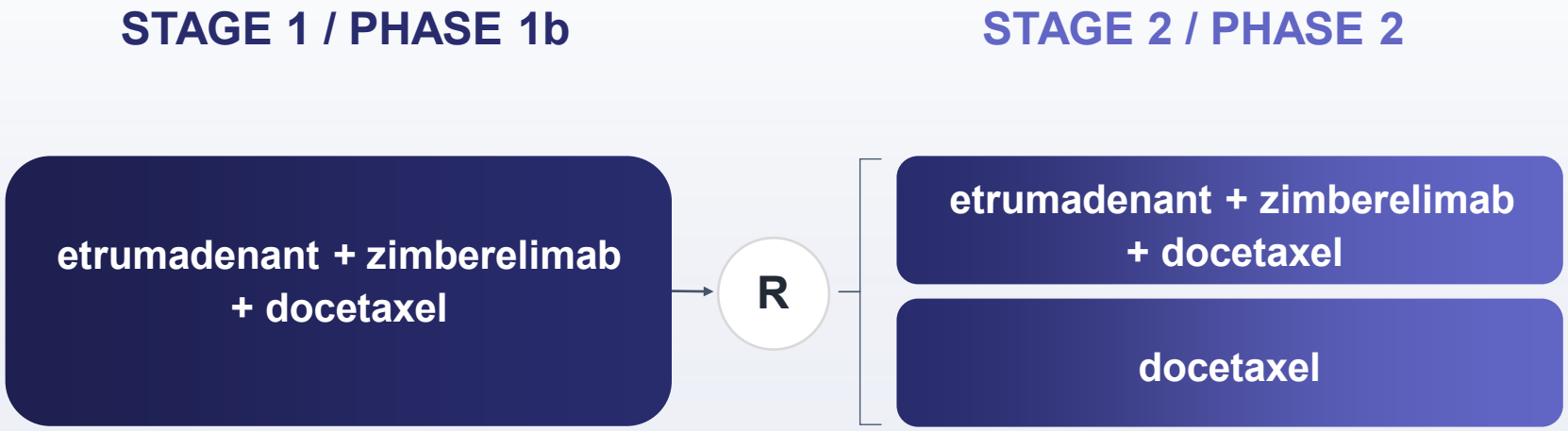


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# Phase 1b/2 Platform Study is Evaluating etruma in second-line mCRPC

- 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 2023

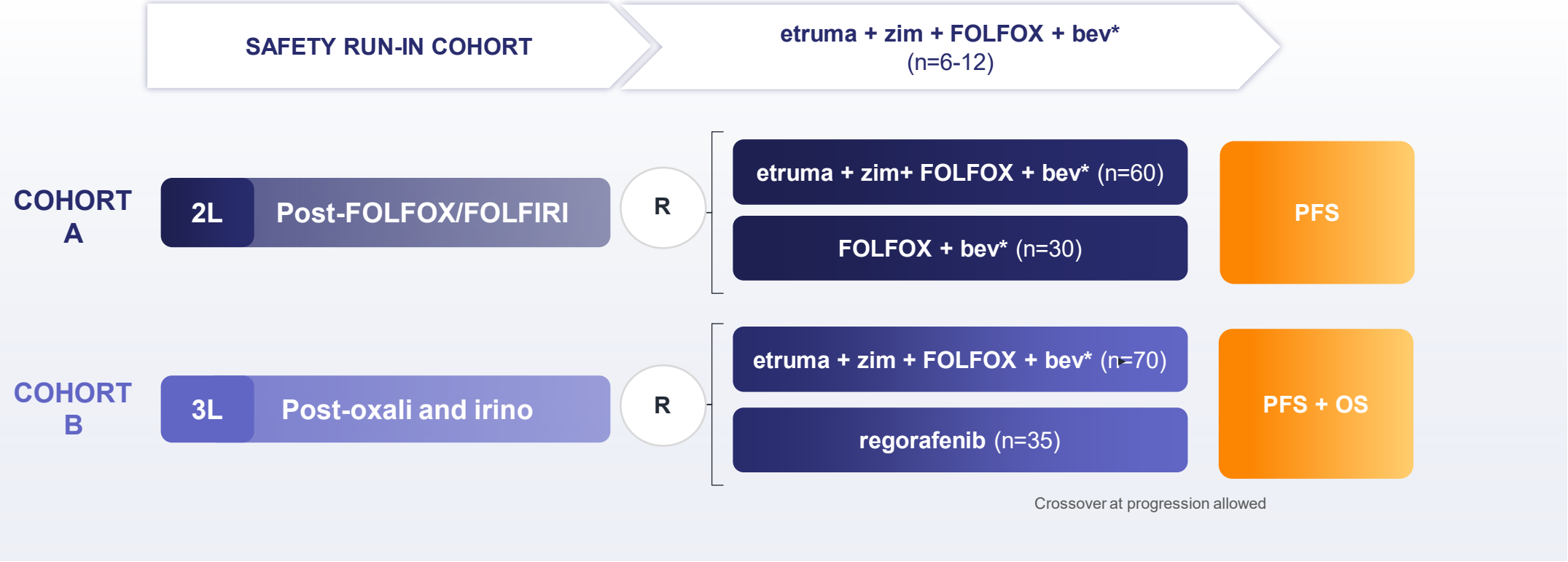



mCRPC: metastatic castrate-resistant prostate cancer; 2L: second-line; ORR: overall response rate; PFS: progression-free survival


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# 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-house in 1H23




*bev will be included for all patients in whom it is not contraindicated
Bevacizumab: bev; etrumadenant: **etruma;** irinotecan: irino; oxaliplatin: oxali; zimberelimab: zim:


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# 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

Potential for oral delivery established in healthy volunteers

**POTENTIAL ADVANTAGES OVER CD73 ANTIBODIES**

Extremely potent and selective inhibition of **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 support potential of CD73 inhibition in Stage 3 NSCLC

Rapidly growing number of CD73 antibodies in clinical development

quemliclustat is an investigational molecule and its safety and efficacy have not been established.

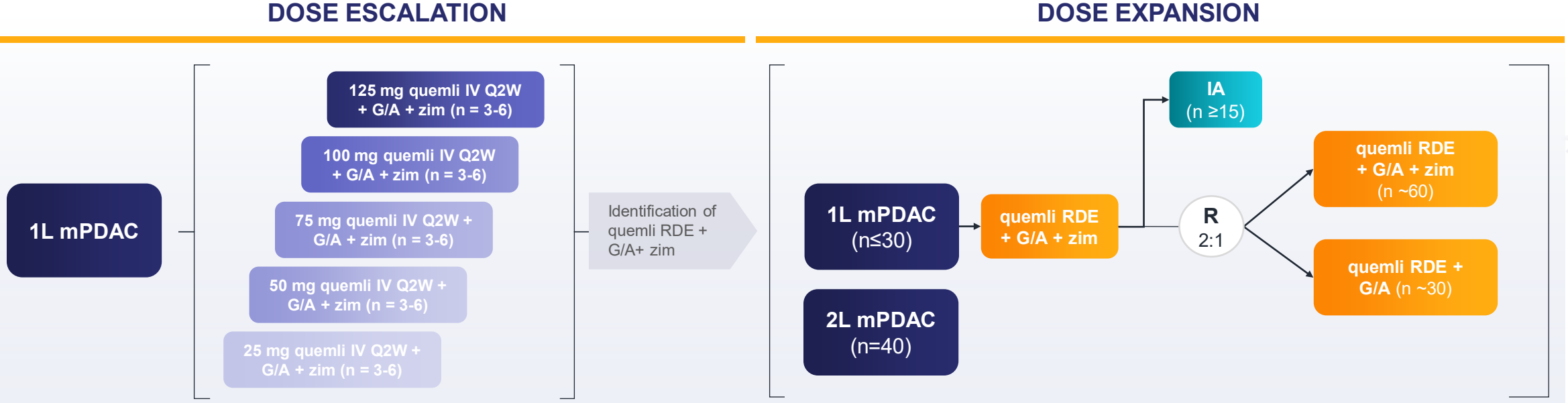
-Manji, GA et al; ASCO GI 2021 (Abstract 404): ARC-8: Phase 1/1b Study to Evaluate Safety and Tolerability of AB680 + Chemotherapy + Zimberelimab (AB122) in Patients with Treatment-Naive Metastatic Pancreatic Adenocarcinoma

-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



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# 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

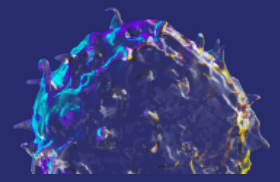
- **Primary:** Safety and tolerability
- **Secondary:** PK and clinical activity

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



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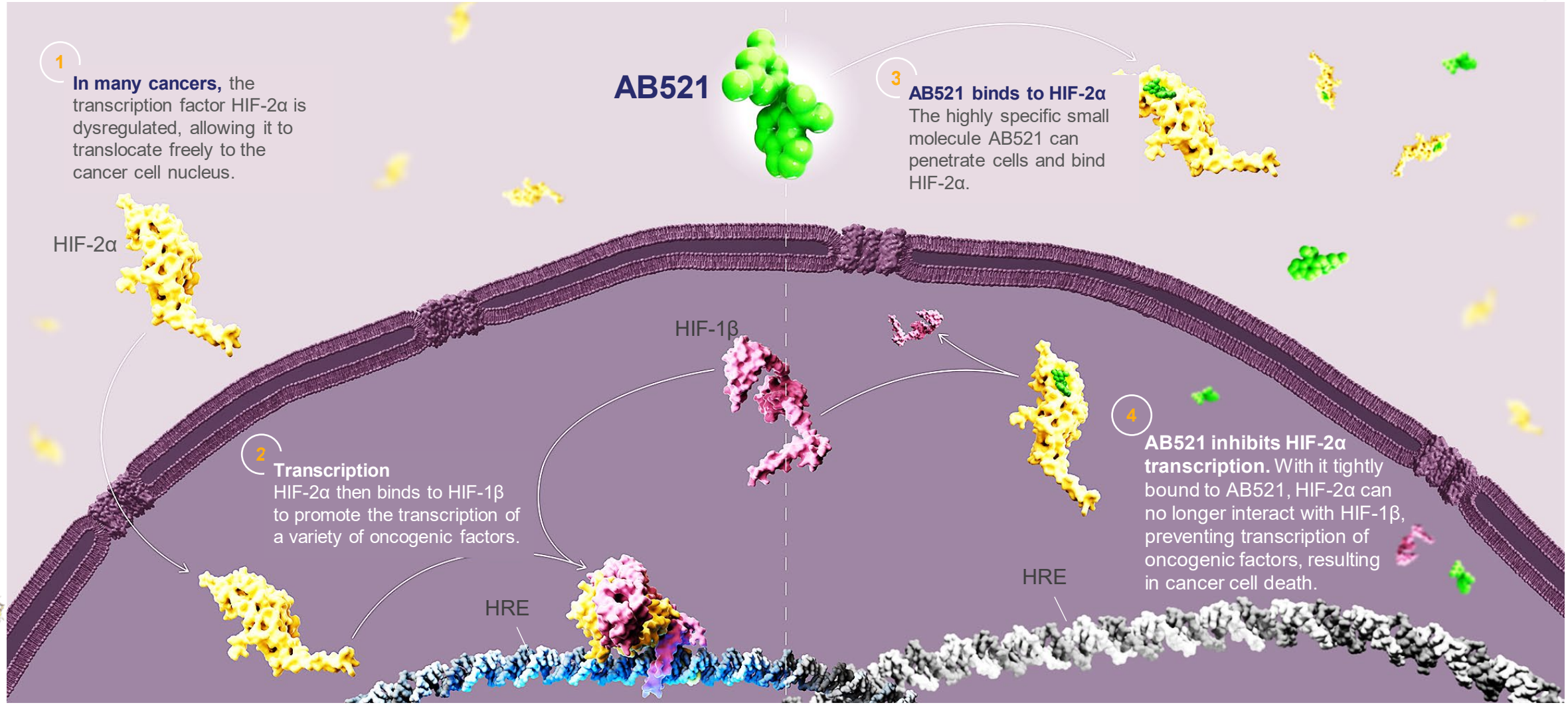
# HIF-2α Program





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# AB521 in the Tumor Cell Nucleus




AB521 is an investigational molecule and its safety and efficacy have not been established.
HRE, Hypoxia Response Element.



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# 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 on-target 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

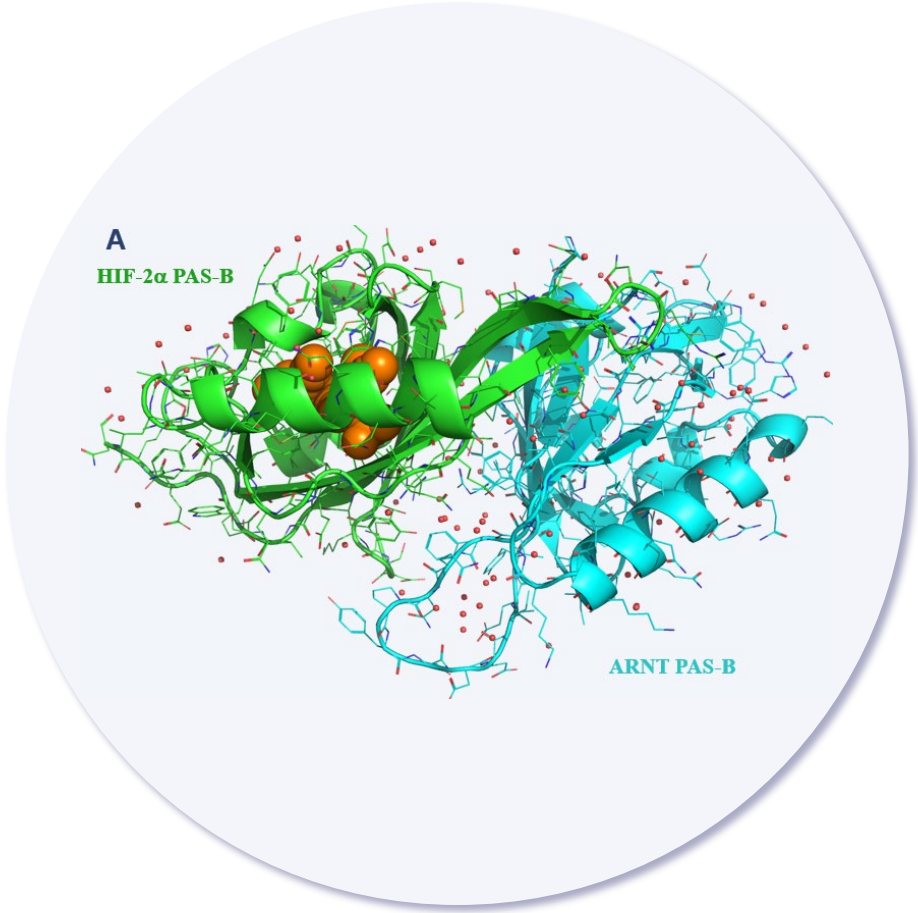


etrumadenant: etruma; quemliclustat: quemli

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# Extensive Preclinical Characterization Confirms Greater Potency of AB521 Relative to that of 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)** |
| CELLULAR | Control 786-O Luc Reporter $IC_{50}$ (nM) | **> 10,000 (n=6)** | **> 10,000 (n=7)** |
| CELLULAR | HIF-2α 786-O Luc Reporter $IC_{50}$ (nM) [in 100% Serum] | **46.5 ± 14.2 (n=24)** | **61.8 ± 6.6 (n=4)** |
| CELLULAR | 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)** |
| BIOCHEMICAL | HIF-2α MST $K_D$ (nM) | **2.4 ± 0.8 (n=3)** | **15.4 ± 2.7 (n=3)** |
| BIOCHEMICAL | HIF-2α ITC $K_D$ (nM) | **53.6 ± 17.9 (n=3)** | **53.8 ± 19.3 (n=3)** |
| BIOCHEMICAL | HIF-2α SPA $IC_{50}$ (nM) | **16.6 ± 5.0 (n=8)** | **22.3 ± 5.6 (n=5)** |

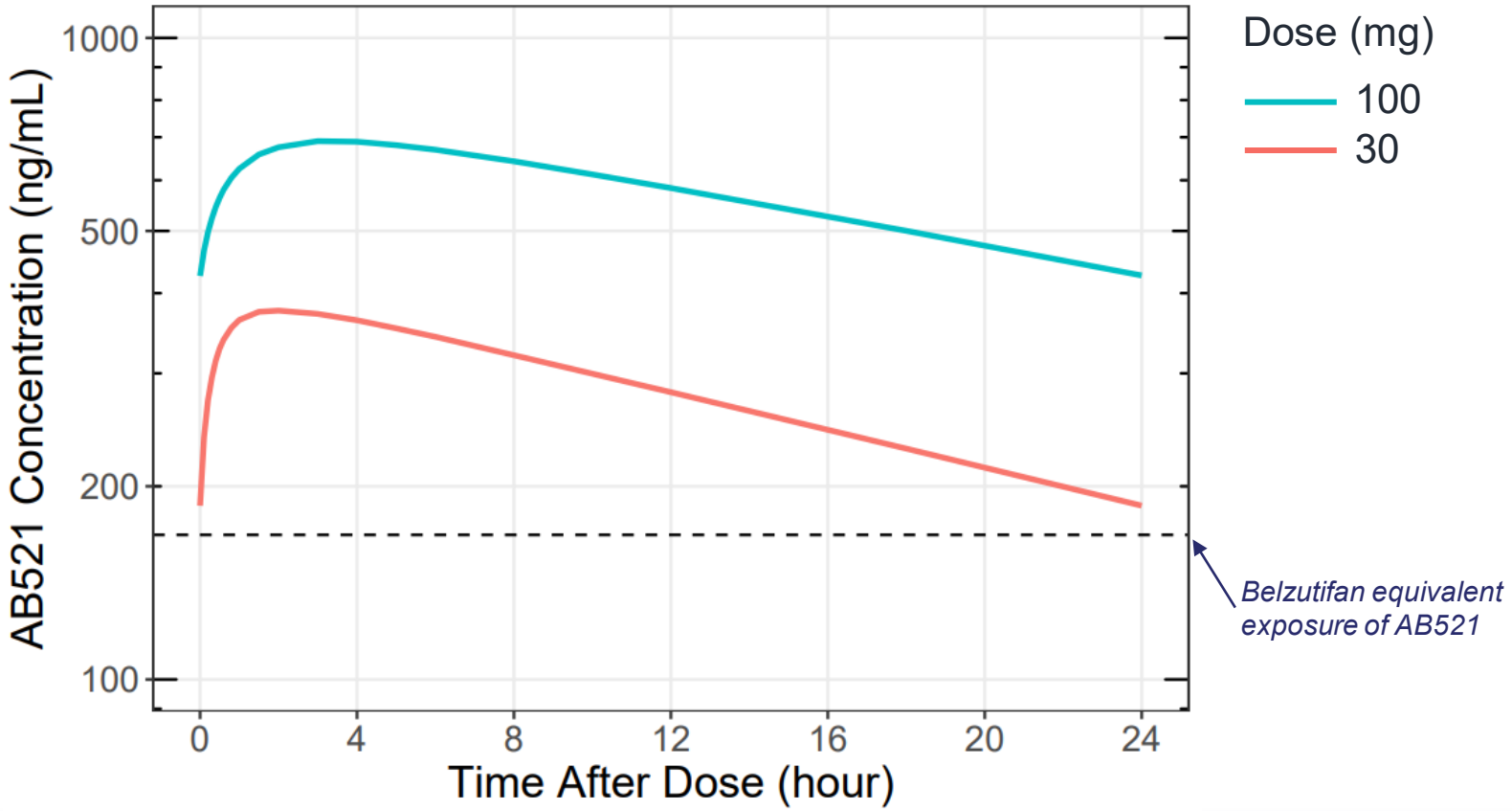



[a] MK-6482 was synthesized according to Xu *et al.* 2019 J Med Chem; DOI: 10.1021/acs.jmedchem.9b00719



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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


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# AB521 Monotherapy Dose Escalation/Expansion in ccRCC is Ongoing

## PH 1 DOSE ESCALATION

3+3 design with 21-day DLT window

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

**Key Inclusion Criteria**

- At least 1 measurable lesion per RECIST 1.1
- Adequate organ and marrow function
- ccRCC (in dose expansion)

**Key Exclusion Criteria**

- No prior HIF-2α inhibitor (dose expansion only)




**Expected to start Q3:23**

**Ph1 Dose Expansion**
*(n=30 x 2-3 doses)*
*2L+ ccRCC*

**AB521 monoTx (multiple doses)**

**Ph 1b/2 AB521 + TKI combo study in 2L ccRCC**

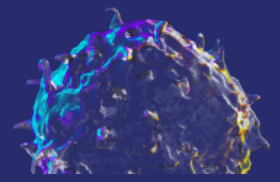
**Current Status:**

**100mg daily dose cohort is enrolling (3rd dosing cohort)**

**This dose should achieve 3x+ the level of HIF-2α inhibition as the approved dose of belzutifan**


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# APPENDIX





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# Gilead is Co-Developing Four Optioned Programs with Arcus

GILEAD

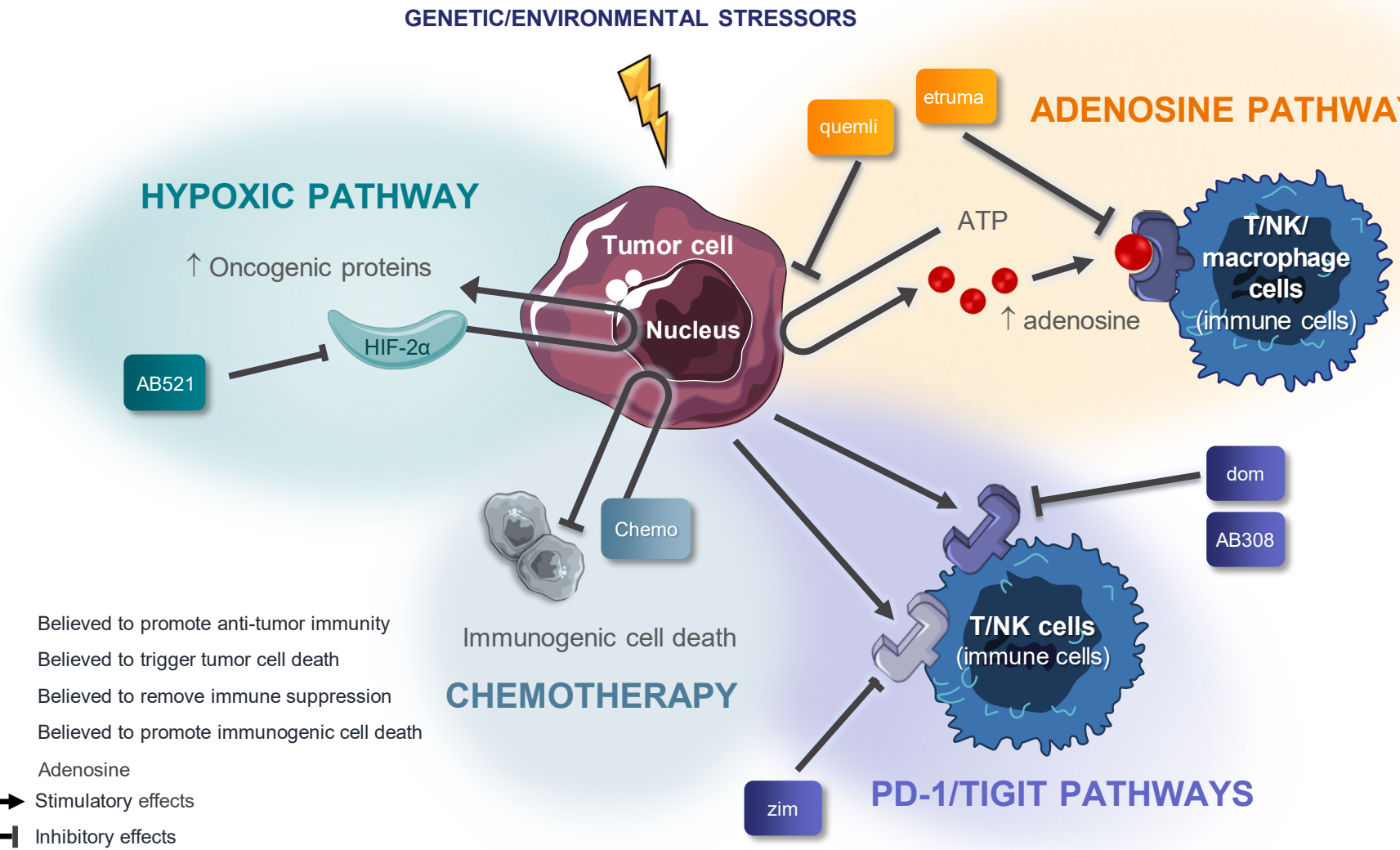
- Currently has rights to five of our clinical-stage candidates through its exercised options:
  - domvanalimab and AB308: anti-TIGIT antibodies
  - etrumadenant: A2a/A2b receptor antagonist
  - quemliclustat: small-molecule CD73 inhibitor
  - zimberelimab: anti-PD-1 antibody
- Arcus and Gilead share 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
- 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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# Biology-Driven Combination Strategy Intended to Enhance Anti-Cancer Activity




## NEW INTRA-PORTFOLIO COMBINATIONS

- TIGIT domvanalimab + PD-1 zimberelimab + CD73 quemliclustat + $A_{2A}R/A_{2B}R$ etrumadenant
- TIGIT domvanalimab + PD-1 zimberelimab + Chemo
- CD73 quemliclustat + PD-1 zimberelimab + Chemo + $A_{2A}R/A_{2B}R$ etrumadenant
- HIF-2α AB521 + $A_{2A}R/A_{2B}R$ etrumadenant

All of these molecules are investigational and Arcus (and Gilead for optioned molecules) has not received approval from any regulatory authority for their use.



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# 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

## NEAR-TERM 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**

## NEWLY INITIATED & UPCOMING STUDIES

Next generation molecules

Key molecule(s): AB521 (HIF-2α), AB801 (Axl), AB598 (CD39), AB375 (KIT)

### Phase 1 Studies

ARC-20

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

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

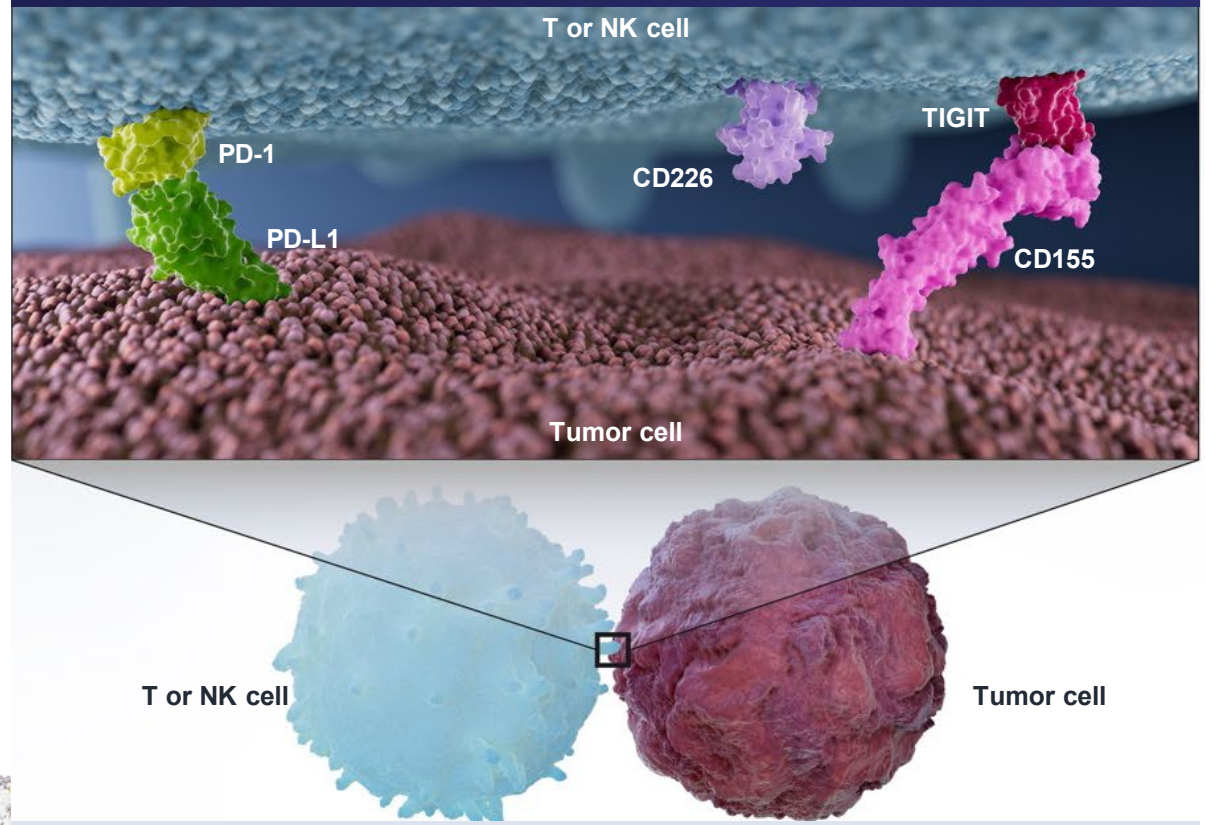


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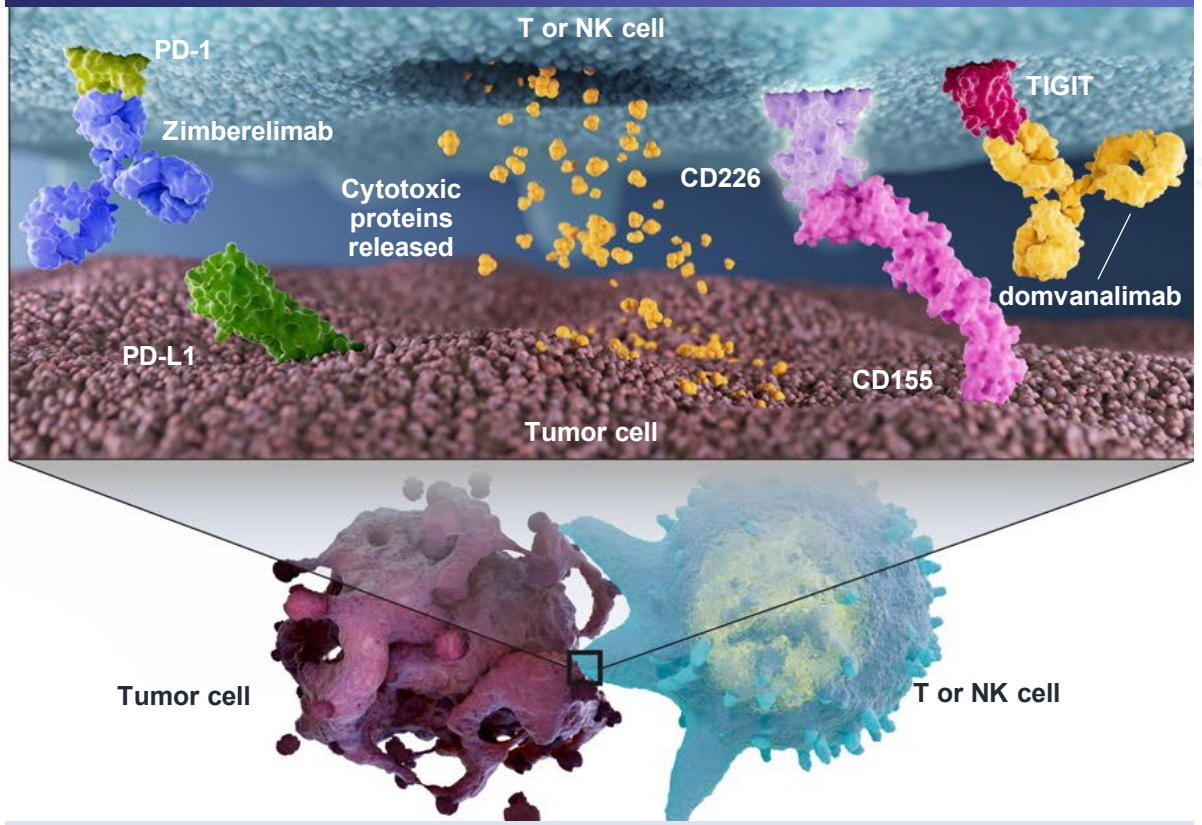
# Domvanalimab (dom): Most Advanced Fc-Silent TIGIT Antibody in Clinical Development

## IMMUNOSUPPRESSION




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

## IMMUNE CELL ACTIVATION & TUMOR CELL KILLING

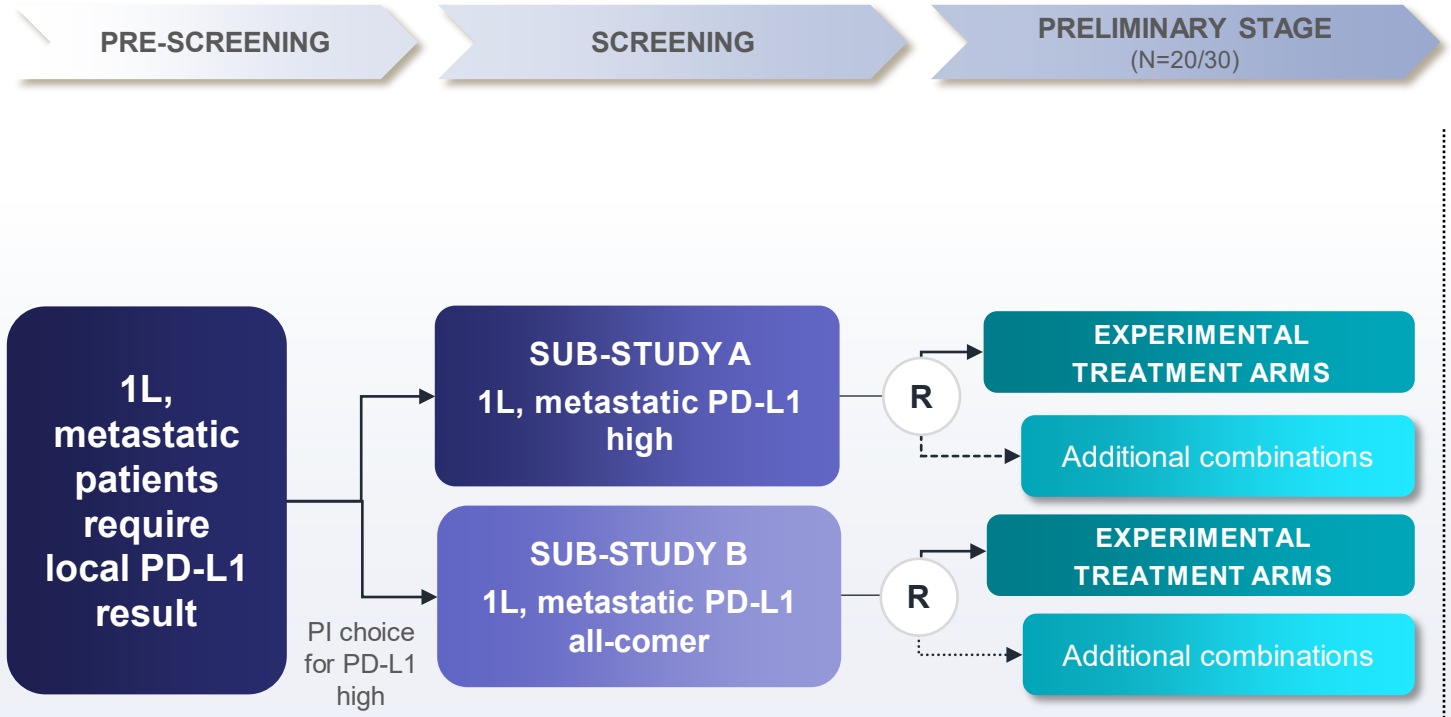



Dom is an investigational molecule designed to block TIGIT, enable CD155:CD226 interaction and immune cell activation

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


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




Treatment arm(s) may be expanded to **N=40 total between both preliminary + expansion**

**PRIMARY ENDPOINTS**

- ORR
- Safety and tolerability

**SECONDARY ENDPOINTS**

- PFS
- DOR
- OS
- PK

**EXPLORATORY ENDPOINTS**

- Biomarkers, PD

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.



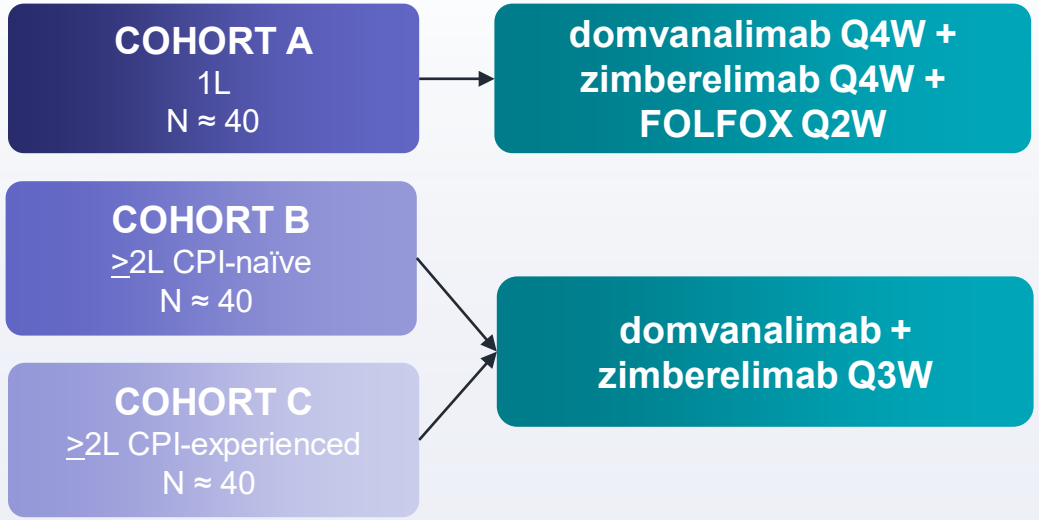
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# Phase 2 Trial to Evaluate Dom + Zim + Chemo vs Dom + Zim in Advanced Upper Gastrointestinal Tract Malignancies

EDGE-Gastric

**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

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# 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 designed to yield safety/combinability benefits<br>• Only TIGIT in Stage 3 NSCLC combining with durva, the dominant PDx SOC<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; incidence of certain irAEs (rash, pruritus)<br>• Limited Atezo use in NSCLC | • 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>• 1L NSCLC (all comer)<br>• Stage 3 NSCLC | • 1L NSCLC (PD-L1 ≥1%)<br>• 1L NSCLC (all comer)<br>• Stage 3 NSCLC<br>• ES-SCLC |

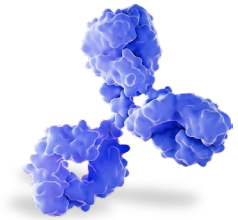
[1]Includes indications relevant to current Arcus/Gilead development program



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# Zimberelimab (zim) Preclinical and Clinical Activity is Consistent with Approved Anti-PD-1 Class

## Broad Clinical Experience



- **Approved** in China for R/R classical Hodgkin Lymphoma (cHL)[1]
- Studied in over **1000** patients[1,2,3,8]
- Currently being studied in over **20** indications globally[3]
- Licensed for development and commercialization by[8]:

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## Clinical Outcomes

**Zim clinical data** indicates single-agent activity shown across multiple tumor types, including NSCLC, gastric, and esophageal[1,2]

- Pooled incidence of ADAs was low (<10%) across 9 Ph1/2 studies (n=747)3
- No impact of neutralizing antibodies on efficacy or safety for patients in ARC-7 to date

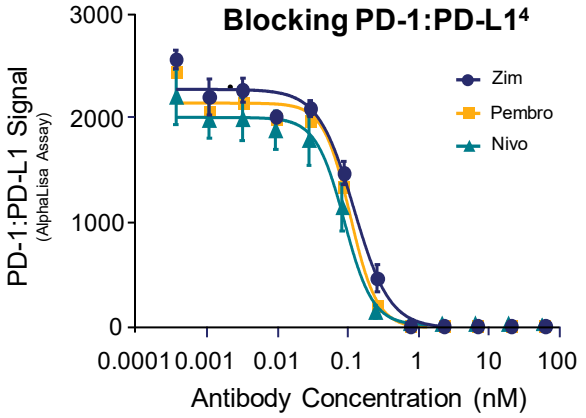
### Zimberelimab Efficacy in cHL and Cervical cancer

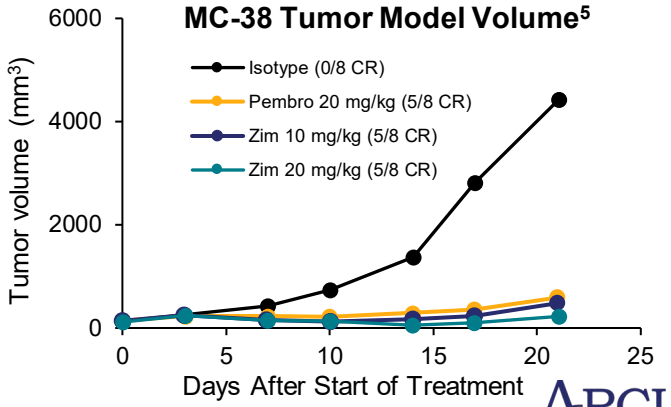
Zimberelimab alone has demonstrated activity consistent with that of marketed anti-PD-1 antibodies in these disease settings.

| R/R Classical Hodgkin Lymphoma | Zim[2] |
|---|---|
| 12-mo PFS | 78% |
| 12-mo OS | 99% |
| ORR | 91% |
| **PD-L1+ Cervical Cancer** | **Zim[6]** |
| ORR | 28% |
| mPFS | 3.7 mo |
| mOS | 16.8 mo |

## Preclinical Characterization

**Zim preclinical activity** shows consistency with pembrolizumab and nivolumab binding potency and tumor model activity[3]

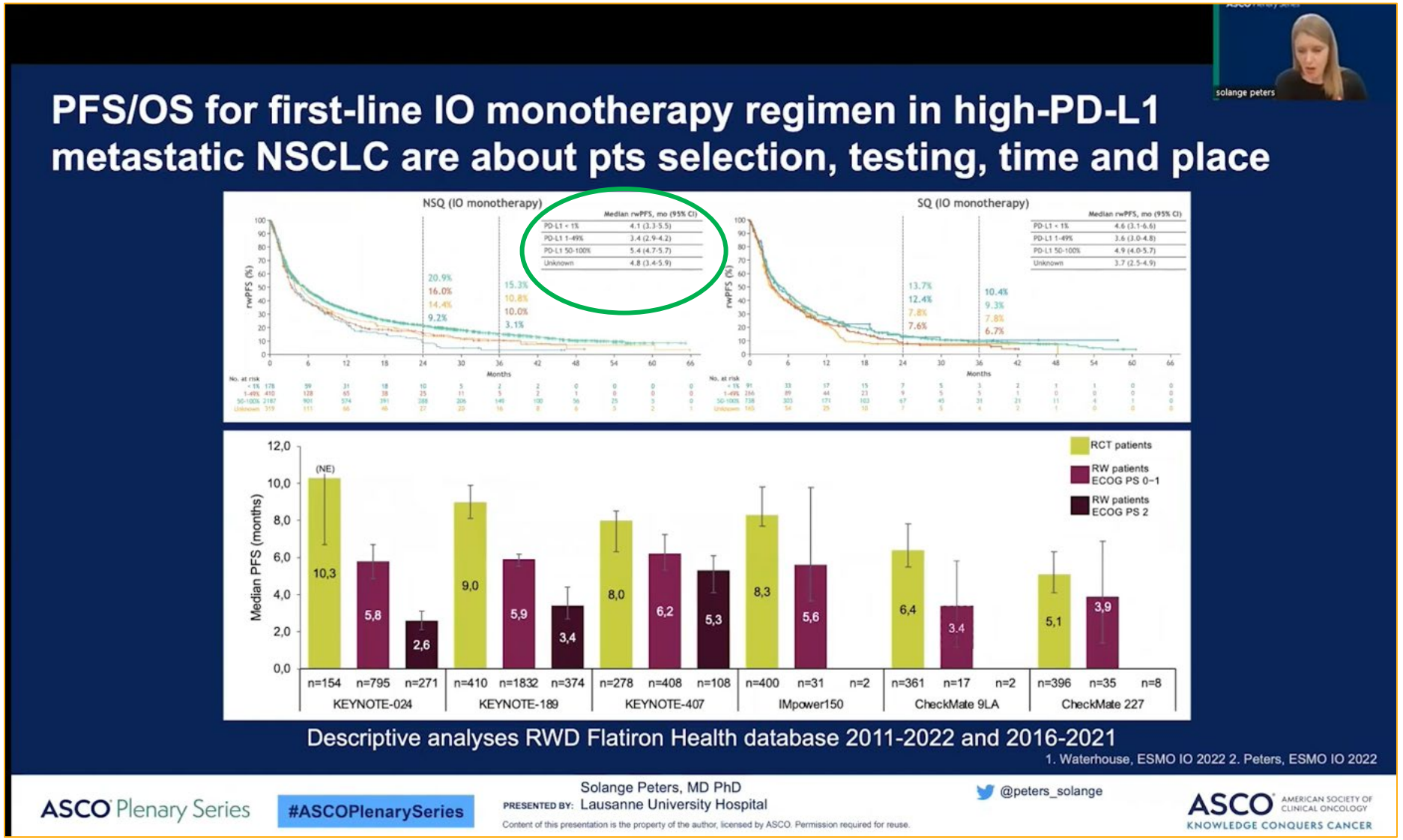



1. Johnson et al. ASCO Plenary Series, Dec. 2022; Gloria Biosciences obtained approval and conducts its activities independent of Arcus. 2. Lin et al Eur J Cancer 2021. 3. Data on file. 4. AlphaLISA. 5. Lou (2023) Front Oncol DOI:10.3389/fonc.2021.736955. 6. Wu et al ESMO IO 2022; Wu SITC 2022 #673. 8. Arcus and Gloria are independent licensees of WuXi Biologics; Gilead and Taiho are licensees of Arcus.


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# RWD Presented at ESMO IO 2022 for PD- Antibodies in PD-L1 High NSCLC

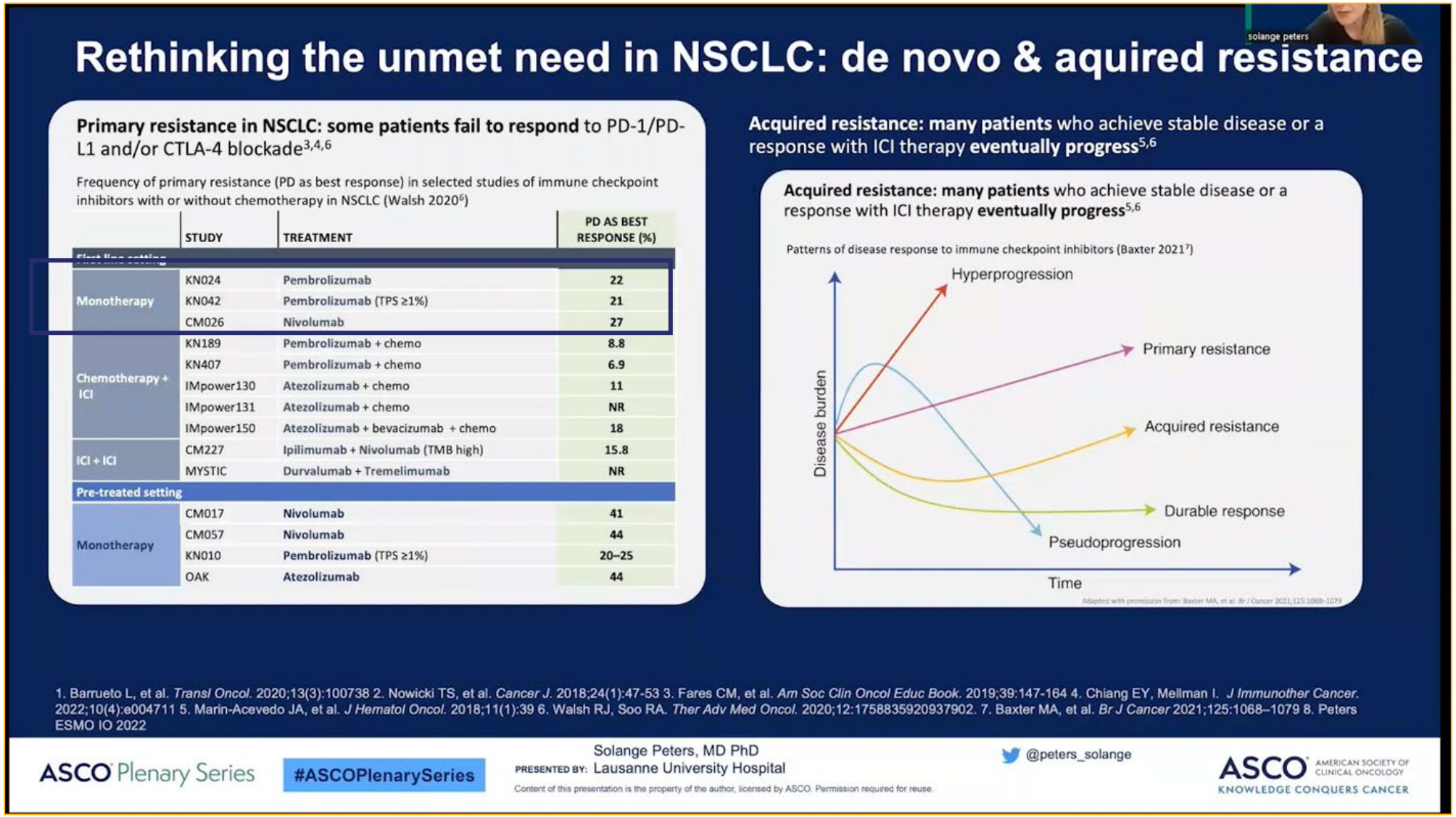





Peters discussion, ASCO Plenary Series, Dec. 2022

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# “Progressive Disease” as BoR for zim (25%) is Consistent with Earlier PD-1 Datasets




| | STUDY | TREATMENT | PD AS BEST RESPONSE (%) |
|---|---|---|---|
| **First-line setting** | | | |
| Monotherapy | KN024 | Pembrolizumab | 22 |
| | KN042 | Pembrolizumab (TPS ≥1%) | 21 |
| | CM026 | Nivolumab | 27 |
| Chemotherapy + ICI | KN189 | Pembrolizumab + chemo | 8.8 |
| | KN407 | Pembrolizumab + chemo | 6.9 |
| | IMpower130 | Atezolizumab + chemo | 11 |
| | IMpower131 | Atezolizumab + chemo | NR |
| | IMpower150 | Atezolizumab + bevacizumab + chemo | 18 |
| ICI + ICI | CM227 | Ipilimumab + Nivolumab (TMB high) | 15.8 |
| | MYSTIC | Durvalumab + Tremelimumab | NR |
| **Pre-treated setting** | | | |
| Monotherapy | CM017 | Nivolumab | 41 |
| | CM057 | Nivolumab | 44 |
| | KN010 | Pembrolizumab (TPS ≥1%) | 20–25 |
| | OAK | Atezolizumab | 44 |


Peters discussion, ASCO Plenary Series, Dec. 2022; BoR: Best Overall Response
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# Zim Has Been Approved in China since 2021

## Ligand's Partner Gloria Biosciences Receives Approval in China for Zimberelimab for the Treatment of Recurrent or Refractory Classical Hodgkin's Lymphoma

*First regulatory approval of an OmniAb-derived antibody*

August 30, 2021 04:01 PM Eastern Daylight Time

EMERYVILLE, Calif.--(BUSINESS WIRE)--**Ligand Pharmaceuticals Incorporated (NASDAQ: LGND)** today announced that its partner Gloria Biosciences (GloriaBio) has received approval from China's National Medical Products Administration (NMPA) for zimberelimab (GLS-010), an OmniAb-derived anti-PD-1 monoclonal antibody for the treatment of recurrent or refractory classical Hodgkin's lymphoma (cHL). GloriaBio has development and commercialization rights in China with respect to zimberelimab through a sublicense agreement with Ligand's licensee Wuxi Biologics Ireland Limited.

"We are delighted to see GloriaBio's progress with zimberelimab including receipt of NMPA approval. When we acquired the OmniAb technology in 2016, there were no OmniAb-derived antibodies in the clinic. GloriaBio's

Zimberelimab is a fully human monoclonal antibody that belongs to a class of immuno-oncology agents known as immune checkpoint inhibitors. It is designed to bind to PD-1, a cell surface receptor that plays an important role in the downregulation of the immune system by preventing the activation of T cells. Other anti-PD-1 antibodies have been approved by the U.S. FDA in multiple cancer types. In addition to cHL, GloriaBio is investigating zimberelimab in advanced solid tumors and in March 2021 was granted Breakthrough Therapy Designation for


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# Zimberelimab* Approved for R/R cHL in China since 2021 (Gloria Biosciences Data)

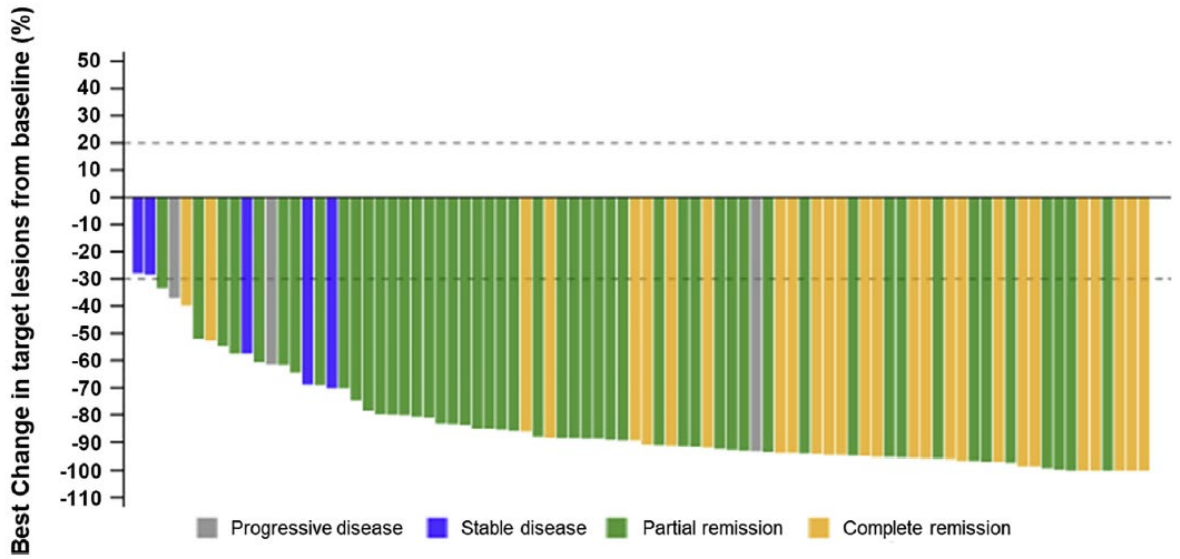



Fig. 1. Waterfall plot of the evaluation of the best overall response by the independent review committee (n = 85).

## BASELINE CHARACTERISTICS

| | Patients with r/r-cHL (n = 85) |
|---|---|
| Age (years), median (min, max) | 31 (18, 59) |
| Sex, n (%) | |
| Male | 49 (57.6) |
| Female | 36 (42.4) |
| Current tumor stage, n (%) | |
| II | 12 (14.1) |
| III | 19 (22.4) |
| IV | 48 (56.5) |
| Other | 6 (7.1) |
| ECOG, n (%) | |
| 0 | 54 (63.5) |
| 1 | 31 (36.5) |
| Previous therapies, n (%) | |
| Chemotherapy | 85 (100) |
| Autologous stem cell transplantation | 12 (14.1) |
| Brentuximab vedotin | 2 (2.4) |
| Targeted drug[a] | 10 (11.8) |
| Lines of prior therapy, n (%) | |
| 2 | 48 (56.5) |
| 3 | 25 (29.4) |
| 4-6 | 12 (14.1) |

## BEST OVERALL RESPONSE: 90.6%[1]

| | Assessed by IRC (n = 85) | Assessed by the investigator (n = 85) |
|---|---|---|
| Complete response, n (%) | 28 (32.9) | 31 (36.5) |
| Partial response, n (%) | 49 (57.6) | 46 (54.1) |
| Stable disease, n (%) | 5 (5.9) | 5 (5.9) |
| Progressive disease, n (%) | 3 (3.5) | 3 (3.5) |
| Objective response rate, n (%) | 77 (90.6) | 77 (90.6) |
| 95% CI | (82.3–95.9) | (82.3–95.9) |

- Pembro, in similar setting, generated ORRs of **65%** (KN-013), **72%** (KN-087) and **65.6%** (KN-204)
- Nivo generated ORR of **69%** (CM-205)

*Also known as GLS-010 in China (Gloria Biosciences); Gloria Biosciences conducts its activities independently from Arcus

[1]Best Overall Response is the sum of all complete responses and partial responses

Lin et al., Efficacy and safety of GLS-010 (zimberelimab) in patients with relapsed or refractory classical Hodgkin lymphoma: A multicenter, single-arm, phase II study. (2021) doi: 10.1016/j.ejca.2021.07.021.



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# Zimberelimab in 2L Cervical Cancer (Gloria Biosciences Data; ESMO IO 2022)

## Results

- In stage 2, 105 patients were enrolled and received zimberelimab (GLS-010), and 90 patients were in FAS, because there were 15 patients who did not received platinum -based standard therapy defined by CDE, NMPA;
- As of 29 April, 2022, after a median follow-up of 16.9 months, 83 patients had discontinued, and 22 were still on treatment.
- CR and PR were achieved by 5 and 20 patients, corresponding to an ORR of 27.8%.
- The median PFS was 3.7 months, and the median OS was 16.8 months.

**Table 1. Baseline characteristics of patients**

| Parameter | Patients (n=45) | Parameter | Patients (n=45) |
|---|---|---|---|
| Age, years, median (range) | 51 (31-75) | Histology, n (%) | |
| ECOG PS | | Adenomatous carcinoma | 9 (10.0) |
| 0 | 34 (37.8) | Squamous carcinoma | 79 (87.8) |
| 1 | 56 (62.2) | Adenosquamous carcinoma | 2 (2.2) |
| Previous treatment | | Disease stage (FIGO 2009), n (%) | |
| Surgery | 64 (71.1) | IB | 17 (18.9) |
| Radiotherapy | 86 (95.6) | IIA | 19 (21.1) |
| Chemotherapy | 90 (100.0) | IIB | 21 (23.3) |
| Lines of previous chemotherapy | | IIIA | 2 (2.2) |
| 1 | 52 (57.8) | IIIB | 10 (11.1) |
| 2 | 29 (32.2) | IIIC | 11 (12.2) |
| ≥3 | 9 (10.0) | IV | 7 (7.8) |

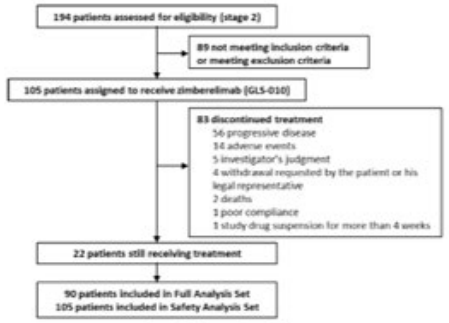



**Fig. 1. Patient disposition**

**Table 2. Efficacy of zimberelimab (GLS-010) in the treatment of recurrent or metastatic cervical cancer**

| Efficacy | IRC-assessed (n=90) |
|---|---|
| Best overall response, n (%) | |
| Complete response | 5 (5.6) |
| Partial response | 20 (22.2) |
| Stable disease | 24 (26.7) |
| ORR, n (%) | 25 (27.8 |
| 95% CI (%) | 18.85-38.22 |
| DCR, n (%) | 49 (54.4) |
| 95% CI (%) | 43.60-64.98 |
| Median PFS (95%CI), months | 3.7 (1.94-5.55) |
| Median OS (95%CI), months | 16.8 (11.50-) |
| Median TTR (95%CI), months | 1.9 (1.84-3.65) |
| Median DoR, months | NR |
| 12-month DoR rate (95%CI), % | 78 (55-90) |

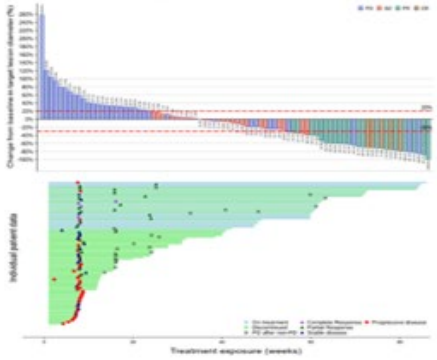


**Fig. 2. Waterfall plot and swimmer plot (N=90)**

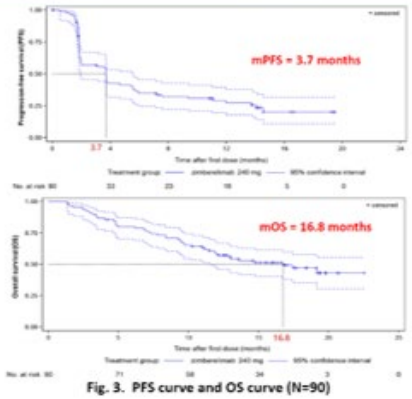



**Fig. 3. PFS curve and OS curve (N=90)**

## Safety and tolerability

- As of 29 April, 2022, TRAEs of any grade were observed in 82 (n=105) patients , mostly Grade 1 or 2;
- Hypothyroidism and anemia were the most common TRAEs.
- Grade ≥ 3 TRAEs were experienced by 26 patients with anemia being the most frequently reported.

**Table 3. Summary of adverse events**

| | AEs, n (%) (N=105) |
|---|---|
| TEAE | 102 (97.1) |
| Grade ≥3 TEAE | 44 (41.9) |
| TRAE | 82 (78.1) |
| Grade ≥3 TRAE | 26 (24.8) |
| irAE | 48 (45.7) |
| Grade ≥3 irAE | 11 (10.5) |
| SAE | 30 (28.6) |
| TRSAE | 16 (15.2) |

**Table 4. Common TRAEs in ≥ 10% of patients at any grade**

| | Any grade, n (%) (N=105) | Grade ≥3, n (%) (N=105) |
|---|---|---|
| Hypothyroidism | 28 (26.7) | - |
| Anemia | 20 (19.0) | 8 (7.6) |
| Hyperthyroidism | 13 (12.4) | - |
| Aspartate aminotransferase elevation | 11 (10.5) | - |
| Alanine aminotransferase elevation | 11 (10.5) | - |
| White blood cell count decreased | 11 (10.5) | 1 (0.7) |

## Conclusion

- In this pivotal registration phase II study, zimberelimab (GLS-010) exhibited encouraging therapeutic activity and manageable safety profile in PD-L1-positive recurrent or metastatic cervical cancer patients.
- The ORR was **27.8%** and DCR was **54.4%**. Responses were durable, with a median DoR that had not been reached and a 12-month DoR rate of 78%. The median OS was **16.8 months**.
- The safety profile was consistent with that previously observed for zimberelimab (GLS-010) in patients with advanced cancer.[3,4] 78.1% patients had any grade of TRAEs , mostly grade 1-2.
- This trial is still ongoing, and we are looking forward to further results.

## References


1. Sung H, Ferlay J, Siegel RL, et al. CA Cancer J Clin. 2021;71(3):209-249.
2. Chung HC, Ros W, Delord JP, et al. J Clin Oncol. 2019;37(17):1470-1478.
3. Liu D, Ma C, Lu P, et al. Eur J Cancer. 2021;148:1-13.
4. Lin N, Zhang M, Bai H, et al. Eur J Cancer. 2022;164:117-126.



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**Wu. X has no conflict of interests to disclose.**


*Sponsored by Guangdong Gloria Biosciences Co. Ltd.*


- Keynote-158 in this same setting (n=82, PD-L1>1%) **generated an ORR of 12.2%**

Gloria Biosciences conducts its activities independently from Arcus.
Source: Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study

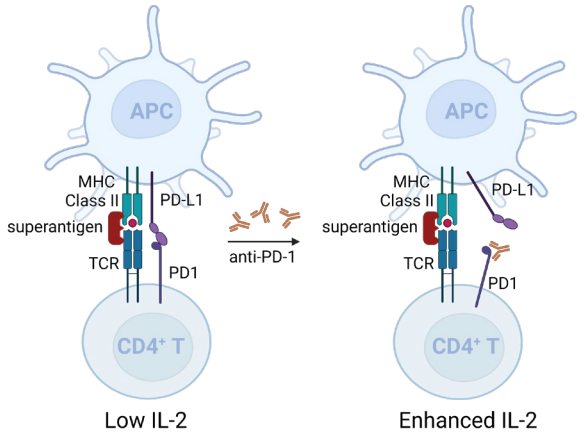


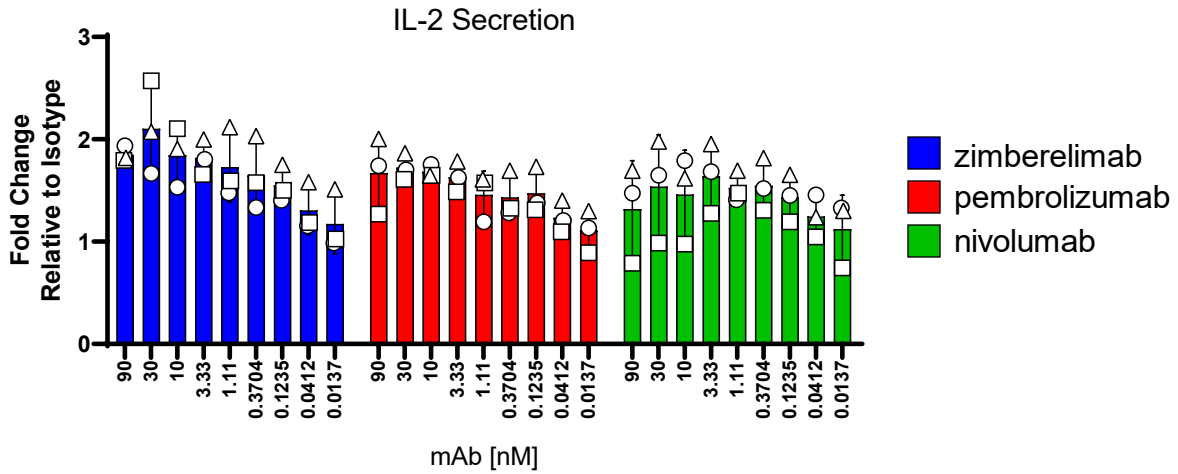

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# Zimberelimab Shows Equivalency to Pembro and Nivo in Preclinical Functional Assays

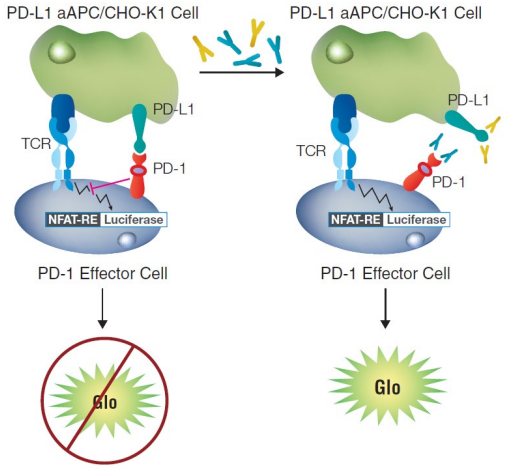
- Arcus in-house data are consistent with preclinical publication on zimberelimab from Gloria Biosciences[1]

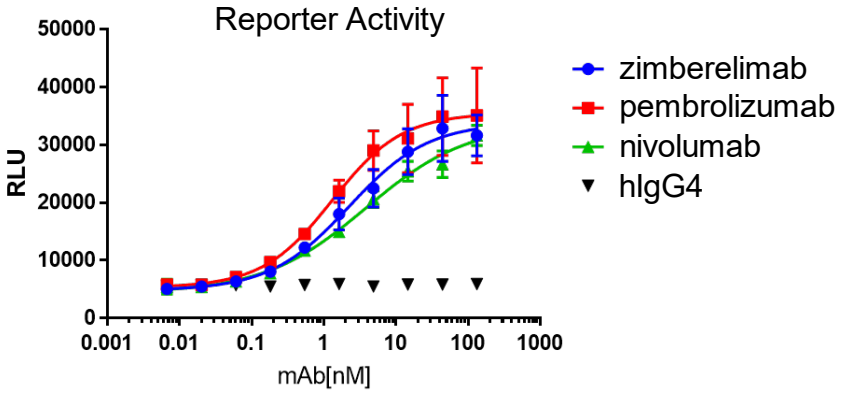
Human PBMC Superantigen Stimulation




Jurkat Reporter Assay (Promega)




[1]Lou (2023) Front Oncol DOI:10.3389/fonc.2021.736955


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