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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.



2022 FULL YEAR EARNINGS - CORPORATE PRESENTATION

February 28, 2023

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.

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.

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 with a Sustainable R&D Engine

~$1.1B
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

2022 Recap

Dom (TIGIT)
- ✓ ARC-7 topline data and presentation
- ✓ Initiated three new Phase 3 studies
- ✓ Completed enrollment of ARC-7

Etruma / Quemli (A2R/ CD73)
- ✓ Initiated two new Phase 2 studies

AB521 (HIF-2α)
- ✓ Completed healthy volunteer study demonstrating best in class potential
- ✓ Initiated Phase 1b study in patients

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 | AB801 | AB375

oncology | oncology | inflammation

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 Presentation Dec. 2022

SELECT PFS TAKEAWAYS:

- With median follow-up of 12 months, **mPFS was 12.0 months for the doublet (DZ) and 10.9 months for triplet (EDZ) vs. 5.4 months** for zim monotherapy
- **Doublet PFS HR=0.55; triplet HR=0.65**
- Doublet resulted in a longer median PFS than reported for PD-1 or PD-1 + chemo combinations in Phase 3 studies

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

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 (ARC-21)** **dom** + **zim** + FOLFOX	**1L NSCLC, PD-L1 ≥50% (ARC-10)** **dom** + **zim** vs. pembro
		1L / 2L NSCLC (Velocity-Lung) ★ **dom** +/- **zim** +/- **etruma** +/- sacituzumab govitecan	**Stage III, unresectable, PD-L1≥1% NSCLC (PACIFIC-8)** ★ **dom** + durvalumab vs. durvalumab
		1L / 2L NSCLC, All Comers (EDGE-Lung) **dom** +/- **zim** +/- **quemli** +/- chemo	**1L NSCLC, PD-L1 All Comers (STAR-121)** ★ **dom** + **zim** + chemo vs. pembro + chemo vs. **zim** + chemo
		1L NSCLC, PD-L1 ≥50% (ARC-7) **dom** + **zim** +/- **etruma** vs **zim**	**1L Upper GI Malignancies (STAR-221)** **dom** + **zim** + chemo vs. nivo + chemo
AB308 (IgG1 WT anti-TIGIT)	**Expansion Cohort (ARC-12)** **AB308** + **zim**		
QUEMLICLUSTAT (QUEMLI) (CD73)		**1L, 2L Pancreatic Cancer (ARC-8)** **quemli** + **zim** + gem/nab-pac vs. **quemli** + gem/nab-pac	
ETRUMADENANT (ETRUMA) (A2a/A2b)		**2L CRPC (ARC-6)** **etruma** + **zim** + docetaxel vs. docetaxel **etruma** + **zim** + sacituzumab govitecan	
		2L / 3L+ mCRC (ARC-9) **etruma** + **zim** + FOLFOX/bev vs. FOLFOX/bev **etruma** + **zim** + FOLFOX/bev vs. regorafenib	
AB521 (HIF-2a)	**HV Study (ARC-14)**		
	2L+, inc. ccRCC (ARC-20) **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 as early as 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

~$1.1B IN CASH AND INVESTMENTS AS OF 12/31/22 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 2023**
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	• **PFS and OS data expected in 1H23**
ARC-9	**etruma** + **zim** + FOLFOX *vs.* SOC	Randomized Phase 2 in 2L/3L+ mCRC	• **Data expected in 2023**
ARC-20	**AB521** (HIF-2α)	Phase 1/1b in cancer patients	• **Initial dose escalation data in house**
ARC-21	**dom** + **zim** + FOLFOX	Phase 2 in 1L/2L upper GI cancers	• **Preliminary data in house**

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

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ARC-7 RESULTS AND DOMVANALIMAB CLINICAL PROGRAM



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 in manner similar to that of pembrolizumab
- **6th PD-1 antibody approved in China** (Gloria Bio has commercial rights in China)

ETRUMADENANT (A_2R ANTAGONIST)

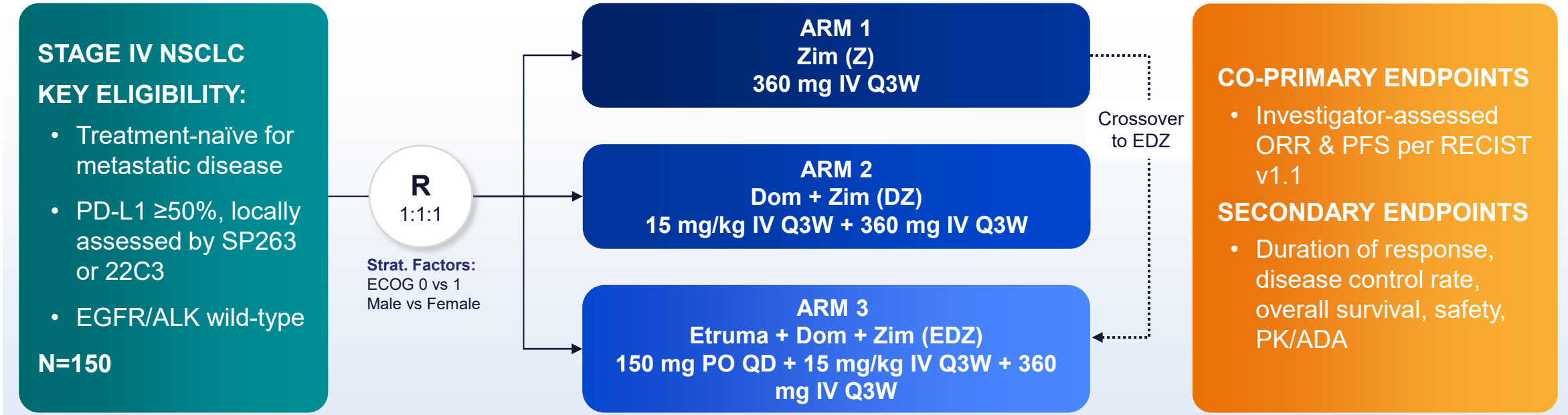
- **First A_2R antagonist to enter clinical development specifically designed for oncology**
- Blocks both $A_{2a}R$ and $A_{2b}R$ receptors
- Multiple advantages over other $A_{2a}R$ antagonists in clinical development:
  - Minimal shift in potency
  - Excellent penetration of tumor tissue
  - Excellent 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**

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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

ITT-13, n (%)	RESPONSE PER RECIST V1.1		
	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)

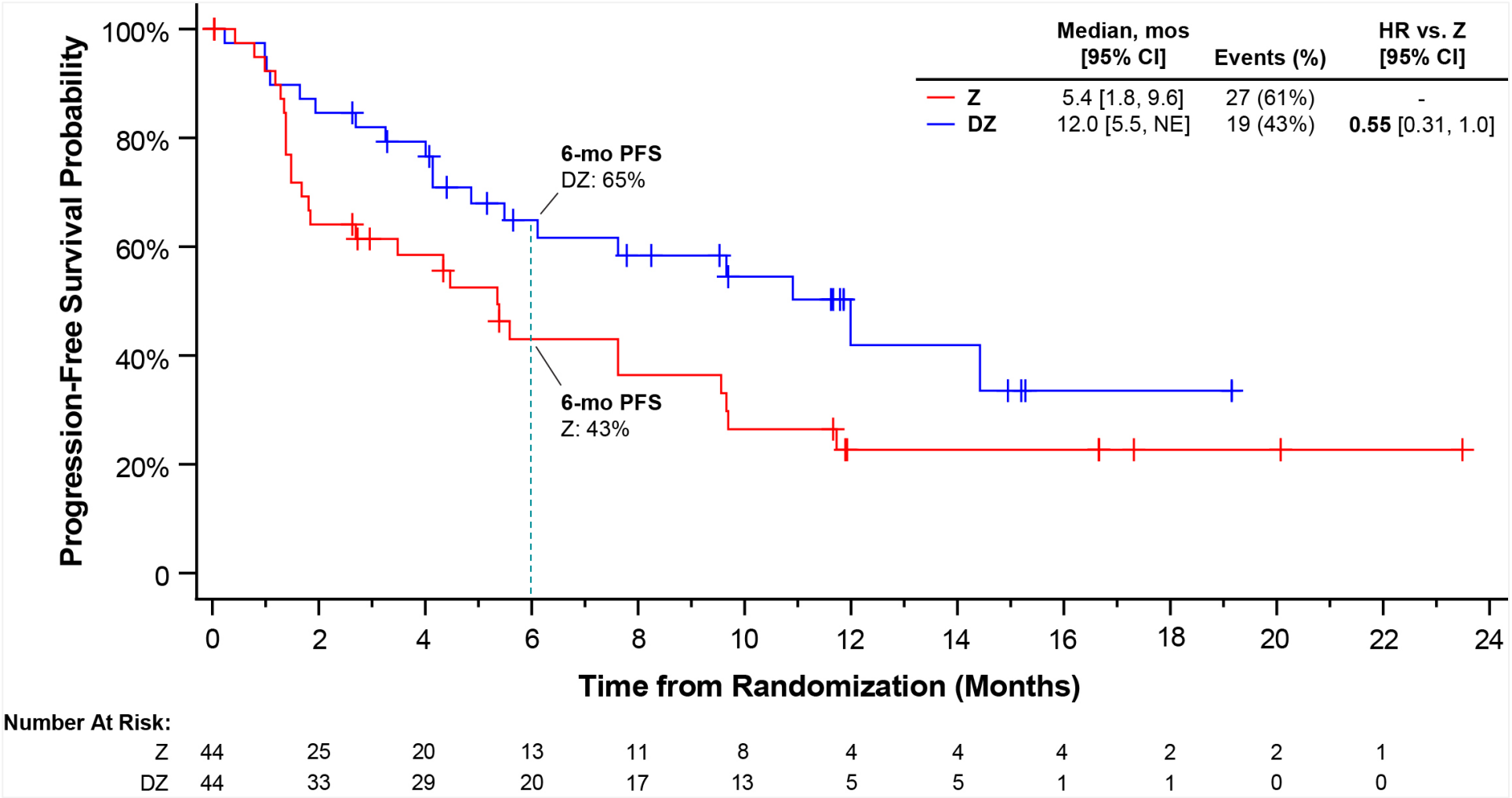
Pending confirmation: subject ongoing study with potential to have confirmed response.
Cannot be confirmed: subject discontinued study without potential to have confirmatory scan.
* Includes subject randomized improperly; not treated.

- 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



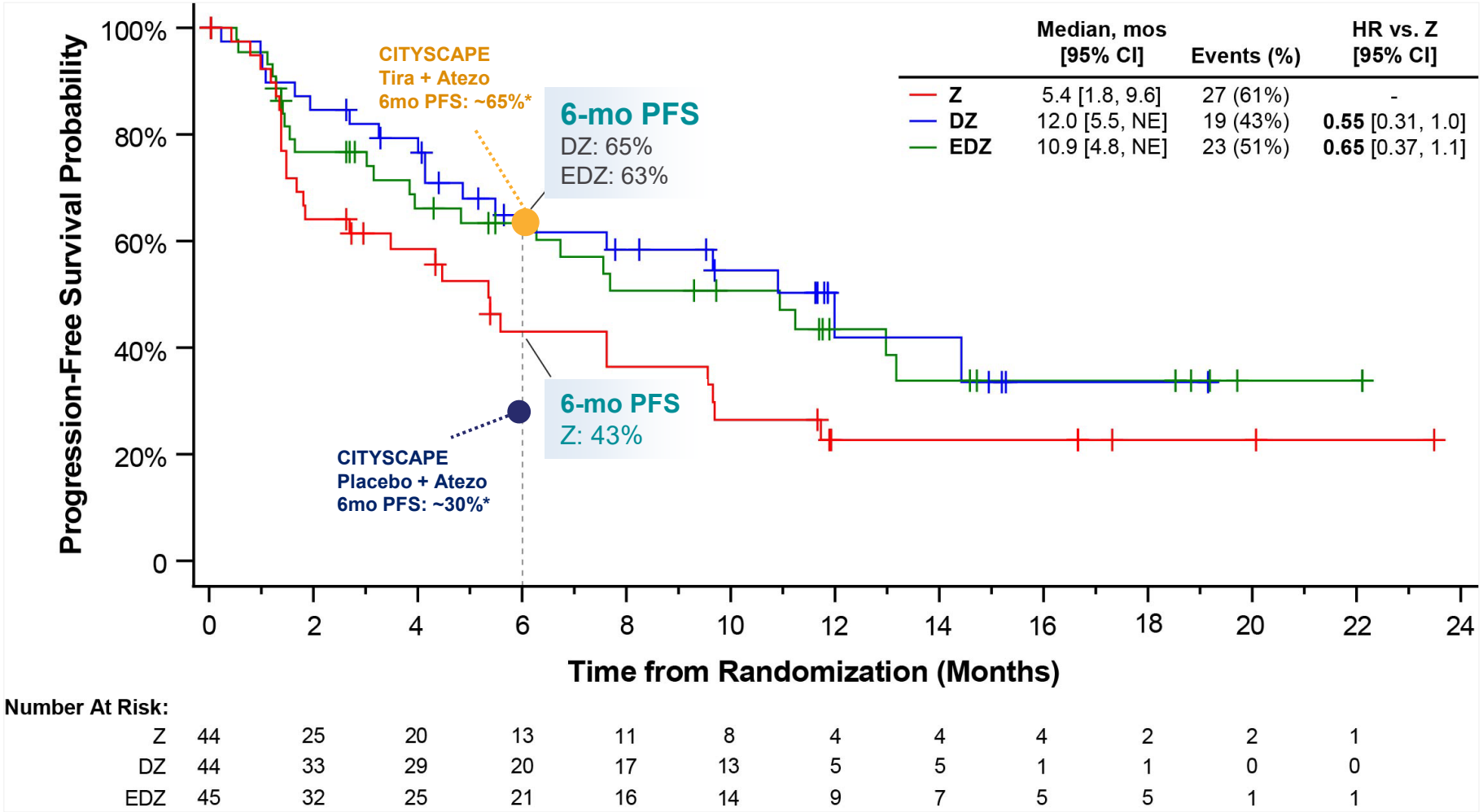
Note: Median follow-up of 12 months

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



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

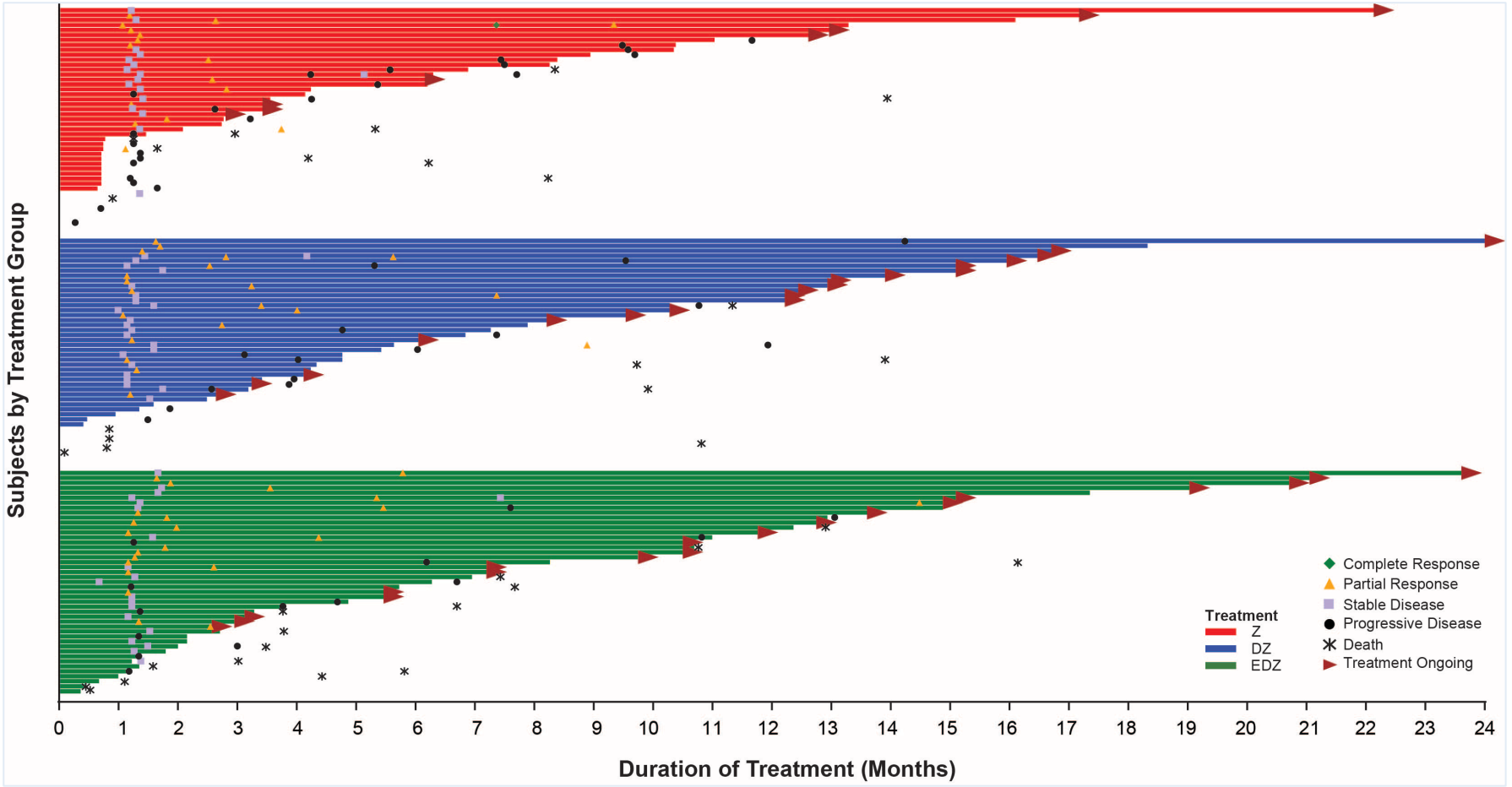
- Earlier PD-1 monotherapy studies likely benefited from 1) long turnaround times for central testing (may have limited rapidly progressing patients) and 2) chemo comparator arm resulting in enrollment of a “fitter” patient population
- Keynote studies conducted scans every 9 weeks which could have benefitted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



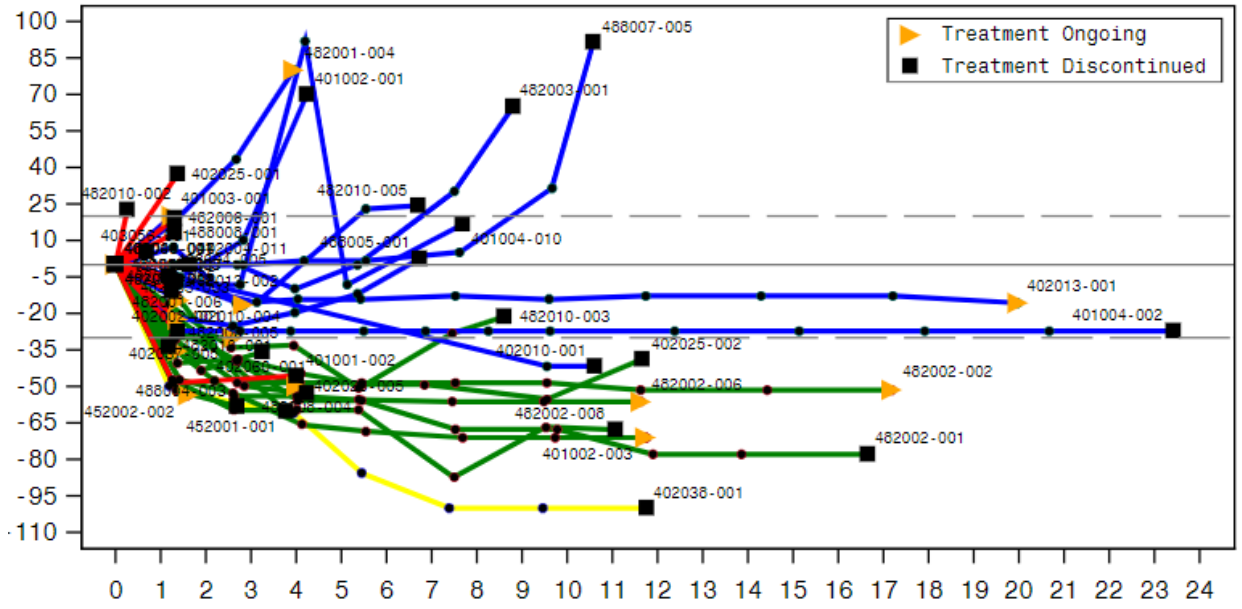
- At the DCO, 31 patients with PRs remain on treatment:
  - **With PRs: Arm 1 (n=5), Arm 2 (n=13), Arm 3 (n=13)**
  - **With SD: Arm 1 (n=3), Arm 2 (n=6), Arm 3 (n=5)**
- Time to initial response ranged from 1.2 – 14.6 months across all arms
- **Median duration of response was not yet reached in any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

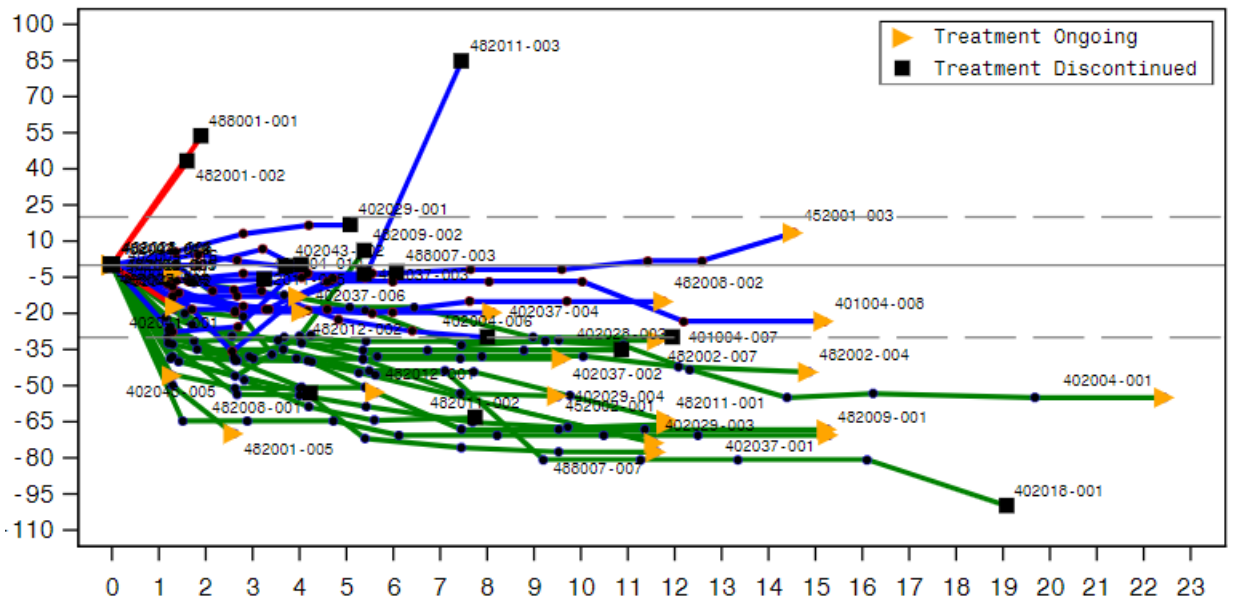
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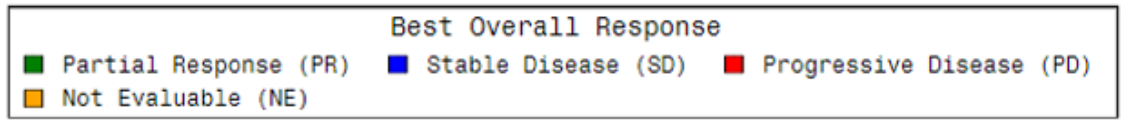
Fewer Rapid Progressors and More Durable Responses are Observed with the Doublet

ZIM MONOTHERAPY



DOM + ZIM

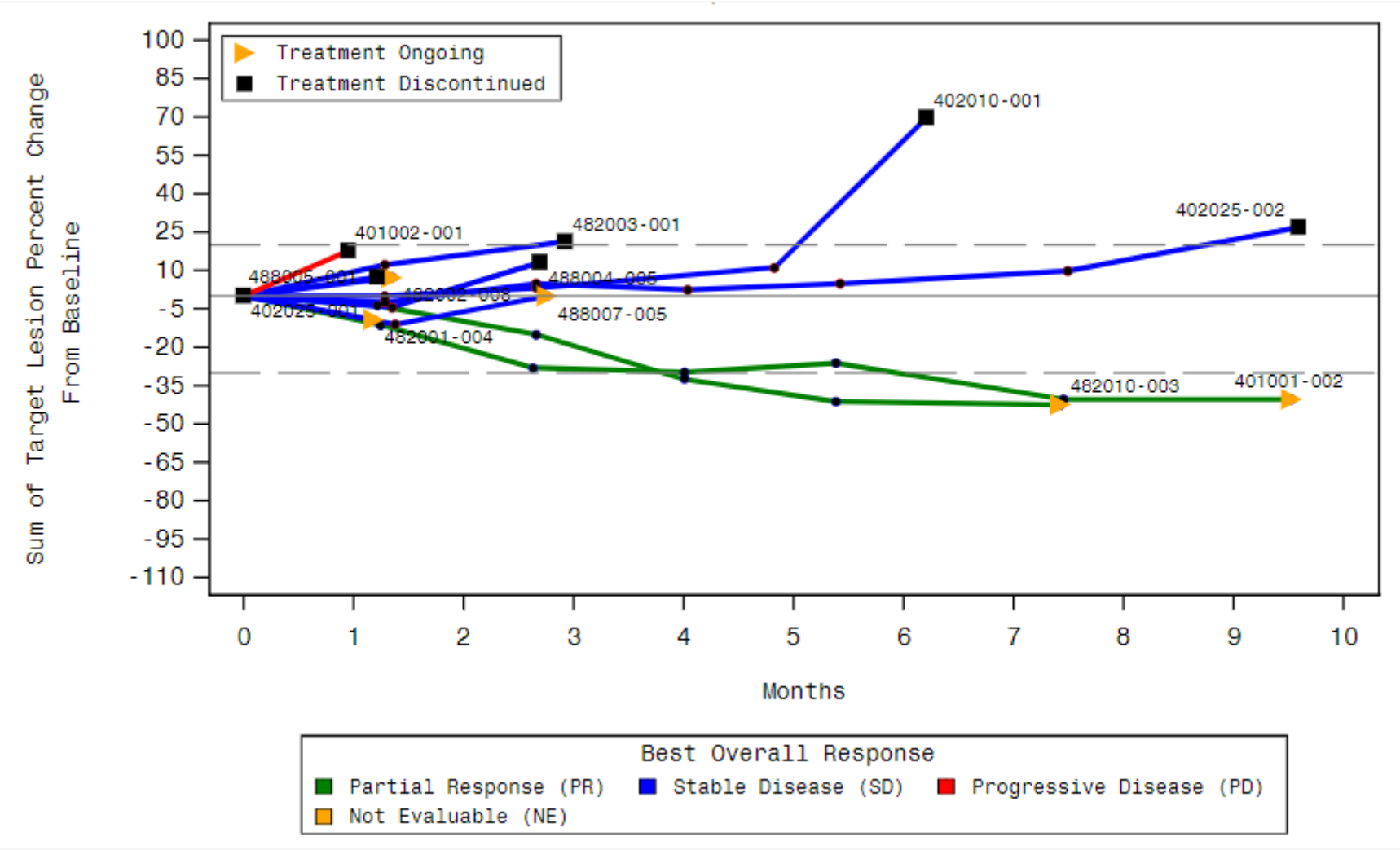




dom: domvanalimab; zim: zimberelimab

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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 Presentation Dec. 2022

SELECT PFS TAKEAWAYS:

- With median follow-up of 12 months, **mPFS was 12.0 months for the doublet (DZ) and 10.9 months for triplet (EDZ) vs. 5.4 months** for zim monotherapy
- **Doublet PFS HR=0.55; triplet HR=0.65**
- Doublet resulted in a longer median PFS than reported for PD-1 or PD-1 + chemo combinations in Phase 3 studies

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

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

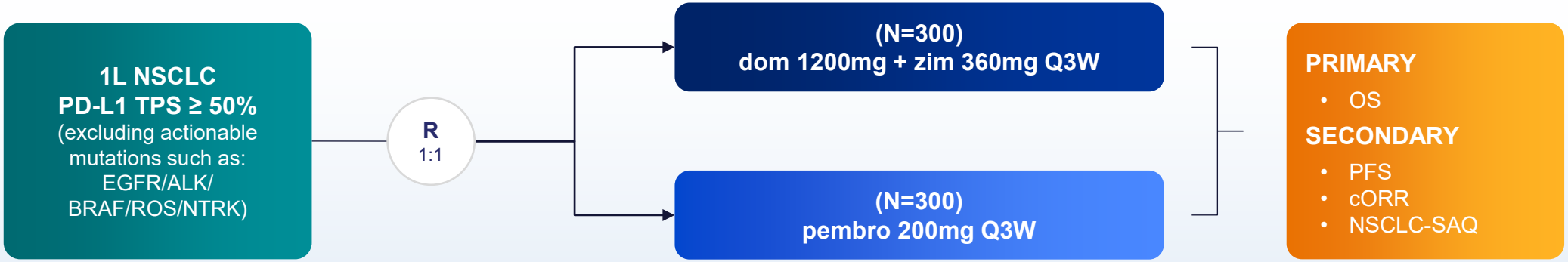
$10B+ addressable market[1]

[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 Trial to Evaluate dom + zim vs. pembro in 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 1L NSCLC All Comer Study evaluating dom + zim + chemo vs. pembro + chemo vs. zim + chemo

STAR-121



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 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

PATIENT POPULATION:

- Patients with unresectable, Stage III NSCLC **who have not progressed following definitive, platinum-based cCRT**
- **EGFR/ALK wt**
- **PD-L1** expression by Ventana SP263 Assay **TC ≥1%**

R
1:1

ARM A (N=430)
domvanalimab Q4W for 12 m
+
durvalumab 1500mg Q4W for 12 m

ARM B (N=430)
durvalumab 1500mg Q4W for 12 m
+
placebo Q4W for 12 m

PRIMARY ENDPOINT:

- PFS in PD-L1 ≥50%

KEY SECONDARY ENDPOINTS

- PFS in ITT (≥1%)
- OS in PD-L1 ≥1%
- OS in ITT
- Safety/tolerability

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 Trial of dom + zim + chemo vs nivo + chemo in Gastric, GEJ and Esophageal Adenocarcinoma

STAR-221

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; 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

ARCUS BIOSCIENCES GILEAD

- 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 PDx agents**
- **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

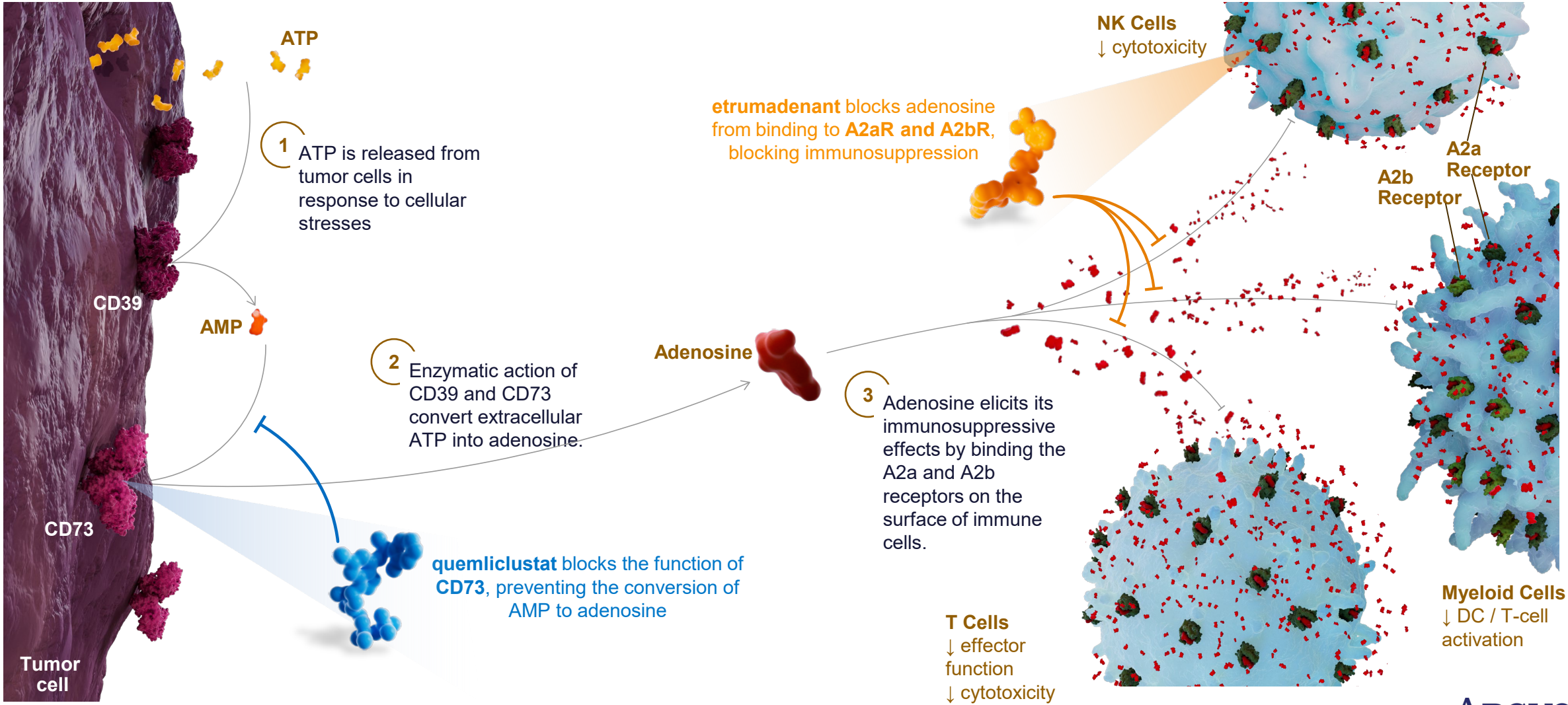
[1]Includes indications relevant to current Arcus/Gilead development program

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CD73-Adenosine Axis Programs



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.

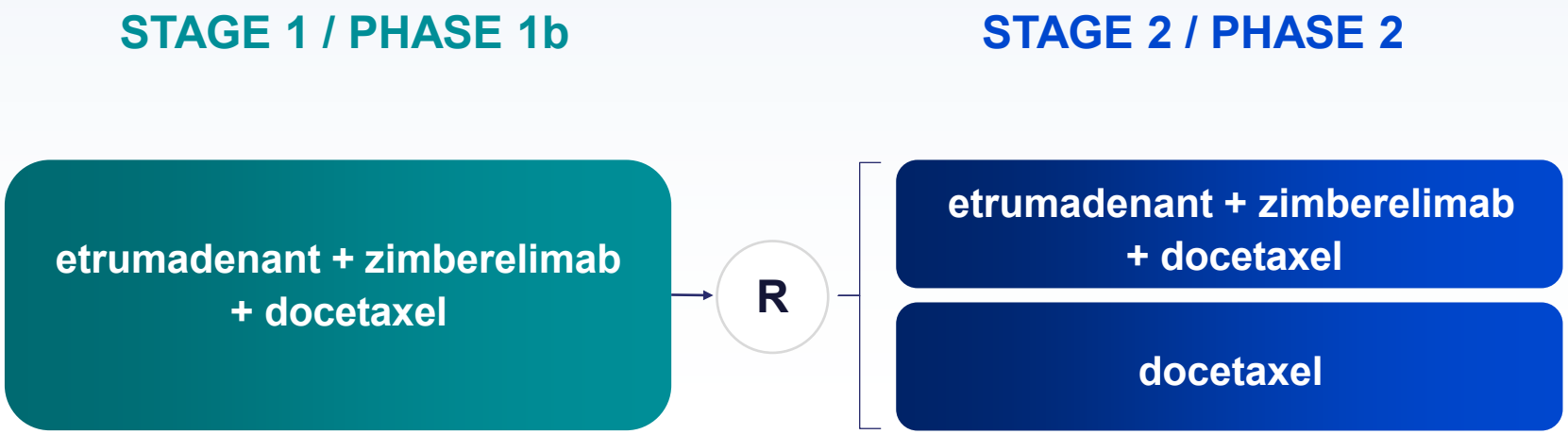
[d] K_B is a measure of a compound's thermodynamic ability to bind/block its target receptor; lower K_B values reflect greater potency for a given receptor.

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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

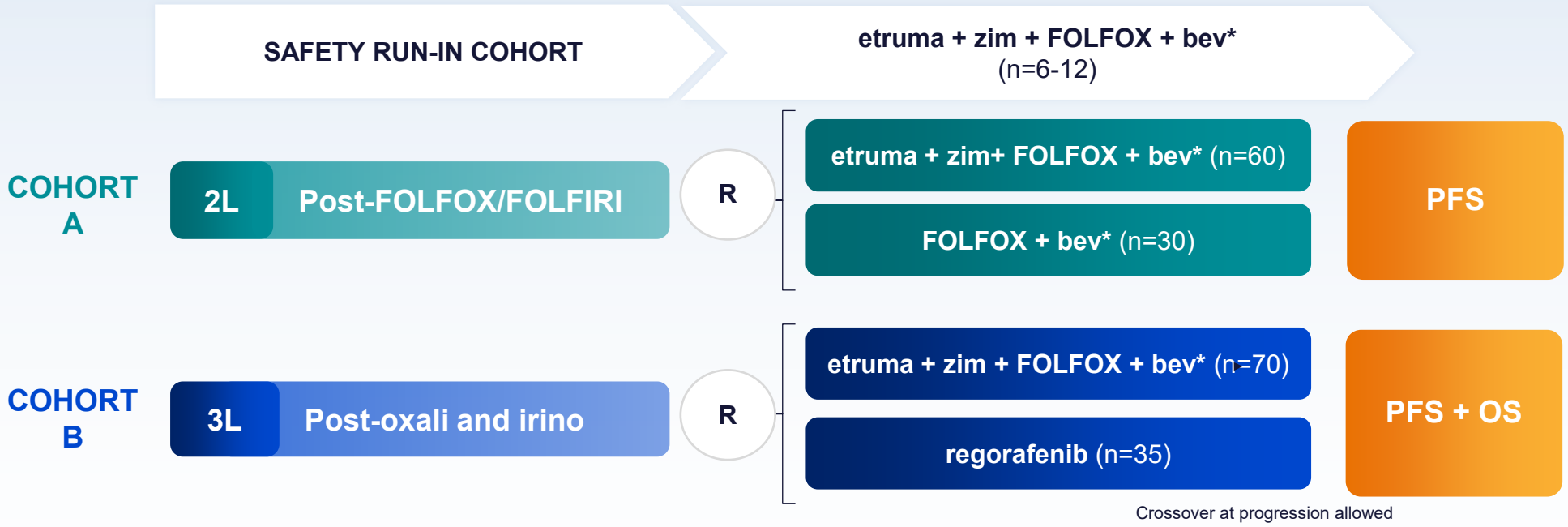


mCRPC: metastatic castrate-resistant prostate cancer; 2L: second-line; ORR: overall response rate; PFS: progression-free survival

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ARC-9 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

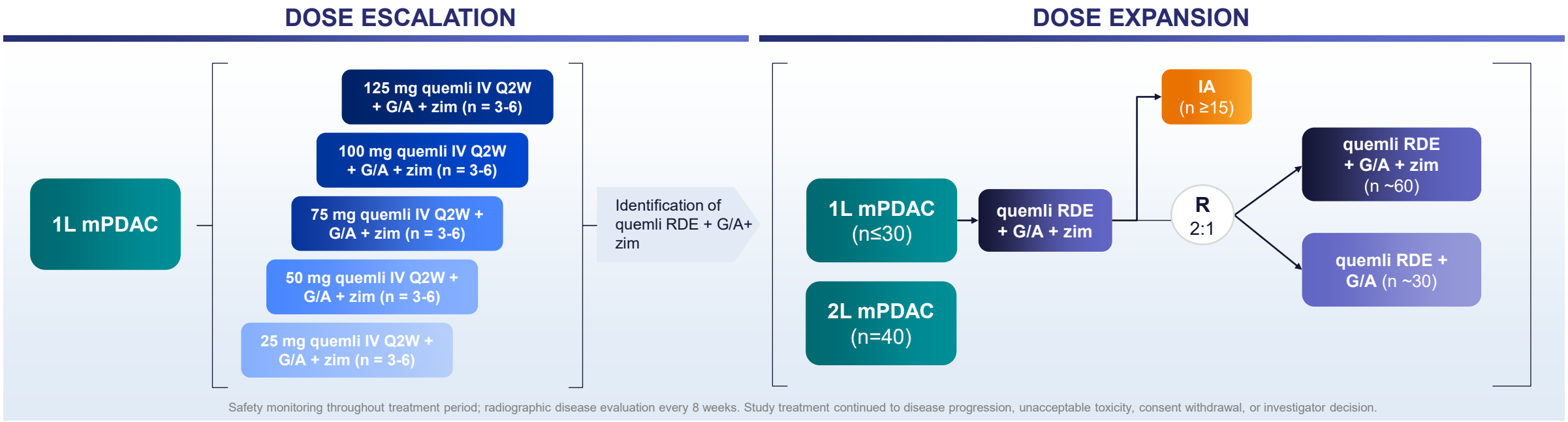
quemliclustat is an investigational molecule and its safety and efficacy have not been established.

-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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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

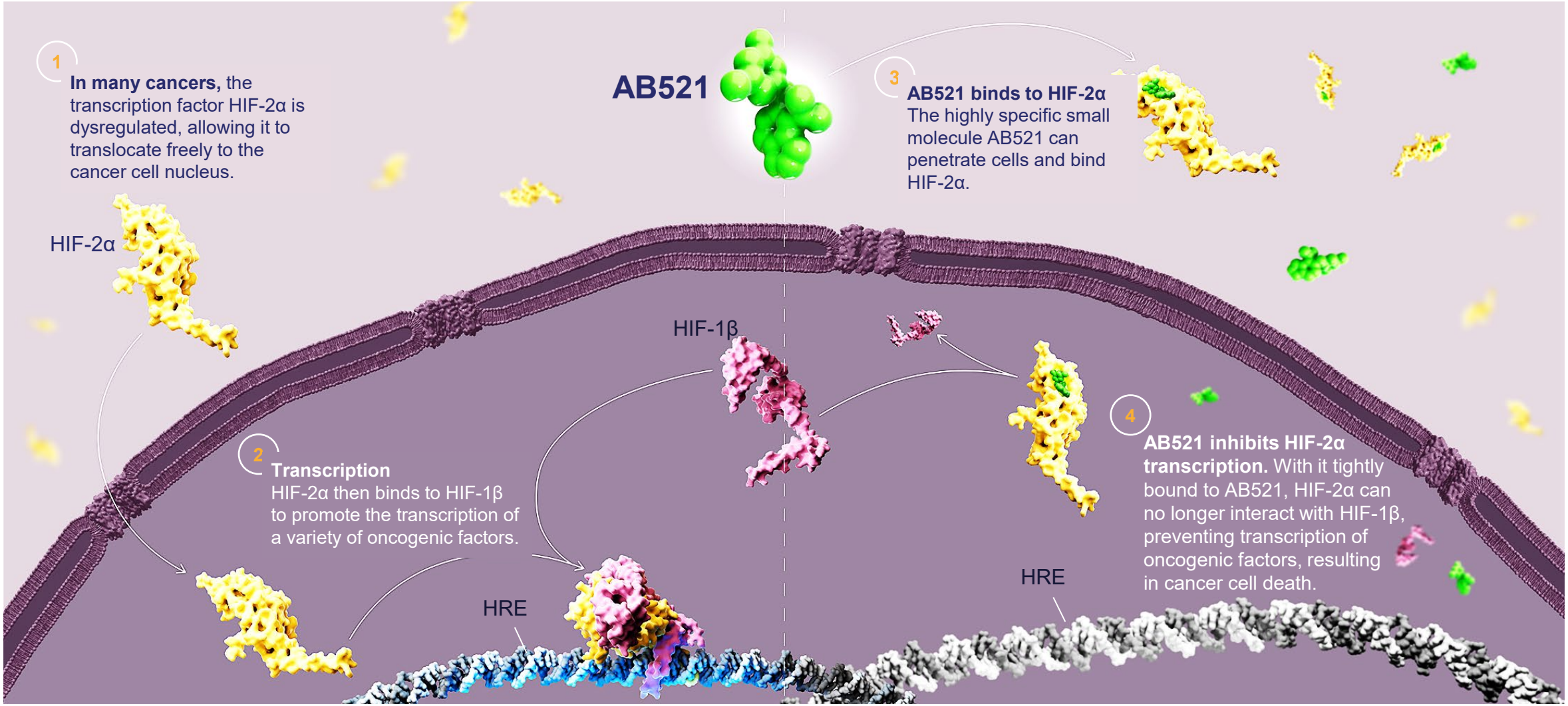
1L, first-line; IV, intravenously; G/A, gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; Q2W, every 2 weeks; R, randomization; RDE, recommended dose for expansion; quemliclustat: quemli; zimberelimab: zim

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HIF-2α Program



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

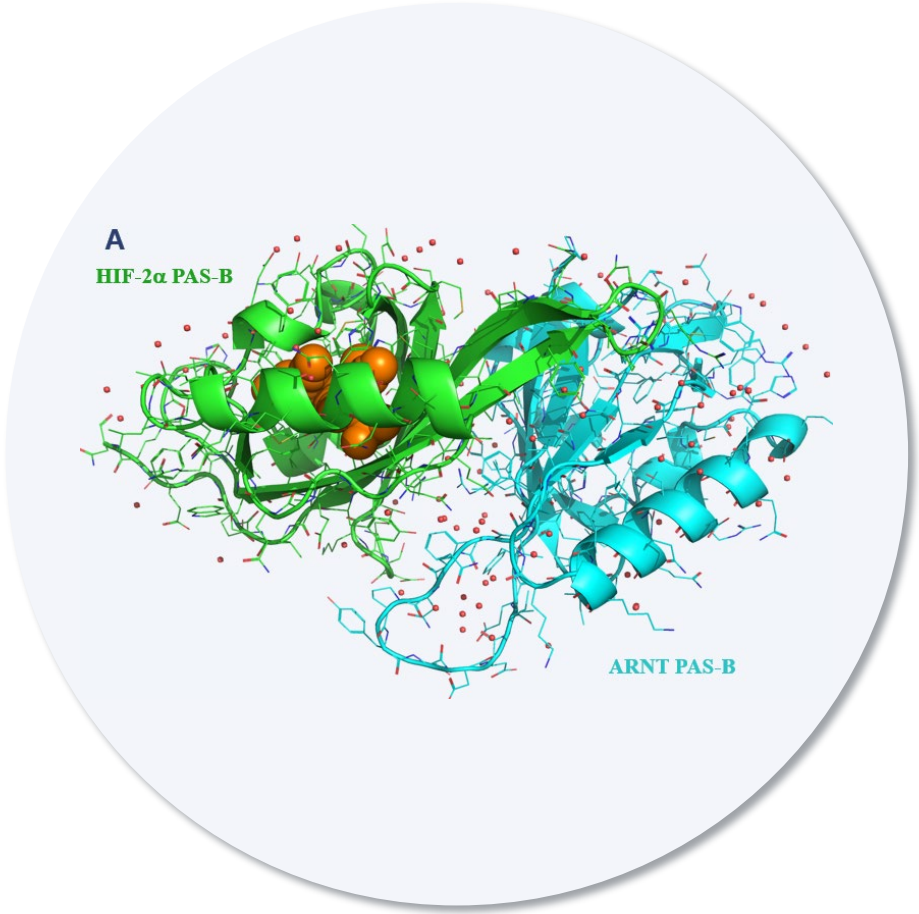
Evaluation of unique combinations and/or unique tumor types

- 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)
	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)

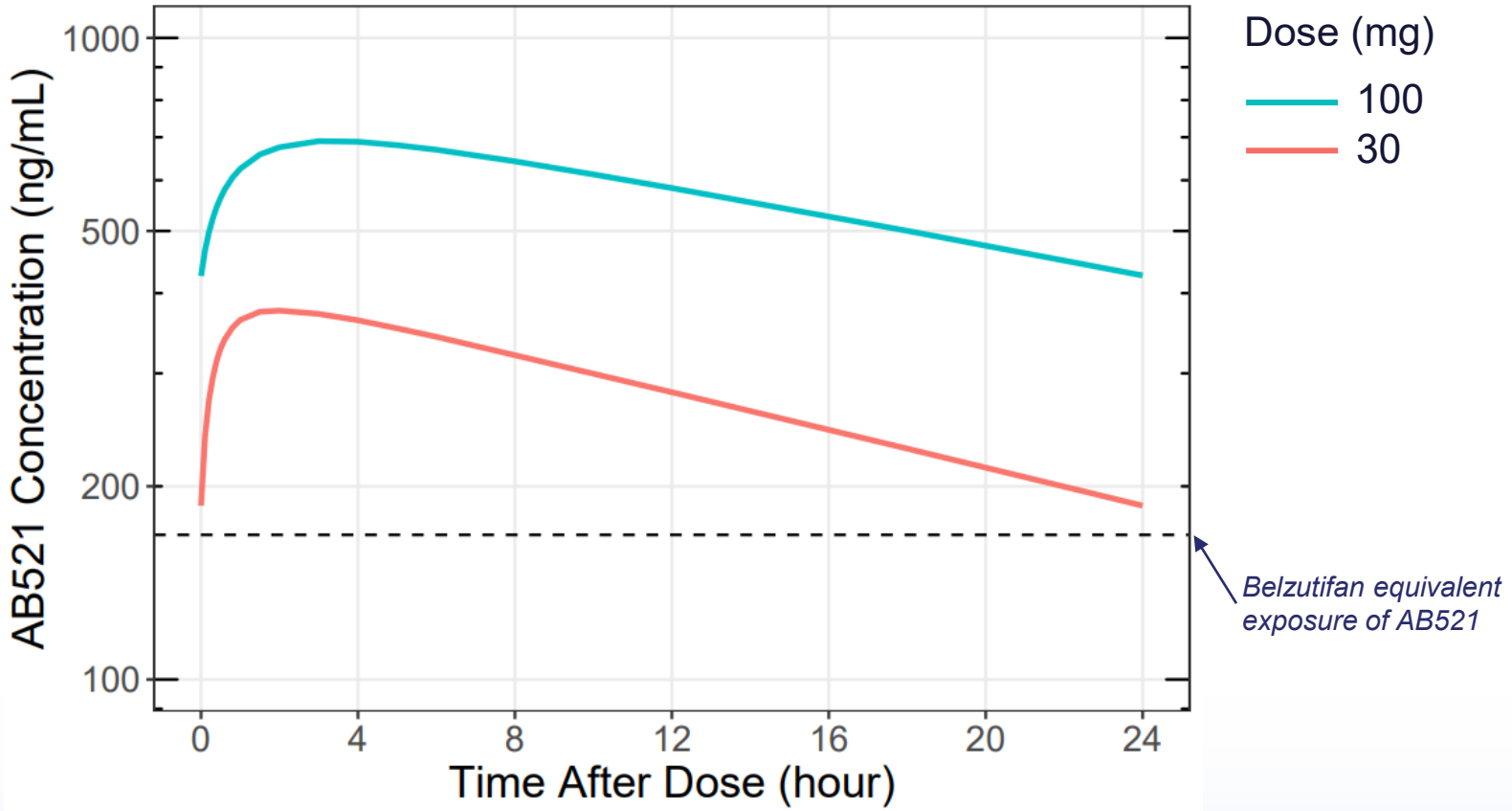


[a] MK-6482 was synthesized according to Xu *et al.* 2019 J Med Chem; DOI: 10.1021/acs.jmedchem.9b00719

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

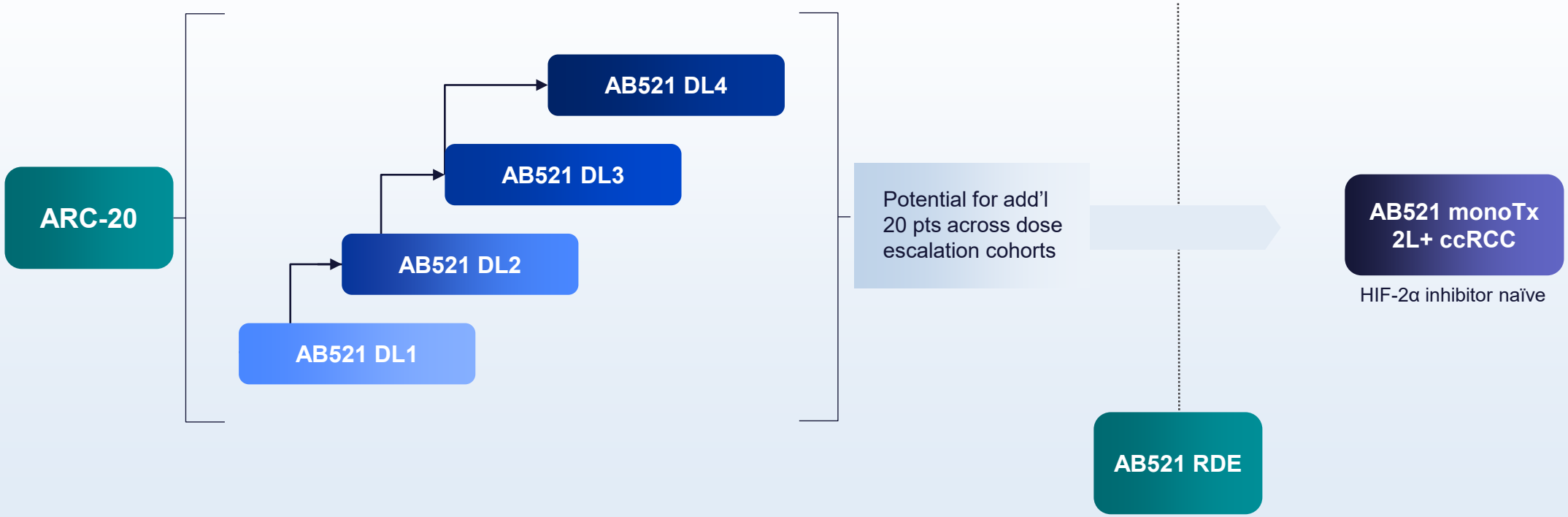
PH 1 DOSE ESCALATION

3+3 design with 21-day DLT window

Solid-tumor patients w/o SOC

PH 1B DOSE EXPANSION

(n=30/cohort)



DL: dose level; RDE: recommended dose for expansion

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APPENDIX



Gilead is Co-Developing Four Optioned Programs with Arcus

GILEAD

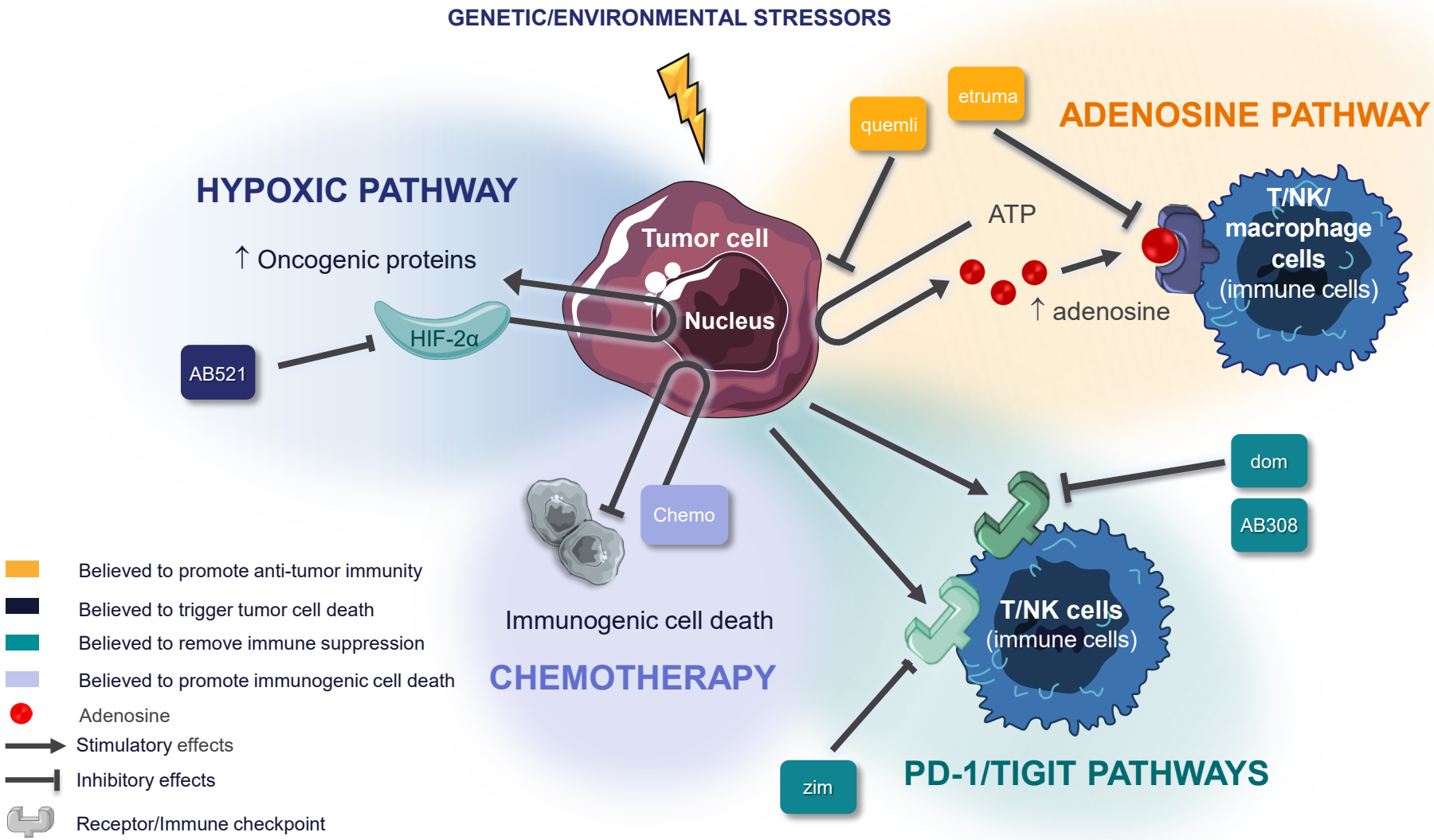
- Currently has rights to five of our clinical-stage candidates through its exercised options:
  - domvanalimab and AB308: anti-TIGIT antibodies
  - etrumadenant: A2a/A2b receptor antagonist
  - quemliclustat: small-molecule CD73 inhibitor
  - zimberelimab: anti-PD-1 antibody
- Arcus and Gilead share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

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 molecules

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

Phase 1 Studies

ARC-20

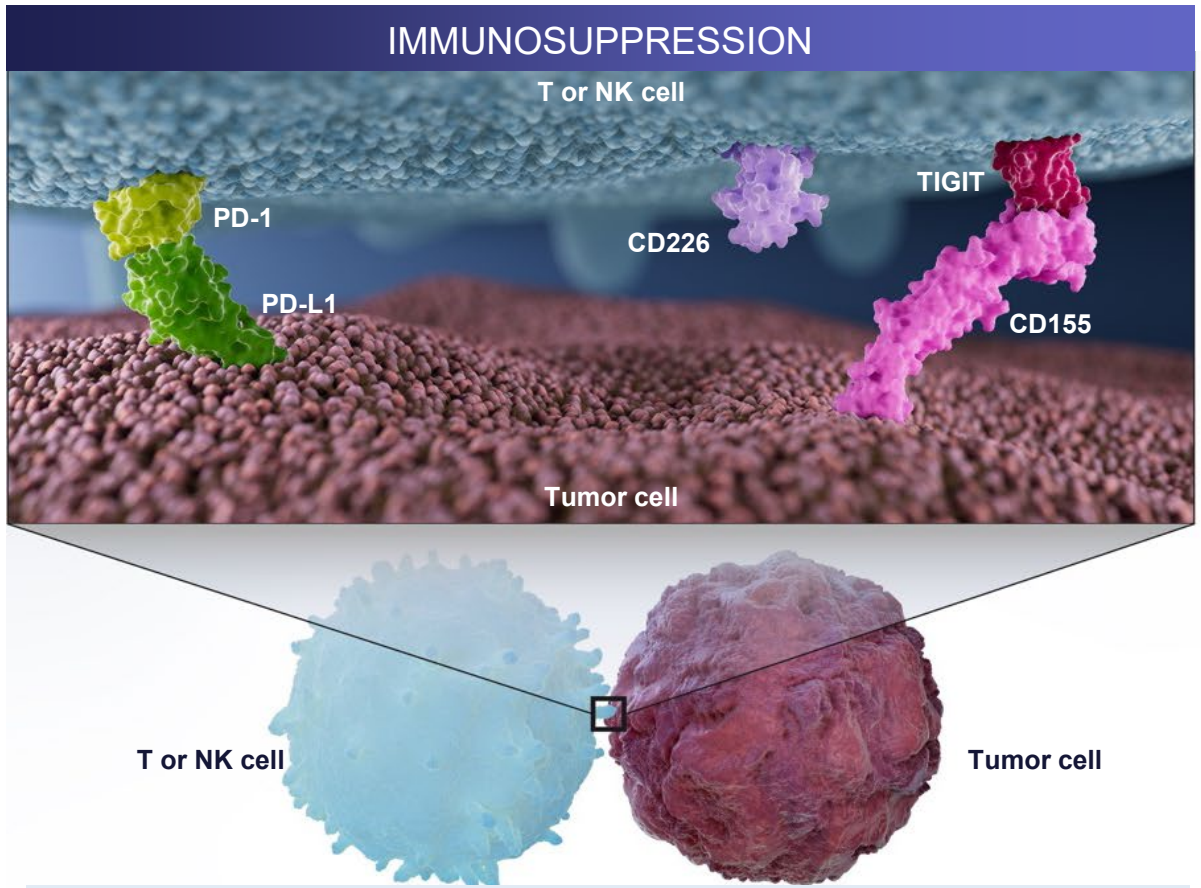
Advancement of next set of molecules into the clinic

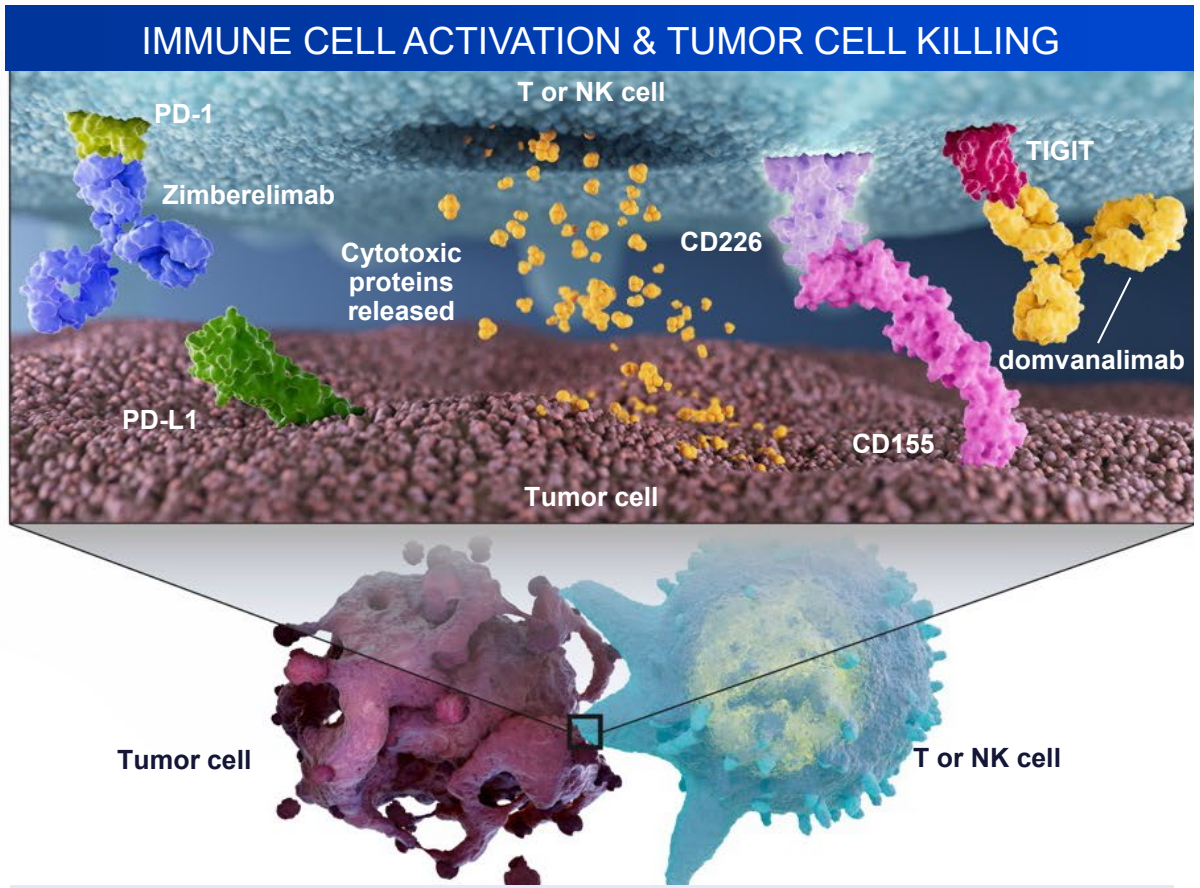
1-2 new development candidates per year

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domvanalimab (dom): Most Advanced Fc-Silent TIGIT Antibody in Development





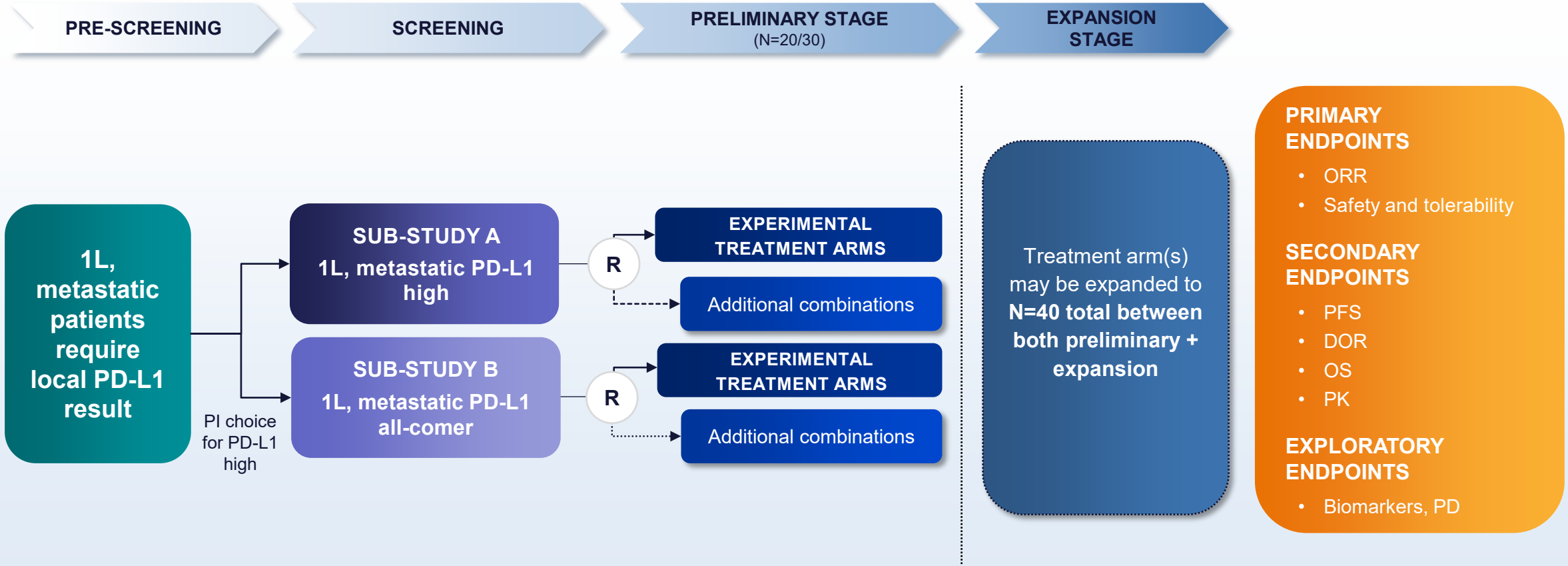
TIGIT is another checkpoint receptor expressed on immune cells that binds CD155 on tumor cells, leading to further evasion of anti-tumor immunity

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



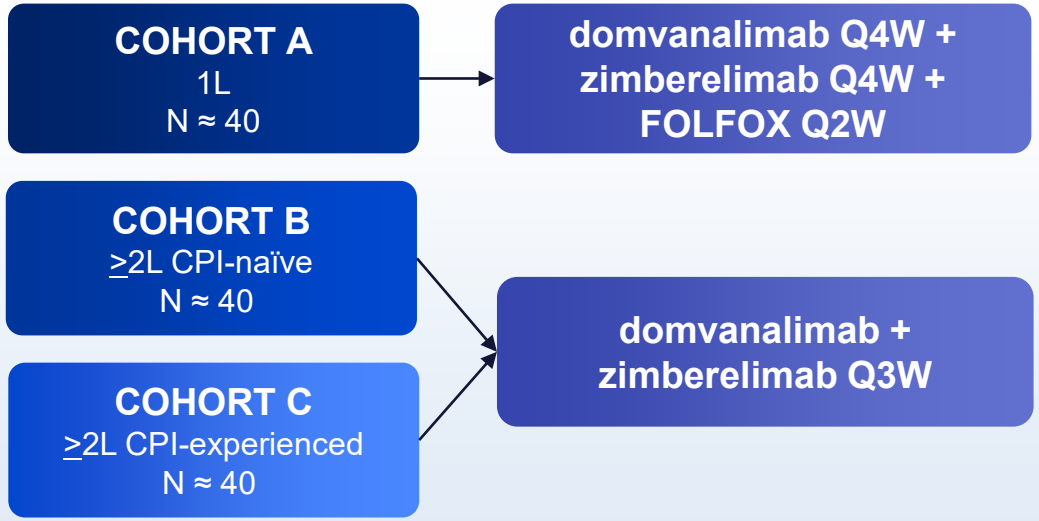
1L, first line; AC, all comer; DOR: duration of response; IO, immuno-oncology; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PD, pharmacodynamics; PD-L1,ORR programmed death-ligand 1; PK, pharmacokinetics; PI, principal investigator; R, randomized.

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Phase 2 Trial to Evaluate dom + zim + chemo vs dom + zim in Advanced Upper Gastrointestinal Tract Malignancies

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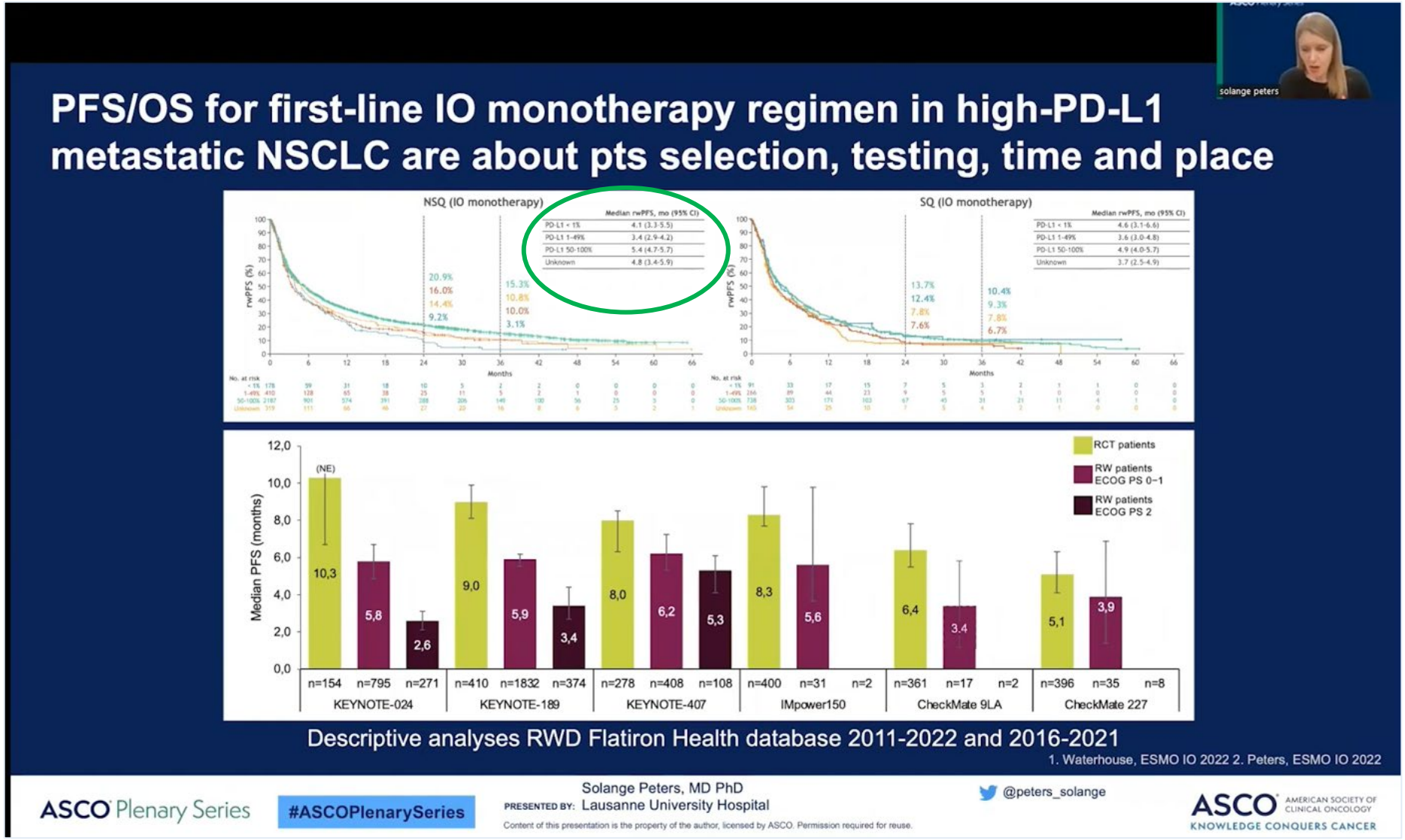
domvanalimab: Compelling Advantages as the First Fc-Silent TIGIT Program that Support Best-in-Class Potential

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

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

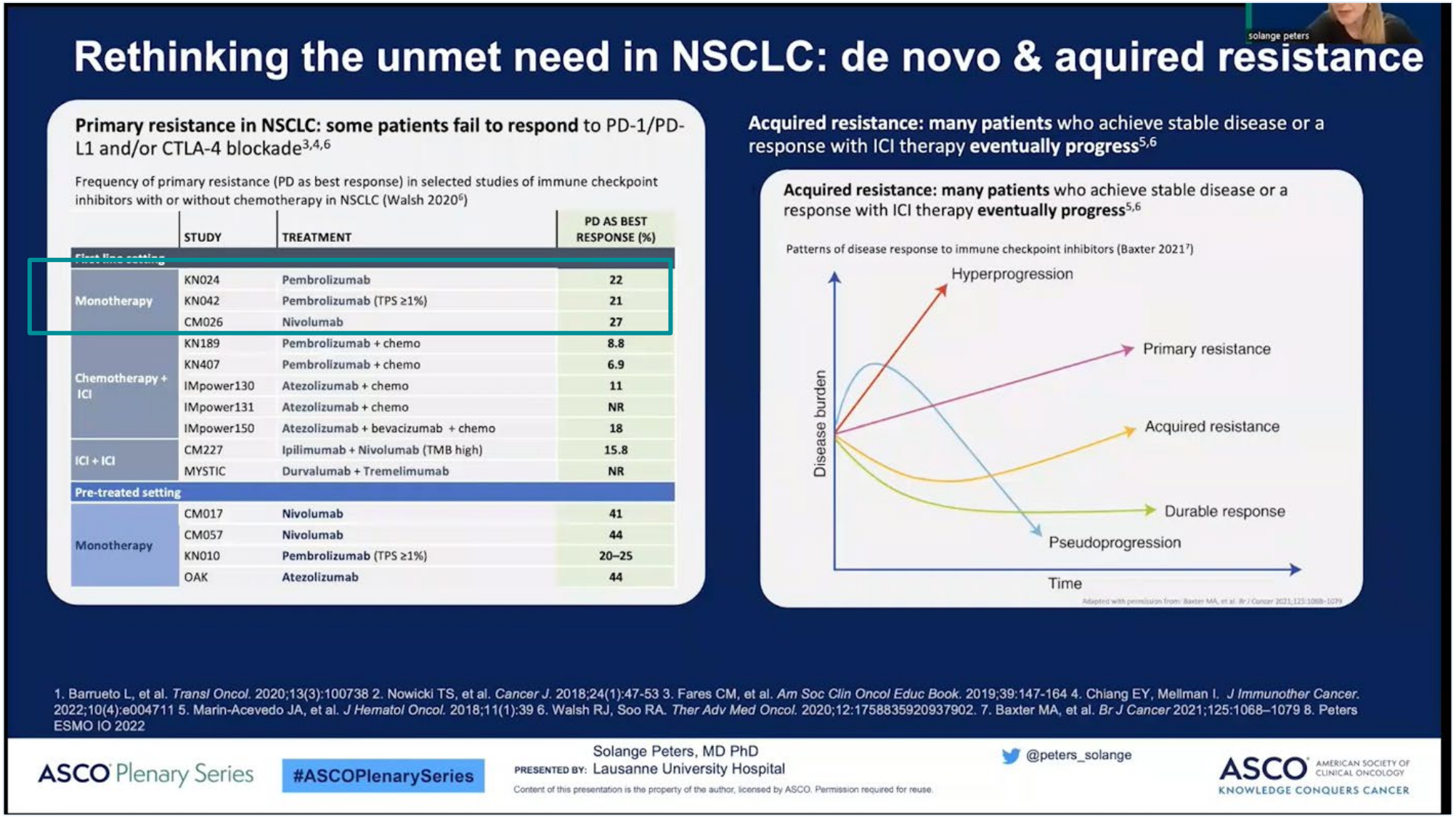
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RWD Presented at ESMO IO 2022 for PD- Antibodies in PD-L1 High NSCLC



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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

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

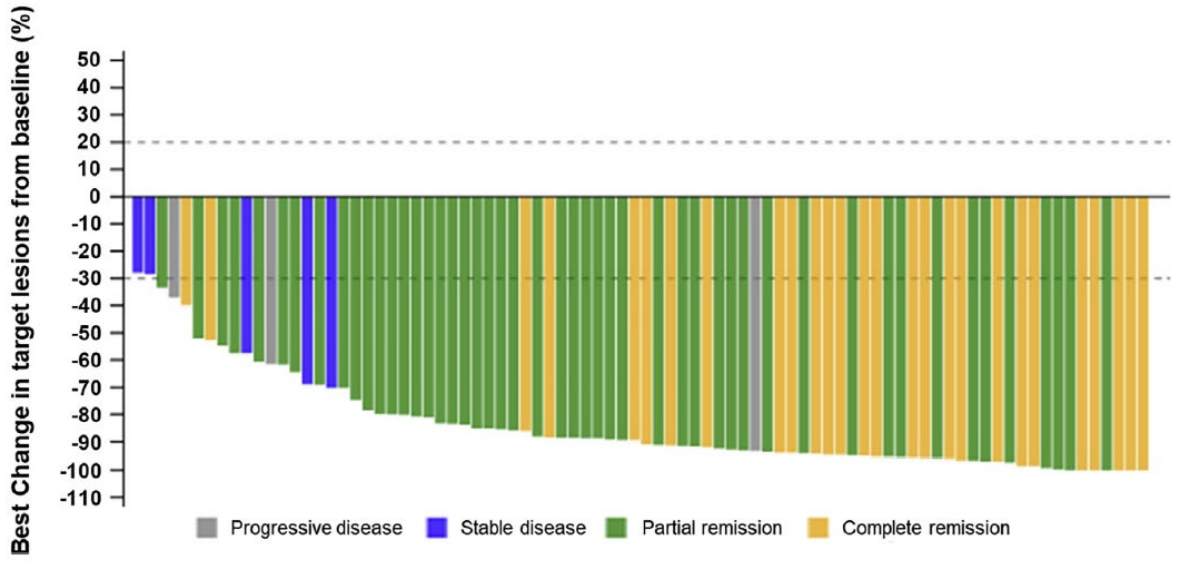


Fig. 1. Waterfall plot of the evaluation of the best overall response by the independent review committee (n = 85).

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%

	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

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)

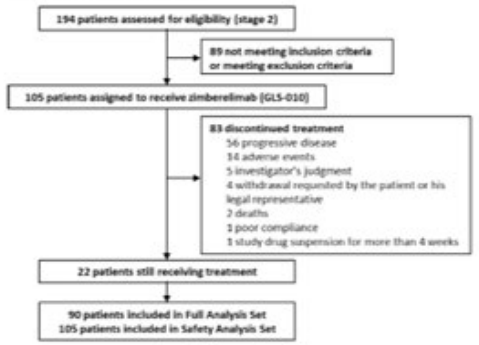


Fig. 1. Patient disposition

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

Efficay	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 (%)	[illegible]
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)

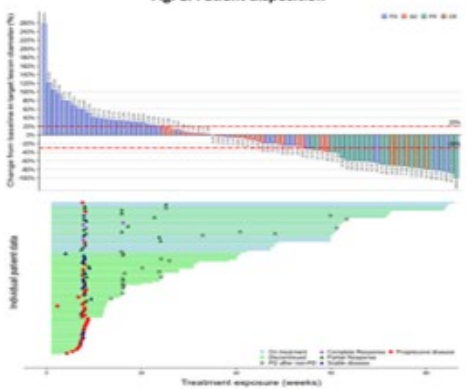


Fig. 2. Waterfall plot and swimmer plot (N=90)

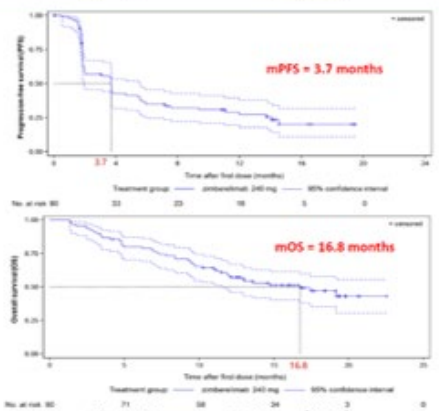


Fig. 3. PFS curve and OS curve (N=90)

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.

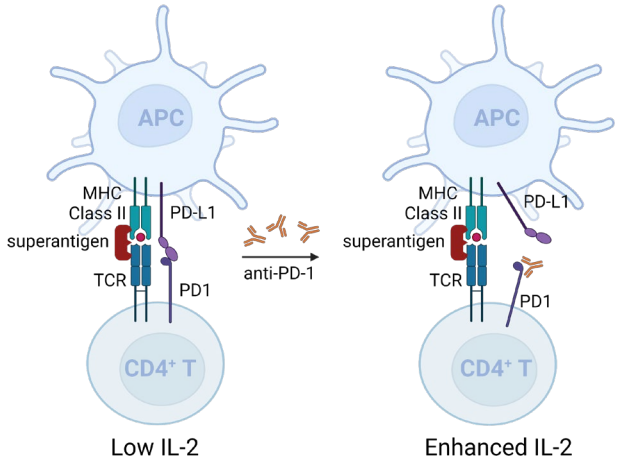
Source: Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study

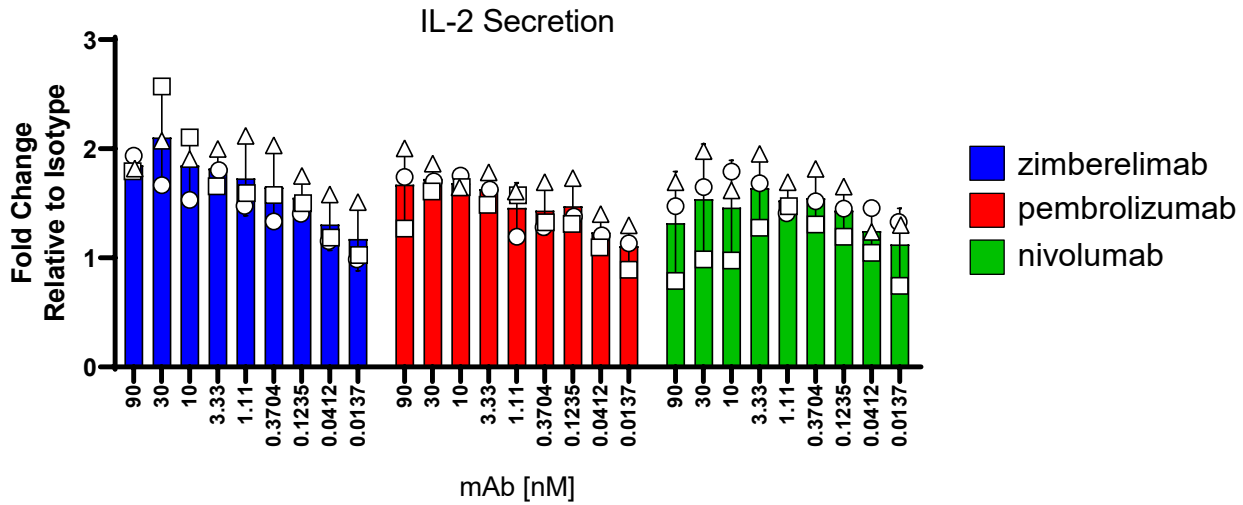
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Zimberelimab Shows Equivalency to Pembro and Nivo in Preclinical Functional Assays

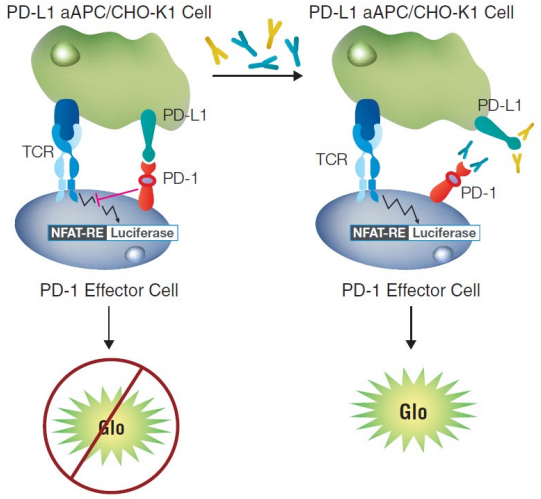
- Arcus in-house data are consistent with preclinical publication on zimberelimab from Gloria Biosciences[1]

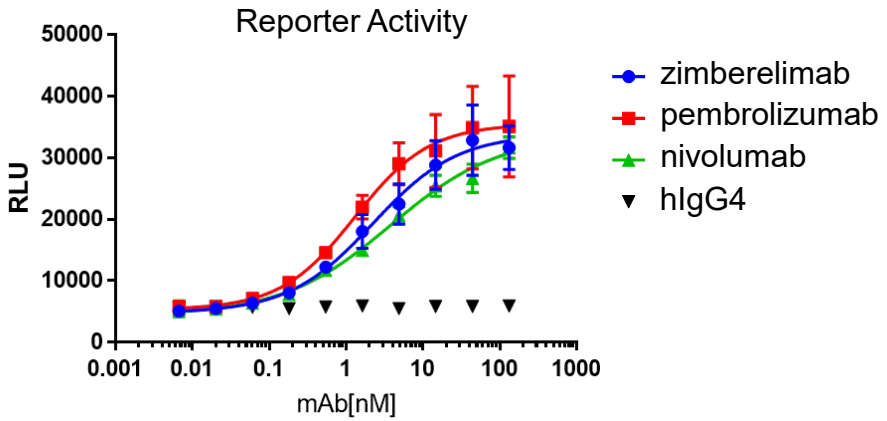
Human PBMC Superantigen Stimulation





Jurkat Reporter Assay (Promega)





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