COMBINING TO CURE®

Arcus is at the forefront of designing combination therapies, with best-in-class potential, in the relentless pursuit of cures for cancer.

CORPORATE PRESENTATION

February 25, 2025

ARCUS BIOSCIENCES

Forward-Looking Statements/Safe Harbor

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 through multiple Phase 3 readouts; potential of our investigational products and portfolio, including our investigational products potential to be best or first in class; anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca; achievement and expected timing of clinical and developmental milestones, including the initiation of clinical trials and the timing of data readouts; excepted timing for clinical data to be available or presented and the scope of such data; launch of our investigational products and such products becoming an available treatment; formulation of our investigational products and the benefits of such formulation; market potential or patient population for any of our investigational products; and possible first to market advantage for any of our investigational products.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions that may cause actual results to differ materially from those contained in any forward-looking statements we may make, including, but not limited to: risks associated with preliminary or interim clinical data or preclinical data not being guarantees that future data will be similar; the unexpected emergence of adverse events or other undesirable side effects; difficulties or delays in initiating, conducting or completing our clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials, all of which may be exacerbated by unfavorable global economic, political and trade conditions; risks associated with our collaboration arrangement with Gilead including our dependence on Gilead for the successful development and commercialization of our investigational products; changes in the competitive landscape; our limited operating history and our ability to manage our growth; 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. 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 periodic reports filed with the U.S. Securities and Exchange Commission filed with the U.S. Securities and Exchange Commission. You should not rely upon forward-looking statements as predictions of future events. Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations.

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Arcus Has Created a Broad Portfolio of Late-Stage Programs, Fueled by a Highly Productive R&D Engine

CASDATIFAN: POTENTIAL BEST-IN-CLASS HIF-2α INHIBITOR

Validated mechanism and compelling market opportunity

Phase 3 initiation expected in 1H25 PEAK-1

DOMVANALIMAB: THREE PHASE 3 STUDIES

STAR-121

1L NSCLC (all comers)
Ongoing

STAR-221

1L Gastric
Approaching Ph 3 Data

PACIFIC-8

Stage 3 NSCLC
Ongoing

WORLD-CLASS DRUG DISCOVERY

Small molecules focused on oncology and I&I

AB801
Potential best-in-class AXL inhibitor in phase 1/1b

>$1 BILLION IN CASH*

Funded through multiple Phase 3 readouts

1H25: first half of 2025; 1L: first-line; 2L: second-line; B: billion; I&I: immunology & inflammation; NSCLC: non-small cell lung cancer
R&D: research & development

* as of December 31, 2024, adjusted for $150 million financing announced in February 2025; includes cash, cash equivalents and marketable securities

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Three Late-Stage Programs Targeting Substantial Market Opportunities and Unmet Medical Need

Designed to improve upon the current standard of care

	PHASE 3 TRIAL NAME	INDICATION	PATIENTS (MAJOR MARKETS[1,2])	MARKET POTENTIAL (MAJOR MARKETS[2])	COMMERCIAL RIGHTS
CAS HIF-2α small molecule inhibitor	PEAK-1	Post-IO ccRCC	19K	**~$2B**	Arcus
	AstraZeneca eVOLVE portfolio	IO-naive ccRCC	21K	**~$3B**	
DOM (+ ZIM) Fc-silent anti-TIGIT mAb + anti-PD-1 mAb	STAR-221	1L Gastric/GEJ/EAC – all comers	105K	**~$3B**	Arcus / Gilead
	STAR-121	1L NSCLC – all comers	307K	**~$10B**	
	PACIFIC-8	Stage 3 NSCLC, PD-L1>1%	35K[3]	**~$2B**	
QUEMLI Small molecule CD73 inhibitor	PRISM-1	1L PDAC	109K	**>$4B**	Arcus / Gilead

1L: first line; 2L: second line; 3L: third line; B: billion; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immuno-oncology; mAb: monoclonal antibody; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat; zim: zimberelimab

1. Drug Treatable Addressable Populations (Major Markets, 2024); Decision Resources Group, Arcus analysis – see appendix for breakout of US patients
2. Major Markets (US, EU5, JP) - total projected 2034 PD-(L)1 + TIGIT opportunity, Q opportunity & Hif2α opportunity
3. cCRT responding patients

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2024 Validating Data Readouts Across the Program Portfolio

CONFERENCE	STUDY	PRODUCT	DATA READOUT
ENA 2024 EORTC NCI AACR 36th Symposium	ARC-20	**cas** (HIF-2α)	Improvement across all efficacy measures evaluated relative to belzutifan data in LITESPARK-005
Society for Immunotherapy of Cancer sitc2024 NOV. 6-10 | HOUSTON	ARC-10	**dom (+zim)** (TIGIT+PD-1)	0.64 OS hazard ratio for dom/zim vs. zim in 1L PD-L1 high NSCLC
2024 ASCO ANNUAL MEETING	EDGE-Gastric	**dom (+zim)** (TIGIT+PD-1)	~13 months mPFS vs. 7-8 months for benchmark data in 1L gastric/GEJ/EAC
2024 ASCO ANNUAL MEETING	ARC-9	**etruma** (adenosine, dual A2R)	19.7 months mOS vs. 9.1 months for regorafenib in 3L CRC
ASCO Gastrointestinal Cancers Symposium	ARC-8	**quemli** (adenosine, CD73)	15.7 months mOS vs. 9 –11 months for benchmark data in 1L pancreatic cancer

1L: first-line; 3L: third-line; cas: casdatifan; CRC: colorectal cancer; dom: domvanalimab; EAC: esophageal adenocarcinoma; etruma: etrumadenant; GEJ: gastro-esophageal junction; mOS: median overall survival; mPFS: median progression-free survival; NSCLC: non-small cell lung cancer; quemli: quemliclustat; zim: zimberelimab

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Multiple Data Milestones in 2025 Expected to Enhance Clarity on Multi-Billion $ Opportunities for Casdatifan and Domvanalimab

TIMING	STUDY	PRODUCT	EVENT
Early 2025	ARC-20	**Casdatifan**	✓ Updated data from 50mg BID, 50mg QD (ORR, PFS) ✓ Initial data from 100mg QD tablet (ORR) mono cohort
Mid 2025	ARC-20	**Casdatifan**	• Safety and initial efficacy data for the cas + cabo cohort
Fall 2025	EDGE-Gastric	**Domvanalimab**	• Phase 2 OS data for dom + zim + chemo in 1L Gastric Cancer
Fall 2025	ARC-20	**Casdatifan**	• More mature safety and efficacy data for all cohorts
2026 (event-driven)	STAR-221	**Domvanalimab**	• Phase 3 data for dom + zim + chemo vs. nivo + chemo in 1L Gastric Cancer

1L: first-line; BID: twice daily; chemo: chemotherapy; dom: domvanalimab; mono: monotherapy; nivo: nivolumab; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; QD: once daily; zim: zimberelimab

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Casdatifan (HIF-2α) in ccRCC

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ARC-20 Results Presented at ASCO GU Support Casdatifan Having a Potential Best-in-Class Profile for ccRCC

Across all three expansion cohorts
(approximately 90 patients)

- ✓ **Lower primary progressive disease (PD) rate** – approximately half the rate observed for belzutifan in LITESPARK-005
- ✓ **Higher ORR*, despite less maturity** – mid-20s to low-30s vs. high teens to low-20s for belzutifan
- ✓ **High DCR** – 80%+ of patients experience some clinical benefit
- ✓ **Highly durable responses** – only 2 (of 26) responders have progressed across all 3 cohorts
- ✓ **Longer mPFS** -- 9.7 mos for 50mg BID / not reached (NR) for other cohorts
- ✓ Comparable rates of on-target and SAEs

100mg QD tablet[1]
(Selected Phase 3 dose and formulation)

15%	Primary PD rate
33%	ORR** (with short follow-up)
85%	DCR
1.6 months	Time to Response
NR	mPFS not reached

**ORR throughout this presentation refers to confirmed ORR unless otherwise noted
*based on casdatifan in ARC-20, a Phase 1 study, and belzutifan in LITESPARK-005, a Phase 3 study
1. Median (range) follow-up for the 100mg QD cohort is 5 (2–6+) months (ongoing)
Source for LITESPARK-005: Albiges L. et al. Abstract LBA88, ESMO 2023

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ARC-20 is a Phase 1 Dose-Escalation and Dose-Expansion Study of Casdatifan

DOSE ESCALATION

Patients with advanced solid tumors

Casdatifan monotherapy

- **200mg QD**
- **150mg QD**
- **50mg BID**
- **50mg QD**
- **20mg QD**

DOSE EXPANSION

N = ~30 per cohort

2L+ ccRCC
Casdatifan mono
50mg BID capsule

2L+ ccRCC
Casdatifan mono
50mg QD capsule

2L+ ccRCC
Casdatifan mono
100mg QD tablet

2L+ ccRCC
Casdatifan mono 150mg QD

Post-IO ccRCC
Casdatifan 100mg QD + Cabozantinib 60mg QD

Favorable-risk 1L ccRCC
Casdatifan mono 100mg QD

1L ccRCC
Casdatifan 100mg QD + Zimberelimab 360mg Q3W

Post-IO ccRCC
Casdatifan mono 100mg QD

KEY INCLUSION CRITERIA

- At least 1 measurable lesion per RECIST v1.1
- Adequate organ and marrow function

PRIMARY OUTCOMES

- AEs
- DLTs

SECONDARY OUTCOMES

- ORR
- PK/PD

EXPLORATORY OUTCOMES

- PFS
- Biomarkers

RECIST: Response Evaluation Criteria in Solid Tumors

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Key Efficacy Measures All Compare Very Favorably to Contemporary Benchmark Studies Despite Shorter Follow-up

Efficacy-Evaluable Population[1,2]	Casdatifan 50mg BID (n = 32)	Casdatifan 50mg QD (n = 28)	Casdatifan 100mg QD (n = 27)
Confirmed ORR (n) [95% CI]	**25% (8)** [11.5, 43.4]	**32% (9)**** [15.9, 52.4]**	**33% (9)** [16.5, 54.0]
Med time to response, mos.	**2.8**	**4.1**	**1.6**
Best Overall Response (n)			
CR	0% (0)	4% (1)	0% (0)
PR	31% (10)*	29%(8)	33% (9)
SD	50% (16)	54% (15)	52% (14)
PD	**19% (6)**	**14% (4)**	**15% (4)[3]**
Disease control rate [95% CI]	**81%** [63.6, 92.8]	**86%** [67.3, 96.0]	**85%** [66.3, 95.8]
Median follow-up, months (range)	15 (7–19+)	12 (9–14+)	5 (2-6+)
Median progression free survival	**9.7 months**	**Not reached**	**Not reached**

*** In the 50mg BID cohort, one unconfirmed responder remains on treatment.**
****In the 50mg QD cohort, ORR includes one unconfirmed responder who became a confirmed responder after the DCO.**

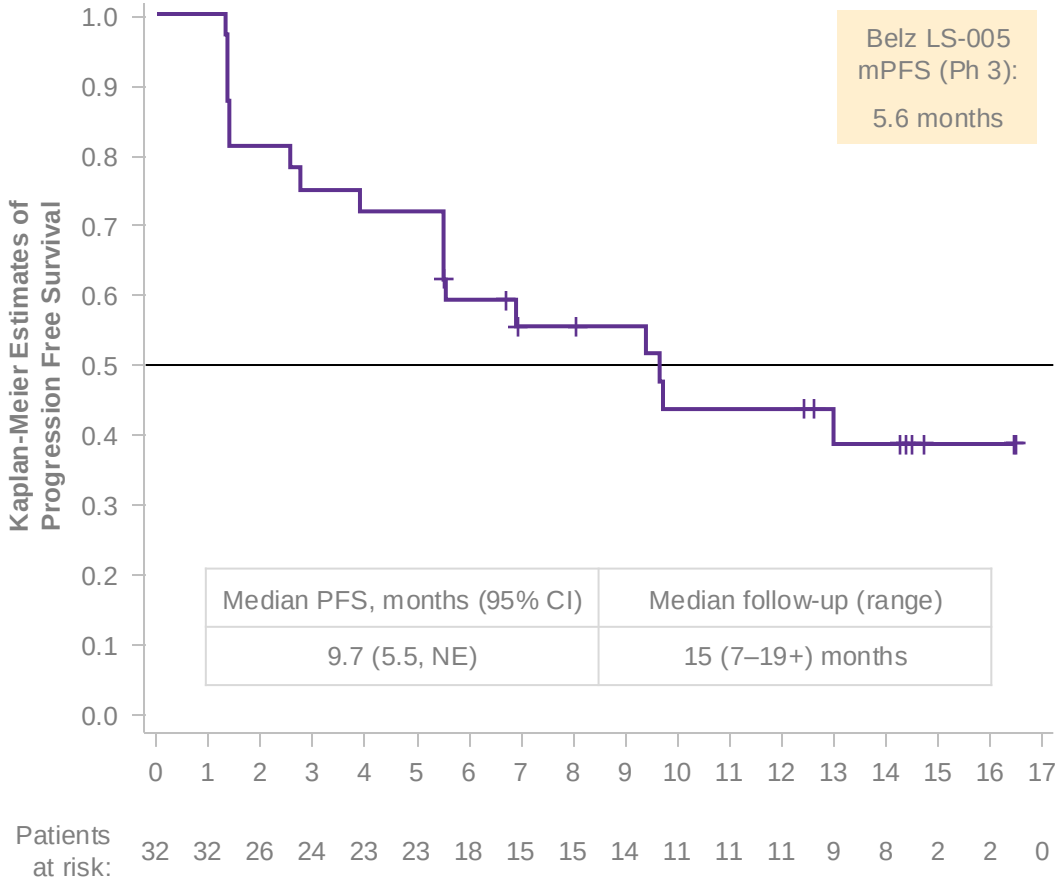
1. For the 50mg BID and 50mg QD cohorts, there were a total of four patients excluded from the efficacy evaluable population. 3 patients deemed ineligible shortly after enrollment (2 patients due to kidney function, 1 patient due to hemoglobin levels). One patient discontinued treatment before the first scan due to an unrelated AE.
2. In the 100mg QD cohort, 2 of 29 patients in the safety population were excluded from the efficacy evaluable population; 1 is ongoing treatment and has not yet received a first scan; the other discontinued prior to the first scan due to an unrelated adverse event.
3. Includes two patients with radiological progressive disease and 2 patients who had clinical progression before the first scan.

Unless otherwise noted, as of DCO date January 3, 2025

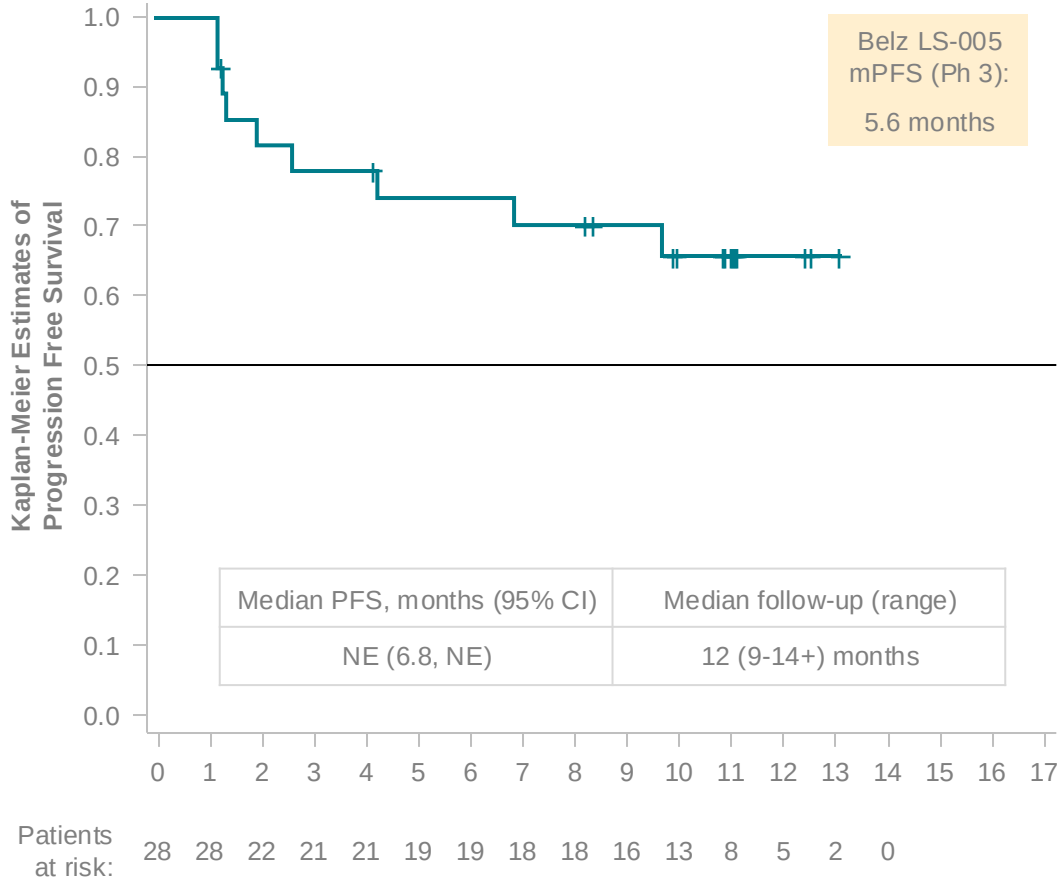
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50mg BID and 50mg QD Cohorts Show Substantially Improved PFS Relative to that of LITESPARK-005

50mg BID Cohort (n=32)



50mg QD Cohort (n=28)



100 mg QD Cohort PFS is immature with 21 pts remaining on treatment

+ Censored

1. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023;
PFS was measured according to RECIST v1.0 and estimated using Kaplan-Meier methodology.
Belz: belzufitan; BID: twice daily; CI: confidence interval; DCO: data cutoff; mPFS: median progression-free survival; NE: not estimable; QD: once daily
Data cutoff date: 03 January 2025

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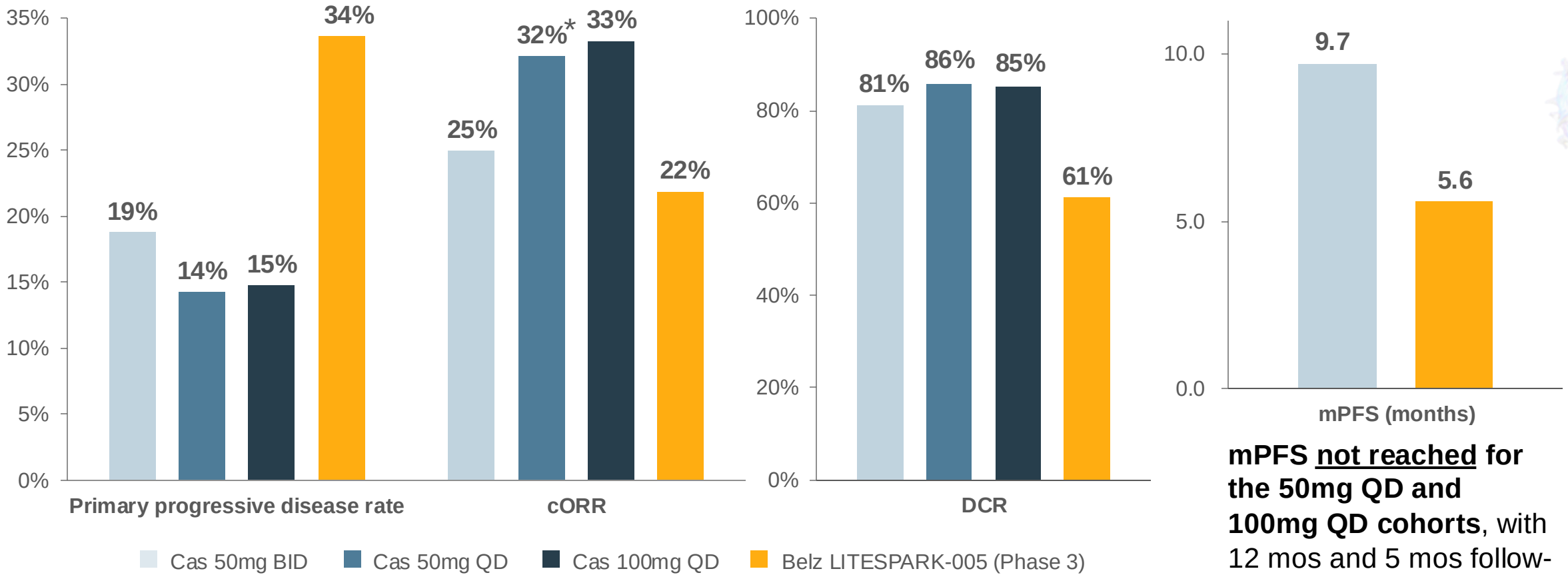
ARC-20 Data Support Casdatifan's Potential Best-in-Class Profile Across All Cohorts and Outcome Measures

Lower Primary PD

Higher ORR*

Higher DCR

Improved mPFS



mPFS <u>not reached</u> for the 50mg QD and 100mg QD cohorts, with 12 mos and 5 mos follow-up, respectively

***In the 50mg QD cohort, the one unconfirmed responder became a confirmed responder after the DCO, increasing the ORR to 32%.**

Data above are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors

Source: Efficacy data from IA1 of LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023

Belz: belzutifan; BID: twice daily; Cas: casdatifan; cORR: confirmed overall response rate; DCR: disease control rate; mg: milligram; mPFS: median progression-free survival; PD: progressive disease; QD: once daily

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Our Vision is for Every ccRCC Patient to Receive a HIF-2α Inhibitor and for Cas to be the HIF-2α Inhibitor of Choice

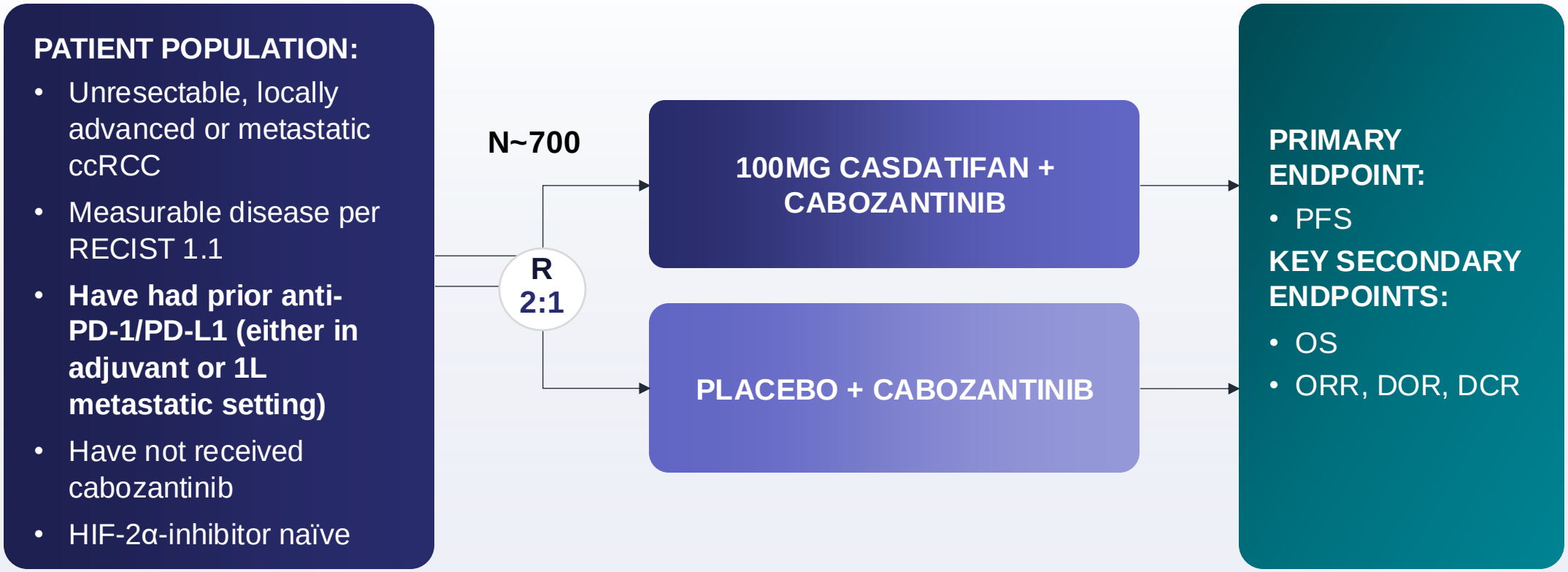
EARLIER LINES OF TREATMENT

SETTING	COMBINATION	EST. 2024 PATIENT POPULATION	DOT (MONTHS)	ARCUS APPROACH
Neoadjuvant ccRCC	**cas** + zimberelimab (anti-PD-1)	57k	3-4	**Investigator-sponsored trial to initiate in March**
Adjuvant	TBD		12	TBD
1L IO-Naive	**cas** + volrustomig (anti-PD-1/CTLA-4 bsp)	21k	18+	**eVOLVE study (AZ operationalizing):** Evaluating a TKI-free regimen in 1L
1L All Comers	**cas** + zimberelimab		24+	**ARC-20:** Cohorts added to evaluate cas as a TKI-free option in 1L
1L Favorable Risk	**cas** monotherapy	9k		
Post-IO (1L-2L)	**cas** + cabozantinib	19k	12+	**PEAK-1:** Combining with the most widely used TKI
Post-IO (1L-2L)	**cas** monotherapy	19k	12+	**ARC-20:** Cohort added to evaluate cas as a TKI-free option
2L+ "Monotherapy"	**cas** monotherapy	12k	9+	TBD

Sources: DRG, Arcus primary research & analysis. Estimated eligible patient population is in "Major Markets" only (US, EU5 and Japan)
1L: first-line; 2L second-line; bsp: bispecific; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; CTLA4: cytotoxic T-lymphocyte associated protein 4; DoT: duration of therapy; HIF: hypoxia-inducible factor; IO: immuno-oncology; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor

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First Phase 3 Study for Cas Has a Simple Design that Utilizes the Preferred SOC in Post-IO ccRCC



PEAK-1 is On Track to Initiate in Q2 2025

1L: first-line; cabo: cabozantinib: cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; HIF: hypoxia-induced factor; IO: immuno-oncology; mg: milligram; ORR: objective response rate; OS: overall survival; PD-1/PD-L1: programmed death protein 1/programmed death ligand 1; PFS: progression free survival; RCC: renal cell carcinoma; RECIST: Response Evaluation Criteria in Solid Tumors

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Cas Will Be Offered as a Single 100mg QD Tablet

PEAK-1

Cas 100mg
(1 x 100mg)



Cabo 20-60mg
(1 x Xmg)



LITESPARK-011 (Merck)

Belz 120mg
(3 x 40mg)



Lenva 20mg
(2 x 10mg)



- Cas tablet strengths will minimize pill burden while enabling dose reductions

AE: adverse event; cas: casdatifan; cabo: cabozantinib; belz: belzutifan; lenva: lenvatinib; mg: milligram; QD: once daily

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Domvanalimab in Non-Small Cell Lung Cancer and Upper GI Cancers

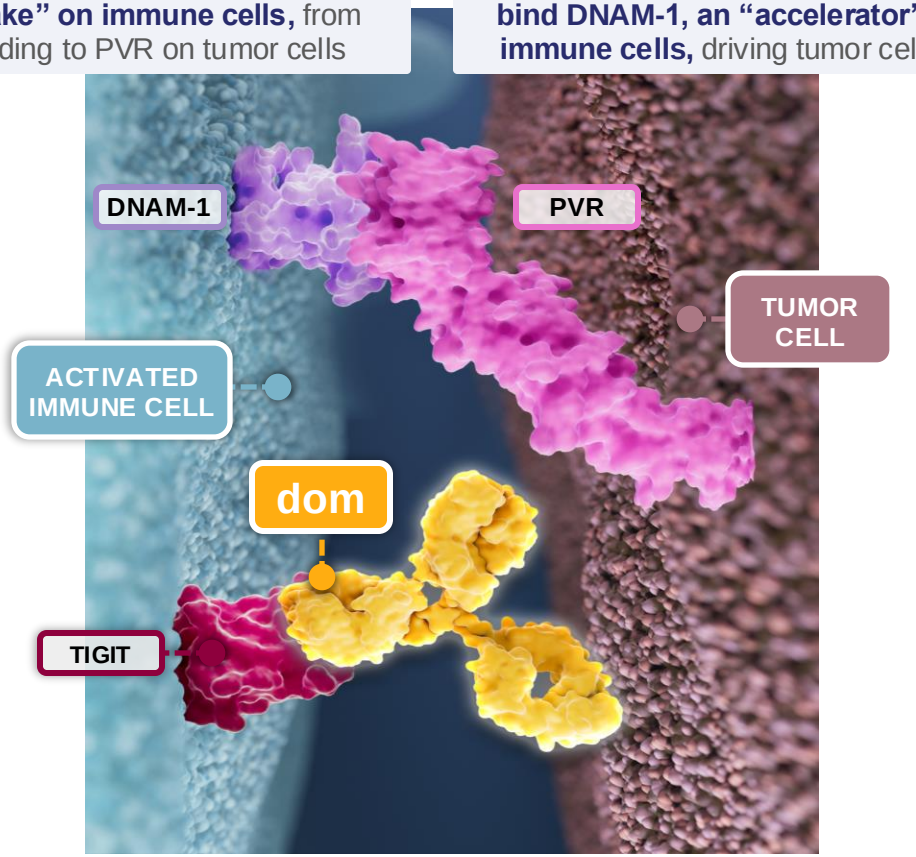
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Dom is the Most Clinically Advanced Fc-Silent Anti-TIGIT Antibody in Development

TIGIT inhibition turns an immuno-suppressive "brake" into an accelerator of adaptive immunity

1 **Dom blocks TIGIT, an inhibitory "brake" on immune cells,** from binding to PVR on tumor cells

2 TIGIT blockade **enables PVR to bind DNAM-1, an "accelerator" on immune cells,** driving tumor cell kill



First-to-Market potential in Upper GI & the only Fc-silent anti-TIGIT in Ph3 NSCLC

Fc-silent

Avoids depletion of TIGIT-bearing cells:

- Minimizes treatment interruptions by avoiding Treg depletion-related immune AEs
- Maximizes efficacy by avoiding potential depletion of cancer-fighting Teff cells

Individual Agents

Administered as individual agents (vs. co-form)

- Pursuing < 1 hour co-administration infusion time for dom and zim

Optimized Development Strategy

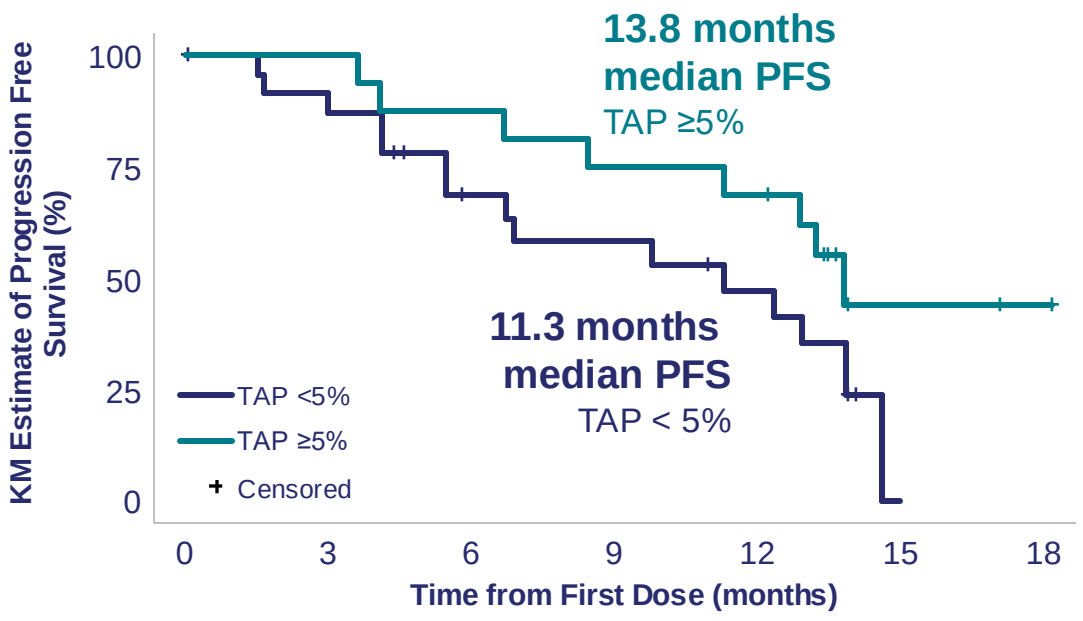
Positioned to be first to market in 1L gastric, 1L NSCLC (all-comers) and Stage 3 NSCLC

DNAM-1: DNAX accessory molecule; dom: domvanalimab; GI: gastrointestinal; NSCLC: non-small cell lung cancer; Ph: phase; PVR: poliovirus receptor; TIGIT, T cell immunoreceptor with immunoglobulin and ITIM domain; Treg: regulatory T-cells; zim: zimberelimab
Note: co-administration of dom + zim was not part of STAR-121 Phase 3 study in 1L NSCLC

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Dom/Zim/Chemo: Unprecedented mPFS in 1L Gastric Cancer

EDGE-Gastric: TAP ≥ 5% (n=16); TAP < 5% (n=24)



NUMBER OF PATIENTS AT RISK

TAP ≥5%	16	16	14	12	11	2	1
TAP <5%	24	20	13	11	8	0	

EDGE-Gastric Data Exceeded Benchmark Data

		EDGE-GASTRIC	CHECKMATE-649[1]	KEYNOTE-859[2]	RATIONALE-305[3]
mPFS	ITT	**12.9m**	7.7m	6.9m	6.9m
	PD-L1 High	**13.8m**	7.7m[4] 8.3m[5]	8.1m	7.2m
mDOR	ITT	**12.4m**	8.5m	8.0m	8.6m
	PD-L1 High	**NE**	9.5m[4] 9.6m[5]	10.9m	9.0m
ORR	ITT	**59%**	58%[6]	51%	47%
	PD-L1 High	**69%**	60%	61%	50%

Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors

EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024

1. Phase 3: Janjigian, 2024. Shitara Nature 2022, Janjigian Lancet 2021, Moehler ASCO 2021 #4003 (36.2m, 24.0m, 12.1m, and 12.1m minimum follow up, respectively) 2. Phase 3: Rha, ESMO Virtual Plenary Feb 2023 and ASCO 2023 #4014 (31.0m median follow up) 3. Phase 3: Moehler, ASCO GI 2023 #286 (15.9m median follow up), and Xu, ESMO 2023 LBA80 (24.6m minimum follow up) 4. With12.1 months minimum follow-up 5. With 36.2 months minimum follow-up 6. ITT population for Checkmate-649 included ~60% patients with PD-L1 high status at baseline. Note that EDGE-Gastric overall population included only 39% PD-L1 high at baseline.

1L: first-line; CI: confidence interval; CPS: combined positive score; dom: domvanalimab; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immuno-oncology; ITT: intent-to-treat; KM: Kaplan Meyer; mDOR: median duration of response; mOS: median overall survival; mPFS: median progression-free survival; NE: not estimable; nivo: nivolumab; ORR: overall response rate; pembro: pembrolizumab; TAP: tumor area positivity; zim: zimberelimab

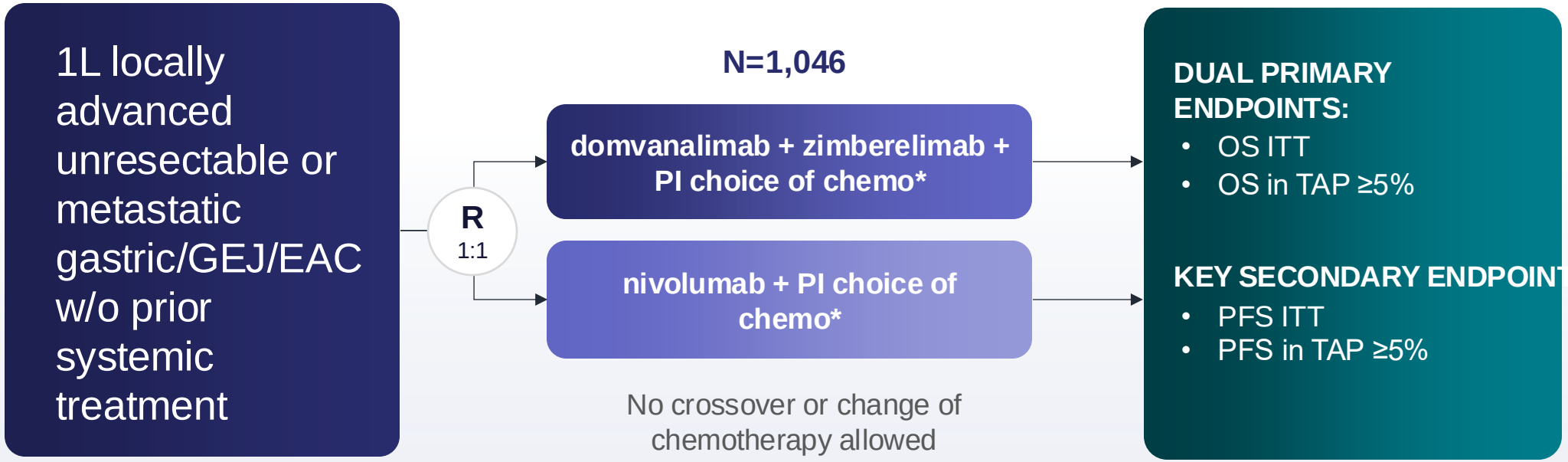
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STAR-221

Phase 3 Study was Fully Enrolled in June 2024

Dom + zim is positioned to be the first anti-TIGIT combination approved

STAR-221 is evaluating the same regimen in the same setting as EDGE-Gastric



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.
NCT #: NCT05568095
1L: first-line; chemo: chemotherapy; dom: domvanalimab; EAC: esophageal adenocarcinoma; ECOG PS: Eastern Cooperative Oncology Group performance status; GEJ: gastroesophageal junction; nivo: nivolumab; ITT: intent to treat; OS: overall survival; PFS: progression-free survival; PI: principal investigator; TAP: tumor area positivity; R: randomized; w/o: without; zim: zimberelimab

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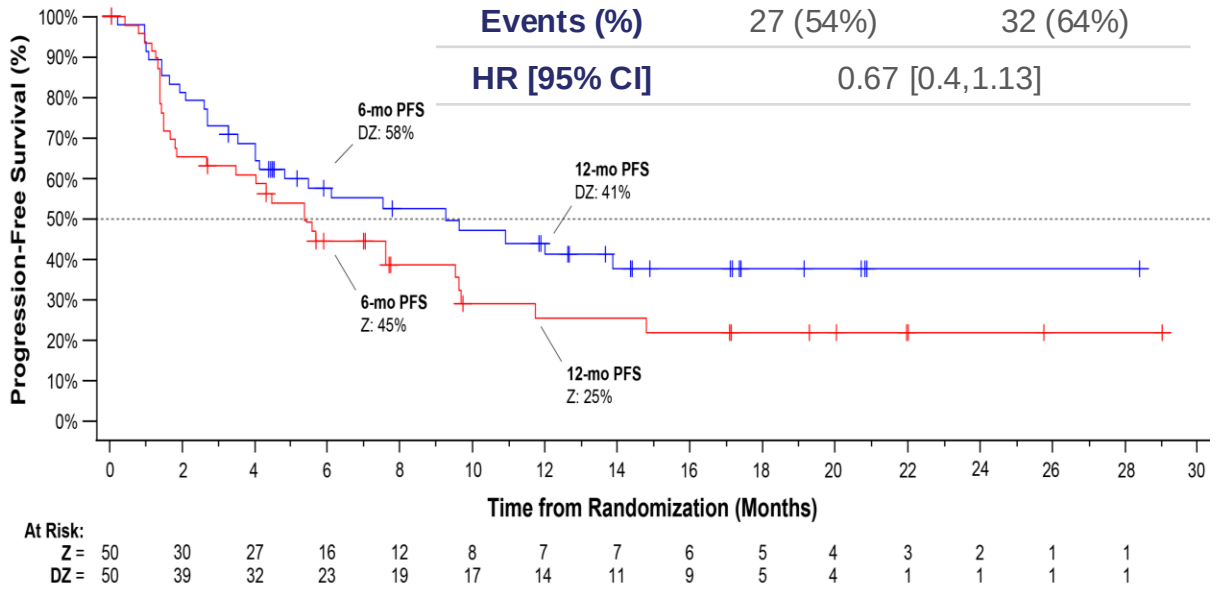
ARC-7 and ARC-10 Demonstrated Consistent Improvement for Dom + Zim in 1L PD-L1 High NSCLC

ARC-7 1L PD-L1 High NSCLC

dom + **zim** *vs.* **zim** *vs.* **etruma** + **dom** + **zim** (n=150)

2023 ASCO ANNUAL MEETING

	Dom + Zim	Zim
Median PFS [95% CI]	9.3 months [4.1,NE]	5.4 months [2.7,9.7]
Events (%)	27 (54%)	32 (64%)
HR [95% CI]	0.67 [0.4,1.13]	



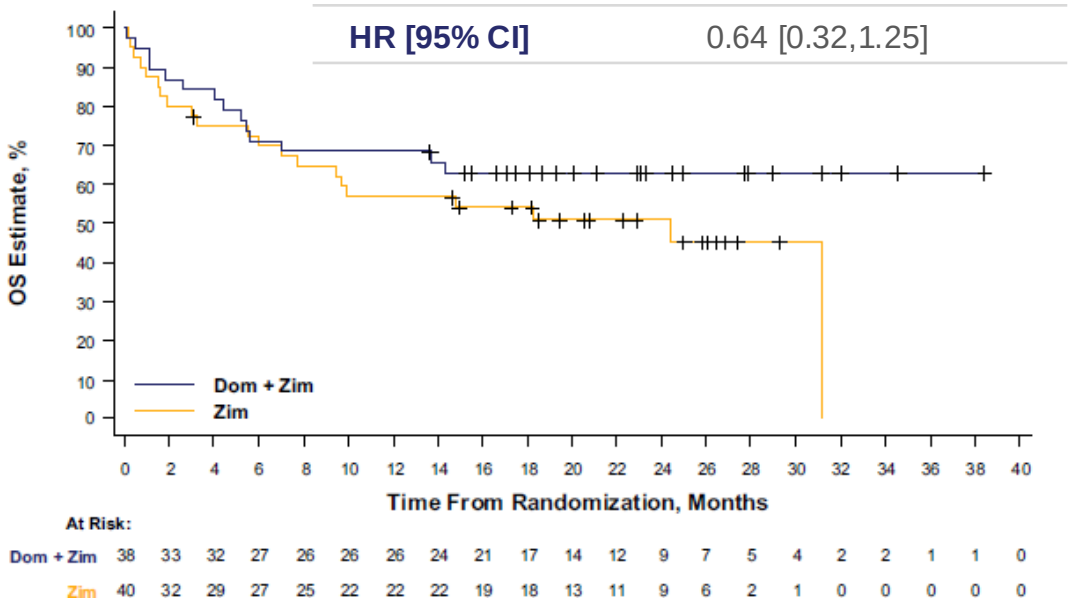
Dom + Zim vs. Zim PFS HR = 0.67

ARC-10 1L PD-L1 High NSCLC

dom + **zim** *vs.* **zim** *or* **chemo** (n=95)

Society for Immunotherapy of Cancer SITC 2024 NOV. 6-10 | HOUSTON

	Dom + Zim	Zim
Median OS [95% CI]	NR [13.7,NE]	24.4 months [7.8, NE]
HR [95% CI]	0.64 [0.32,1.25]	



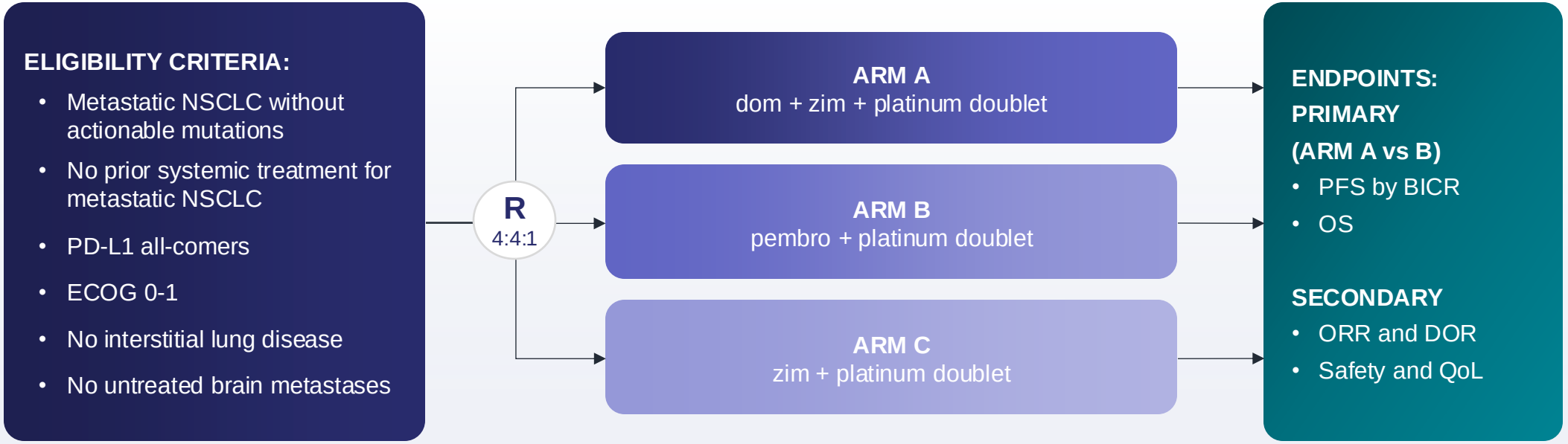
Dom + Zim vs. Zim OS HR = 0.64

ARC-7 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023
ARC-10 – Johnson et al. SITC 2024, Nov. 5 2024, data cut off of May 17, 2024Do
1L: first-line; chemo: chemotherapy; CI: confidence interval; D/dom: domvanalimab; HR: hazard ratio; NE: not estimable; NR: not reached; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression-free survival; Z/zim: zimberelimab

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

- Uses standard of care, pembrolizumab, in the comparator arm



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

★ **ONGOING**

1L: first-line; BICR: blinded independent central review; dom: domvanalimab; DOR: duration of response; ECOG: Eastern Clinical Oncology Group; NSCLC: non-small cell lung cancer; ORR: objective response rate; OS: overall survival; pembro: pembrolizumab; PFS: progression-free survival; QoL: quality of life; R: randomized; sq: squamous; zim: zimberelimab

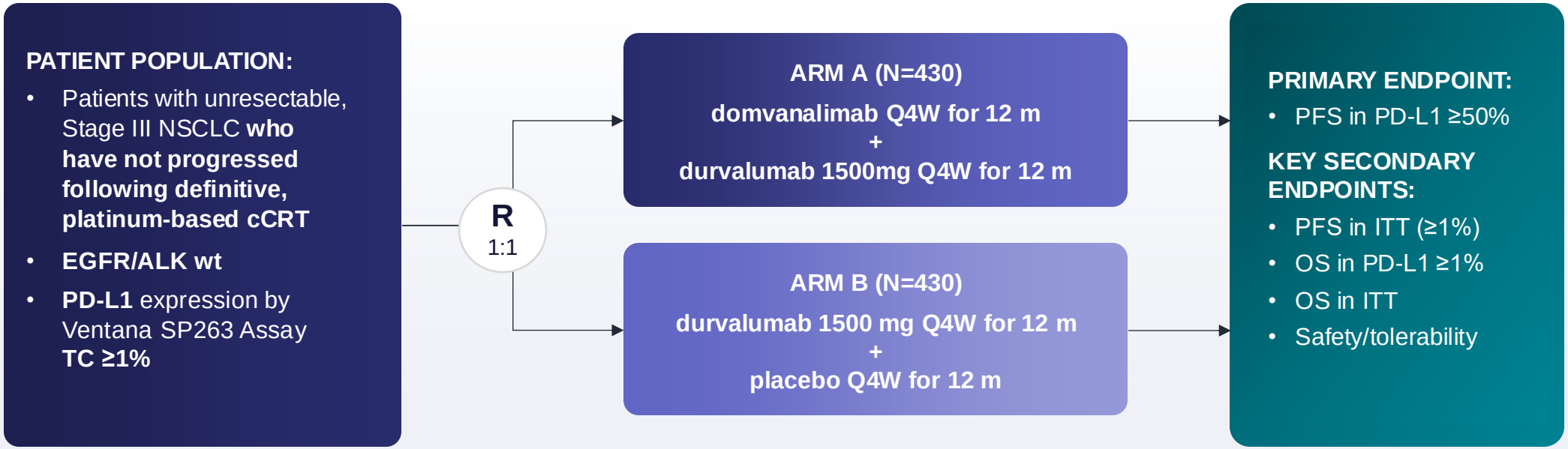
Gilead Sciences is operationalizing STAR-121

NCT #: NCT05502237

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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)

cCRT: concurrent chemoradiotherapy; IHC: immunohistochemistry; ITT: intent to treat; m: months; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression free survival; Q4W: every 4 weeks; TC: tumor count

NCT #: NCT05211895

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CD73-Adenosine Axis Programs

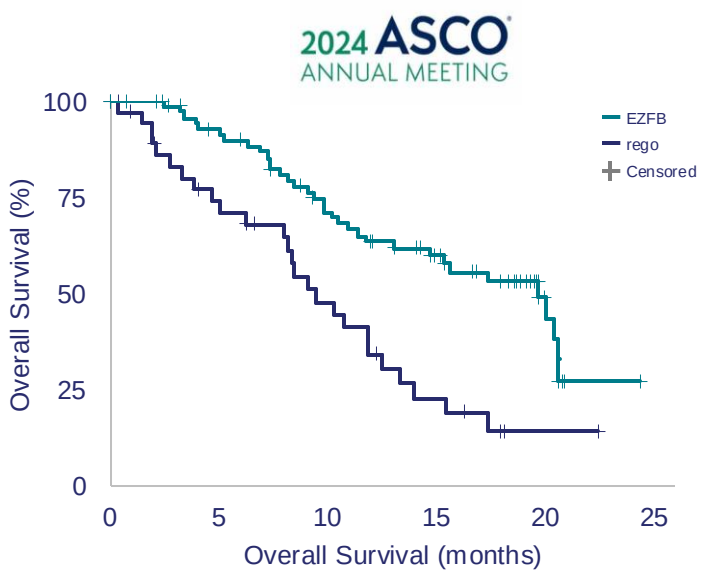
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Three Datasets in Six Months Demonstrate the Potential Benefits of Combining Adenosine Blockade with Chemotherapy

3L Colorectal Cancer

etruma + zim + FOLFOX/bev vs. rego (n=112)

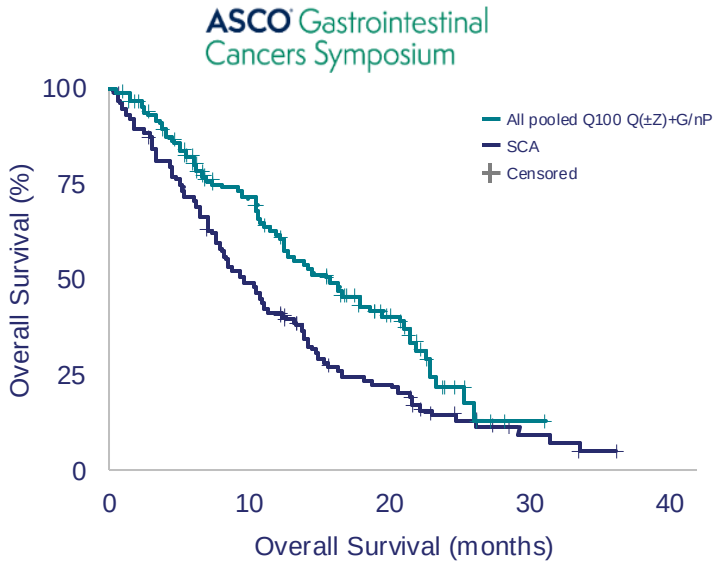
ARC-9



1L Metastatic PDAC

quemli ± zim + G/nP (n=122)

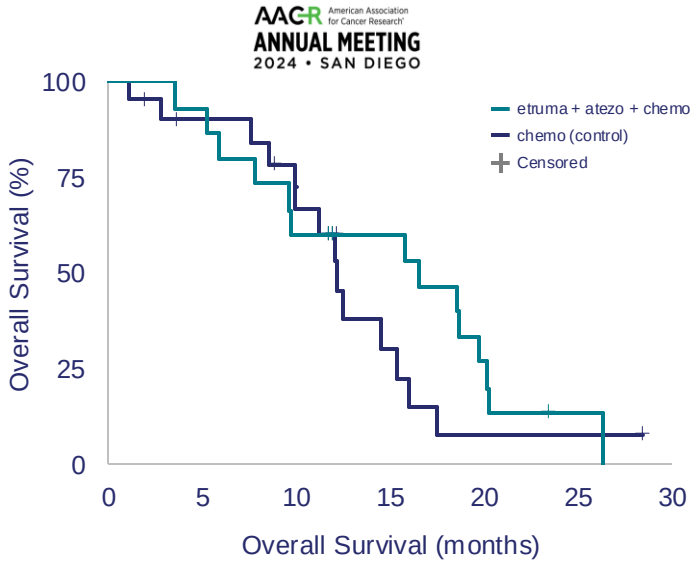
ARC-8



1L Metastatic PDAC

etruma + atezo + G/nP (n=35)

MORPHEUS COMBINATIONS PLATFORM



	EZFB	Rego	HR (95% CI)	Q(±Z)+G/nP	SCA	HR (95% CI)	etruma + atezo + chemo	Chemo	HR (95% CI)
mOS (mos)	19.68	9.13	0.36 (0.2. - 0.66)	15.7	9.8	0.63 (0.47 – 0.85)	16.5	12.1	0.67 (0.3-1.5)

⬇ 63% reduction in risk of death
⬆ 10.2 month increase in mOS
vs. standard of care (rego)

⬇ 37% reduction in risk of death
⬆ 5.9 month increase in mOS
vs. matched synthetic control arm

⬇ 33% reduction in risk of death
⬆ 4.4 month increase in mOS
vs. standard of care (chemo)

1L: first line; 3L: third line; atezo: atezolizumab; bev: bevacizumab; chemo: chemotherapy; E/etruma: etrumadenant; EZFB, etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; FOLFOX: oxaliplatin 85 mg/m2 IV; G/nP: gemcitabine/nab-paclitaxel; HR: hazard ratio; mOS: median overall survival; PDAC: pancreatic ductal adenocarcinoma; Q/quemli: quemliclustat; rego: regorafenib; SCA: Synthetic Control Arm; Z/zim: zimberelimab

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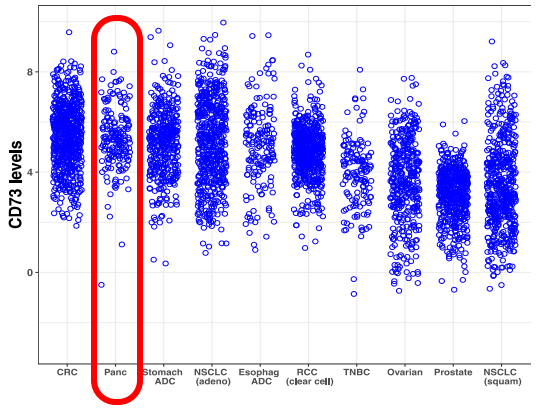
Quemliclustat (quemli): A Small Molecule CD73 Inhibitor with Several Key Attributes

QUEMLICLUSTAT

- Highly potent small molecule
- Target coverage achieved at doses as low as 25 mg every two weeks
- Extremely long (4+ days) half-life, enabling Q2W dosing by IV infusion

Biological rationale for CD73 inhibition in pancreatic cancer

Pancreatic cancer exhibits very high expression levels of CD73



mRNA Levels from analysis of The Cancer Genome Atlas (TCGA)

Potential advantages over CD73 antibodies[1]

- ✓ Highly potent and selective inhibition of both tumor cell-bound and soluble CD73
- ✓ Greater inhibition of enzymatic production of adenosine
- ✓ Orders of magnitude more potent
- ✓ Greater permeability of tumor tissue

Q2W: every 2 weeks

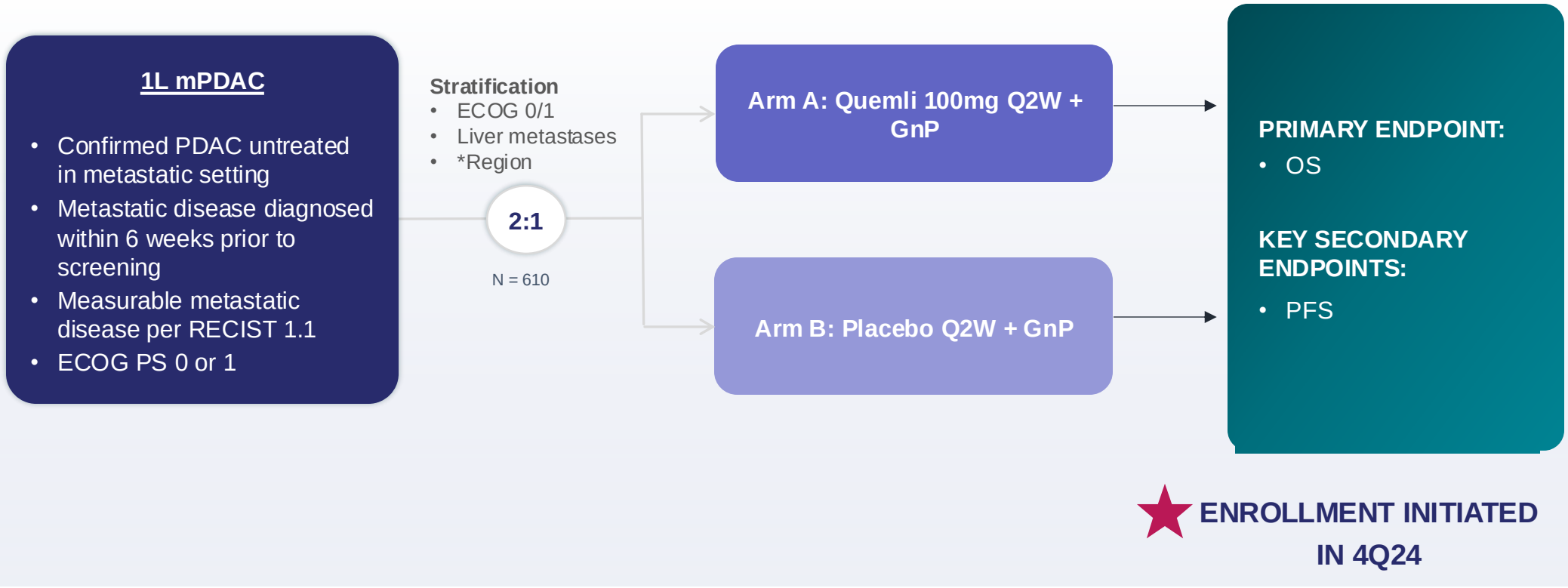
quemliclustat is an investigational molecule and its safety and efficacy have not been established.

1) Arcus Biosciences data on file; based on preclinical studies

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PRISM-1

Phase 3 Study of Quemli + Chemo in 1L Metastatic PDAC



1L: first-line; GnP: gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; OS: overall survival; PFS: progression-free survival; Q2w: every two weeks; quemli: quemliclustat

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Etrumadenant Represents a Potentially Best-in-Class Adenosine Receptor Antagonist

ETRUMADENANT

- Highly potent small molecule that inhibits both the A_{2a} and A_{2b} receptors
- Excellent penetration of tumor tissue and drug properties (PK, etc.)
- MORPHEUS-PDAC (operationalized by Roche) data presented at AACR 2024 (Abstract CT212; see slide 24)
- Data from ARC-9 evaluating etruma + zim + chemo* vs. regorafenib in 3L CRC; mature PFS and OS were presented at ASCO 2024 (Abstract 3508; see slide 24)

Etrumadenant has an ideal profile

- ✓ 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

1H: first half; 3L third-line; CNS: central nervous system; CRC: colorectal cancer; etruma: etrumadenant; PFS: progression-free survival; PK: pharmacokinetics; OS: overall survival; zim: zimberelimab

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

*+/- biologic, e.g. bevacizumab or biosimilar, will be included for all patients in whom it is not contraindicated

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AXL Program

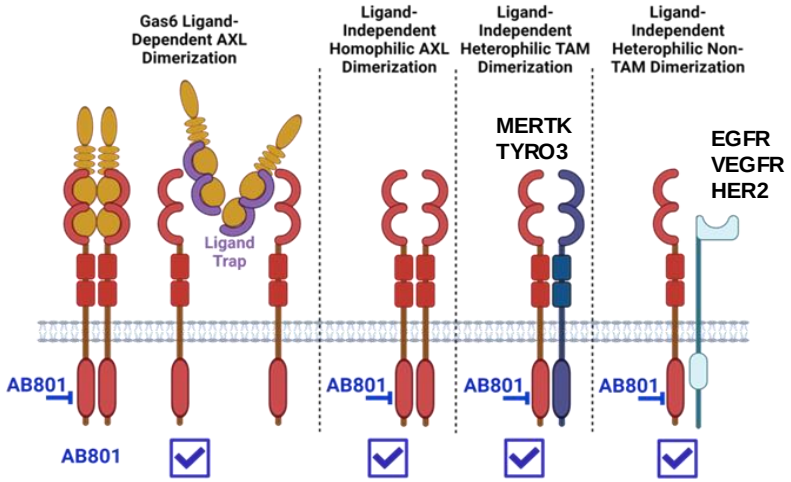
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AB801 is a Potent, Selective AXL Inhibitor

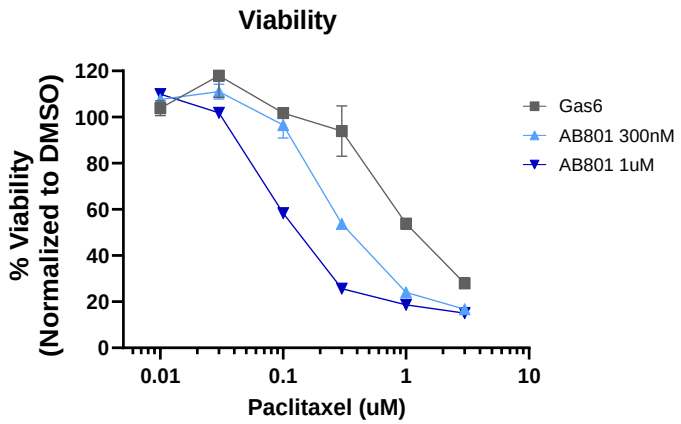
AB801 is a highly potent and selective AXL inhibitor

	Assay	AB801
BIOCHEMICAL	AXL K_i	**0.024 nM**
	Fold selectivity over hMERTK/ hTYRO3 (enzyme K_i over AXL K_i)	**860x / 1400x**
	Kinome Selectivity against 403 kinases at 100x IC_{50} for AXL	**Only one kinase with less that 200-fold selectivity**
CELLULAR	pAXL ELISA IC_{50} (serum-free media)	**17 nM**
	pAXL ELISA IC_{50} (100% serum)	**68 nM**

AXL signals via Ligand-dependent and Ligand-independent mechanisms



AB801 sensitizes cancer cells to chemotherapy



*Syngeneic mouse MC38 tumor model; data on file at Arcus.
AB801 is an investigational molecule and its safety and efficacy have not been established.

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AB801 is Potentially the Most Potent & Selective AXL Inhibitor in Clinical Development

THERAPEUTIC HYPOTHESIS: Inhibiting AXL will overcome resistance against chemotherapy and immunotherapy in human tumors

- AB801 was designed to potently and selectively inhibit AXL signaling in tumors, resulting in enhanced responses to chemotherapy and immunotherapy
  - Other “AXL inhibitors” may not be potent enough or lack selectivity (leading to toxicity) that may limit their use at doses suitable for efficient AXL inhibition
- Phase 1 study in healthy volunteers is completed:
  - No safety issues have been observed to date in the dose-escalation cohorts
  - Pharmacokinetics were dose-proportional and appear to support once-daily dosing
- Phase 1 study (ARC-27) in patients with advanced solid tumors is ongoing; **expansion cohort planned in 2L+ NSCLC in the second half of 2025**

2L: second-line; NSCLC: non-small cell lung cancer

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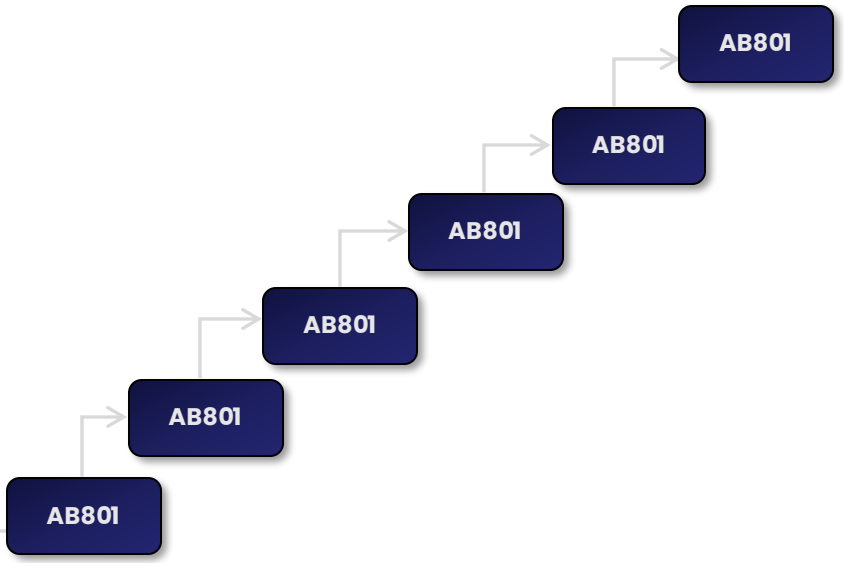
Phase 1 Dose-Finding Study in Patients with Advanced Solid Tumors

ARC-27

PRE-SCREENING / SCREENING | DOSE ESCALATION STAGE | EXPANSION STAGE

Advanced Solid Tumors

NSCLC, CRC, Breast, RCC, Ovarian, HNSCC, Bladder



Cohort 1: NSCLC adenocarcinoma

AB801 + docetaxel

Safety run-in n=6

n=40
Prior α-PD-(L)-1 and chemo

DOSE ESCALATION

PRIMARY ENDPOINT
- Safety / DLT

SECONDARY ENDPOINT
- PK
- ORR

EXPLORATORY ENDPOINTS
- Biomarkers / PD
- PFS, OS

DOSE EXPANSION

PRIMARY ENDPOINT
- Safety

SECONDARY ENDPOINT
- PK
- ORR

EXPLORATORY ENDPOINTS
- Biomarkers / PD
- PFS, OS

- Evaluate AB801 single agent tolerability and activity to inform dose in expansion stage
- Expansion cohort: all comers NSCLC adenocarcinoma designed to generate preliminary safety, PK, and activity signal (ORR), to support randomized POC Phase 2 study

CRC: colorectal cancer; DLT: dose-limiting toxicity; mg: milligram; NSCLC: non-small cell lung cancer; ORR: objective response rate; PD: pharmacodynamics; PFS: progression-free survival; PK: pharmacokinetics; OS: overall survival; RCC: renal cell carcinoma

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COMBINING TO CURE®

Our Partnerships Enable Cost-Efficiency and Greatly Expand Our Opportunities

	GILEAD	TAIHO PHARMA	AstraZeneca
R&D COST-SHARING	STAR-121 STAR-221 EDGE-Gastric EDGE-Lung VELOCITY-Lung	STAR-121 STAR-221 PRISM-1	PACIFIC-8 **Phase 1/1b:** **cas** + volru
RIGHTS / ECONOMICS	• Arcus retains co-promotion rights and profit share in the U.S. • High-teens to low-20's royalties on ex-U.S. sales • Opt-in rights to all programs; 4 exercised to date	• Taiho has development / commercial rights in Japan and rest of Asia (ex-China) • Up to $275mm in milestones per program • High single-digit to mid-teens royalties	• Both parties retain economics on their respective molecules

cas: casdatifan; mm: million; volru: volrustomig

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