



# COMBINING TO CURE<sup>®</sup>

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

CORPORATE PRESENTATION

**August 8, 2024**

# 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 2027; 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 completion of enrollment, presentation of clinical data and launch of our investigational products; and possible first to market advantage for any of our investigational products.

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

## FUNDING INTO 2027

~\$1.0B in cash,  
cash equivalents  
& marketable securities\*\*

## POTENTIAL BEST-IN-CLASS HIF-2a INHIBITOR, CASDATIFAN

Commercially validated  
mechanism

First Phase 3 initiation 1H25



## PHASE 3 STUDIES FOR DOM IN LUNG & UPPER GI PROGRESSING TO DATA



• Fully  
enrolled by  
YE 2024



✓ Fully  
enrolled

PACIFIC8

## MULTIPLE UPCOMING DATASETS

### Casdatifan (HIF-2a)

- **2H24** ARC-20  
(2L+ ccRCC):  
ORR and safety  
data from 100mg  
expansion cohort
- **1Q25:** ARC-20:  
Data from 50mg  
expansion cohort

### Domvanalimab\* (TIGIT)

- **2H24** ARC 10:  
OS & PFS data  
from Part 1
- **2025:** EDGE-  
Gastric: OS data

## TOP TIER PARTNERS

Provides funding and  
resources enabling a  
diversified pipeline



TAIHO PHARMA



## WORLD CLASS DRUG DISCOVERY

1-2 new development  
candidates a year

### AB801

Initiated Phase 1/1b for potential  
best-in-class small molecule  
AXL inhibitor in Jan. 2024

# Multiple Late-Stage Programs and Opportunities to "Win"

**Dom (+ Zim)**  
(anti-TIGIT + anti-PD-1)

**THREE\*** PHASE 3  
STUDIES UNDERWAY

- Potential to be first-in-class in upper GI cancer (\$3B market opportunity) and best-in-class in NSCLC (\$10B+ market opportunity)
- 12.9 - 13.8 months PFS in EDGE-Gastric<sup>1</sup> is meaningfully higher than benchmark studies

**Casdatifan**  
(HIF-2a)

AT LEAST **ONE** PHASE  
3 STUDY IN PLANNING

- Mechanism validated through belzutifan approval
- Data from 30-patient 100mg expansion cohort planned for Fall 2024; multiple datasets from additional expansion cohorts expected to follow
- Cas has potential for a best-in-class efficacy profile – and a differentiated development / combination strategy vs. belzutifan

**Quemli / Etruma**  
(CD73 inhibitor / A2R  
antagonist)

**ONE** PHASE 3 STUDY  
IN PLANNING (PDAC)

- Three recent datasets support the potential of adenosine blockade to prolong survival when combined with chemotherapy
- ~20 months overall survival in ARC-9<sup>2</sup> data is unprecedented in all-comer 3L CRC, meaningfully above benchmark studies for this population

\*includes STAR-121, STAR-221 and PACIFIC-8

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

2. ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023

2H: second half; 3L: third line; B: billion; cas: casdatifan; CRC: colorectal cancer; dom: domvanalimab; etruma: etrumadenant; GI: gastrointestinal; mg: milligram; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; PFS: progression-free survival; quemli: quemliclustat; zim: zimberelimab

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# New Disclosure for the Second Quarter 2024

## **Dom (+ Zim)** (anti-TIGIT + anti-PD-1)

- OS and PFS data for ARC-10 (dom + zim vs. zim vs. chemo) in PD-L1 high NSCLC will be presented by YE 2024
- EDGE Gastric OS Data is expected to be presented in 2025










## **Casdatifan** (HIF-2a)

- First Phase 3 study, PEAK-1, will evaluate cas + cabo vs. cabo in anti-PD-1 experienced ccRCC patients – expected to start 1H25
- For ARC-20, the 150mg expansion cohort has completed enrollment and the 100mg expansion cohort has been re-opened due to high level of interest in the study
- Data from the 100mg expansion cohort has been submitted for presentation at a Fall 2024 medical conference

## **Quemli / Etruma** (CD73 inhibitor / A2R antagonist)

- Taiho exercised its option to quemli; will participate in the Phase 3 PRISM-1 study in pancreatic cancer; this triggered an option payment plus potential milestone payments that could be payable next year
- Next steps for etruma in CRC are being discussed with Gilead

# Targeting Huge Market Opportunities and Unmet Need

	PHASE 1/2 STUDIES	PHASE 3 STUDY	INDICATION	PH 3 STUDY DETAILS	ADDRESSABLE PATIENTS <sup>1</sup>	MARKET POTENTIAL <sup>2</sup>
<b>DOM + ZIM</b> Fc-silent anti-TIGIT MAb + anti-PD-1 MAb	 <b>EDGE</b> -Gastric mPFS presented at ASCO '24	 <b>STAR</b> -221	1L Gastric/GEJ/EAC - all comers	dom + zim + chemo vs nivo + chemo	103K	~\$3B
	 <b>ARC</b> -7 Final PFS presented at ASCO '23	 <b>STAR</b> -121	1L NSCLC – all comers	dom + zim + chemo vs pembro + chemo	303K	~\$10B
	 <b>EDGE</b> -Lung Enrolling dose-optimization cohorts	 <b>PACIFIC</b> -8 Recruiting	Stage 3 NSCLC	dom + durva vs durva + placebo	48K	~\$2B
<b>CAS</b> HIF-2α small molecule inhibitor	 <b>ARC</b> -20 100 mg expansion cohort data: 2H24	 <b>PEAK</b> -1 Initiating 1H25	Post-IO ccRCC	cas + cabo vs cabo	20K	~\$2B+
<b>QUEMLI</b> Small molecule CD73 inhibitor	 <b>ARC</b> -8 OS data presented Q124	 <b>PRISM</b> -1 Initiating early '25	1L PDAC	quemli + G/nP vs G/nP	106K	~\$4B
<b>ETRUMA</b> Small molecule A2a & A2b receptor antagonist	 <b>ARC</b> -9 OS data (3L cohort) presented ASCO '24	Next steps in planning	CRC	Next steps to be determined	82K	~\$2B

1. Drug Treatable Addressable Populations (G7, 2023); Decision Resources Group

2. G7 Markets (US, EU5, JP) - total projected 2034 PD-(L)1 + TIGIT opportunity, Q opportunity & Hif2α opportunity

1L: first line; 2L: second line; 3L: third line; B: billion; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; CRC: colorectal cancer; dom: domvanalimab; durva: durvalumab; EAC: esophageal adenocarcinoma; etruma: etrumadenant; GEJ: gastroesophageal junction; GI: gastrointestinal; G/nP: gemcitabine/nab-paclitaxel; IO: immuno-oncology; mAb: monoclonal antibody; mPFS, progression-free survival; nivo: nivolumab; NSCLC: non-small cell lung cancer; OS: overall survival; PDAC: pancreatic ductal adenocarcinoma; PD: pharmacodynamic; pembro: pembrolizumab; Ph: phase; PK: pharmacokinetic; quemli: quemliclustat; zim: zimberelimab

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# Our Partnerships Greatly Expand & Accelerate Our Opportunities



## 10-YEAR COLLABORATION

- Gilead has opted into 5 molecules to date -- shares costs for studies within the joint development plan
- Arcus retains U.S. co-commercialization rights



TAIHO PHARMA

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

- Taiho has optioned dom, zim, etruma and, most recently, quemli
- Up to \$275mm in development, regulatory and commercial milestones per program
- Tiered royalties from high-single digit to mid-teens on net sales



## CLINICAL COLLABORATION FOR DOMVANALIMAB PLUS DURVALUMAB

- Companies collaborating on PACIFIC-8, a Phase 3 registrational trial sponsored by AstraZeneca
- Leverages AstraZeneca's leadership in the curative-intent Stage 3 NSCLC setting with funding shared
- Retained economics on respective molecules



## CLINICAL COLLABORATION FOR CAS + ZANZALINTINIB

- Companies collaborating on STELLAR-009, a Phase 1b/2 trial sponsored by Exelixis
- Potential to create a "best-in-class" TKI/HIF2 $\alpha$  combination
- Enables cost-effective path for development

**ENABLES MULTIPLE "SHOTS ON GOAL" AND FUNDING INTO 2027**



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



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

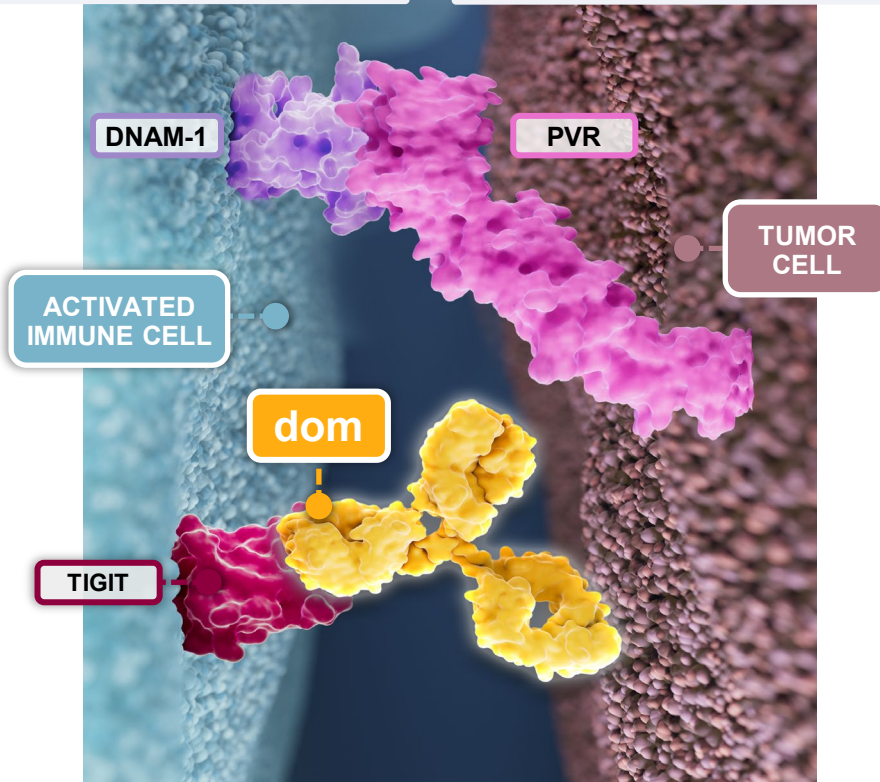
TIGIT inhibition turns an immuno-suppressive “brake” into an accelerator of adaptive immunity

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 peripheral T<sub>reg</sub> depletion that can lead to immune-related adverse events and treatment interruptions

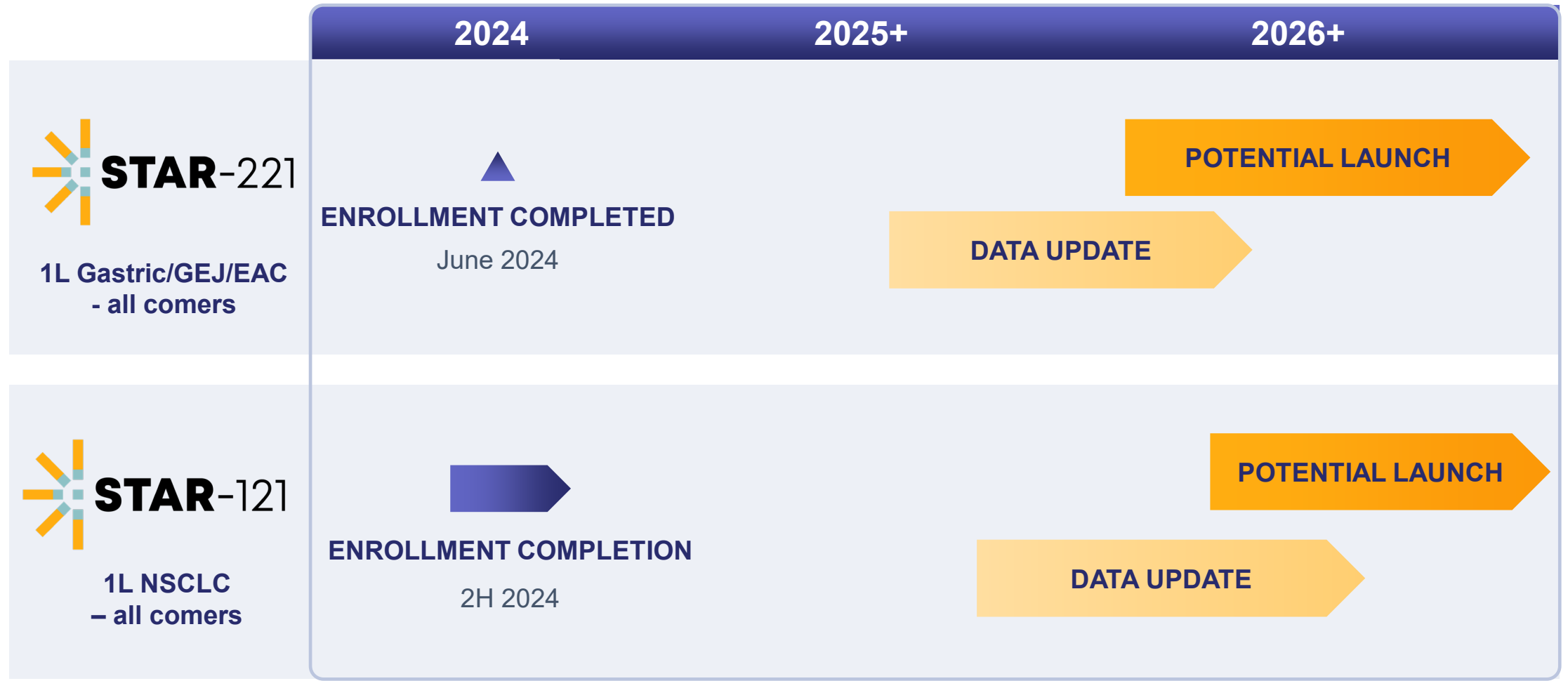
Optimized dose

1200 mg dose selected for maximum efficacy, without the potential safety concerns of Fc effector function

Co-administered dosing

Co-administered dom + zim can reduce infusion times, without the constraints of fixed-dose co-formulation

# Approaching Pivotal Data & Launch Windows for Dom + Zim



# Two De-Risking Phase 2 Datasets Have Been Presented for Domvanalimab Plus Zimberelimab Regimens



## 1L Gastric/EAC/GEJ

dom + zim + FOLFOX (n=40)

2024 ASCO<sup>®</sup>  
ANNUAL MEETING

**mPFS well beyond historical benchmarks of 7 to 8 months<sup>1-3</sup>**

- **PD-L1-high\*: 13.8 months**
- **Overall: 12.9 months**
- **Incidence of adverse events was similar to prior experience with anti-PD-1 + FOLFOX**

**STAR-221, the registrational Phase 3 study evaluating the same regimen in the same setting, is fully enrolled**



## 1L PD-L1 high NSCLC

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

2023 ASCO<sup>®</sup>  
ANNUAL MEETING

- **PFS HRs:**
  - **0.67** for DZ vs. Z
  - **0.72** for EDZ vs. Z
- **ORRs for DZ and EDZ vs. Z**
  - **Up to 14% improvement** in ORR
  - **Lower incidence** of progressive disease
- **Similar rates of immune-related adverse events observed for DZ and Z – including rates of infusion-related reactions, rash and pruritis**

\*PD-L1 high population defined as TAP≥5

1L: first-line; D/dom: domvanalimab; EAC: esophageal adenocarcinoma; E/etruma: etrumadenant; GEJ: gastroesophageal junction; HR: hazard ratio; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; TAP: tumor area positivity; Z/zim: zimberelimab

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)

ARC-7 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

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# Summary of EDGE-Gastric Arm-A1 Results and Domvanalimab Plus Zimberelimab Clinical Program in Upper GI Cancers

Data presented at 2024 ASCO Annual Meeting, based on data cut off of March 12, 2024.

# Arm A1: 1L Metastatic Gastric/GEJ/EAC Cohort

EDGE-Gastric (NCT05329766) is a Phase 2 study evaluating the safety and efficacy of treatment combinations with and without chemotherapy in adults with advanced upper gastrointestinal tract malignancies

## KEY ELIGIBILITY CRITERIA

- First-line locally advanced unresectable or metastatic gastric/GEJ/EAC
- Measurable disease per RECIST v1.1
- ECOG 0-1
- Known HER-2-positive tumors excluded
- Irrespective of PD-L1 levels

N ≈ 40

DOM 1600 mg Q4W  
ZIM 480 mg Q4W  
FOLFOX Q2W

Treatment continues until PD or unacceptable toxicity

Scanning interval: Q6W for first year,  
and Q12W thereafter

## PRIMARY ENDPOINTS:

- Safety
- Investigator ORR

## SECONDARY ENDPOINTS:

- Efficacy by PD-L1 (OS, PFS, DCR, DOR)
- PK and biomarker data

At the 12, March 2024 data cutoff, the median follow-up was 13.9 months

# Baseline Characteristics

	Arm A1 N=41, n (%)
<b>Mean age, years (range)</b>	61 (30 to 82)
<b>Female</b>	17 (41)
<b>Country</b>	
United States/France	22 (54)
Korea	19 (46)
<b>Baseline ECOG performance status 1</b>	25 (61)
<b>Histologically confirmed diagnosis</b>	
Esophageal	10 (24)
Gastric	26 (63)
Gastroesophageal Junction (GEJ)	5 (12)

	Arm A1 N=41, n (%)
<b>Current disease status</b>	
Locally advanced unresectable disease	3 (7)
Metastatic disease	38 (93)
<b>Liver metastases</b>	13 (32)
<b>Peritoneal metastases</b>	15 (37)
<b>TAP category (Central Lab)*</b>	
TAP ≥ 5%	16 (39)
TAP < 5%	24 (59)
Unavailable†	1 (2)
<b>Microsatellite instability status</b>	
High	1 (2)
Low/Stable	35 (85)
Unknown	5 (12)

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

\* Ventana SP263 assay used for all TAP scores.

† 1 patient did not have tissue available for central testing.

ECOG: Eastern Cooperative Oncology Group; TAP: tumor area positivity

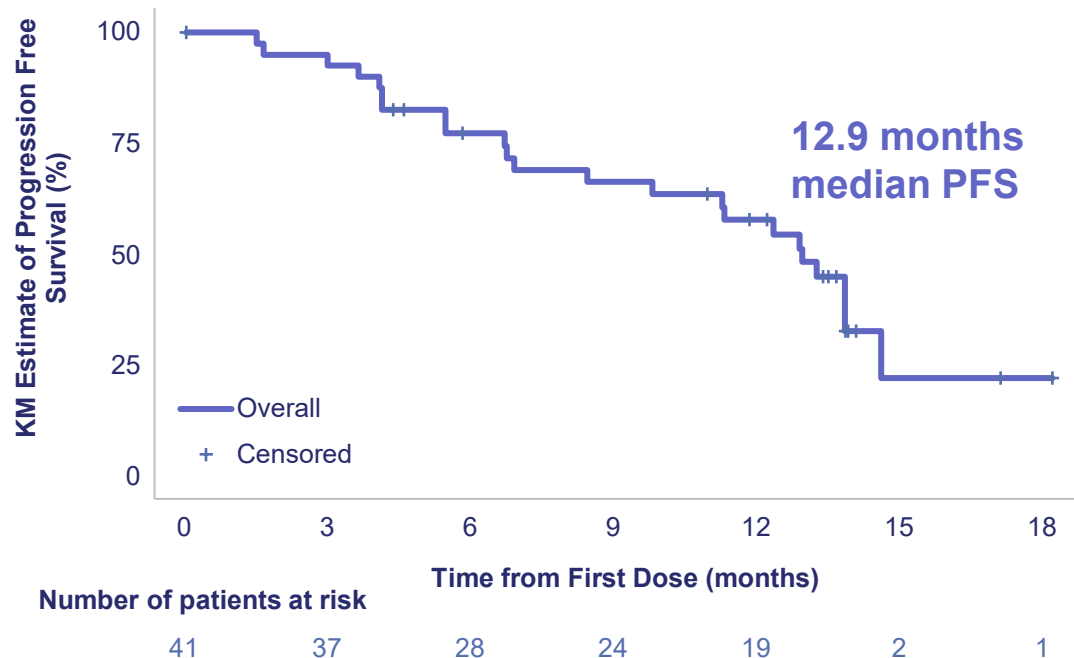




# Unprecedented Median PFS of 12.9 months in the Overall Population

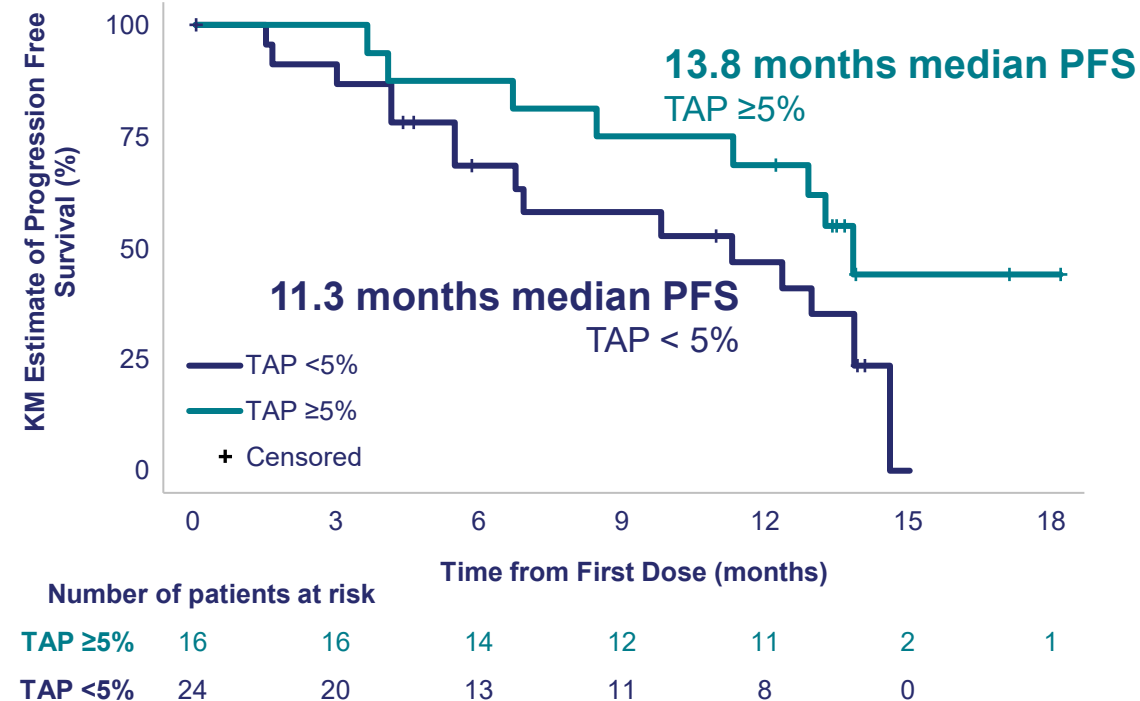
## Efficacy-Evaluable (N=41)

	Median, months (95% CI)	Month 12 rate, % (95% CI)	Median PFS follow-up time, months (95% CI)	Events, n (%)
Overall (N=41)	12.9 (9.8, 13.8)	58 (42, 74)	13.9 (13.5, 14.1)	24 (59)



## TAP ≥ 5% (n=16); TAP < 5% (n=24)

	Median, months (95% CI)	Month 12 rate, % (95% CI)	Median PFS follow-up time, months (95% CI)	Events, n (%)
TAP ≥ 5% (n=16)	13.8 (11.3, NE)	69 (46, 91)	13.8 (13.5, 17.1)	8 (50)
TAP < 5% (n=24)	11.3 (5.5, 13.8)	47 (25, 69)	13.9 (10.9, 14.1)	16 (67)



# Dom + Zim + Chemo Has the Potential to Become the New SOC in 1L Gastric/GEJ/EAC

Data below 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

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

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. With 12.1 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.

CPS: combined positive score; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immuno-oncology; ITT: intent-to-treat; mOS: median overall survival; mPFS: median progression-free survival; NE: not estimable; nivo: nivolumab; ORR: overall response rate; pembro: pembrolizumab; TAP: tumor area positivity

# Phase 3 Evaluating Dom + Zim + Chemo vs Nivo + Chemo in 1L Gastric/GEJ/EAC

STAR-221 is evaluating the same regimen in the same setting as EDGE-Gastric – and dom + zim has the potential to be the first anti-TIGIT combination approved for 1L Gastric/GEJ/EAC

## 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

## Stratification Factors:

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

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  $\geq 5\%$

## KEY SECONDARY ENDPOINTS:

- PFS ITT
- PFS in TAP  $\geq 5\%$



ENROLLMENT COMPLETED

\*PI choice of chemo: FOLFOX or CAPOX.

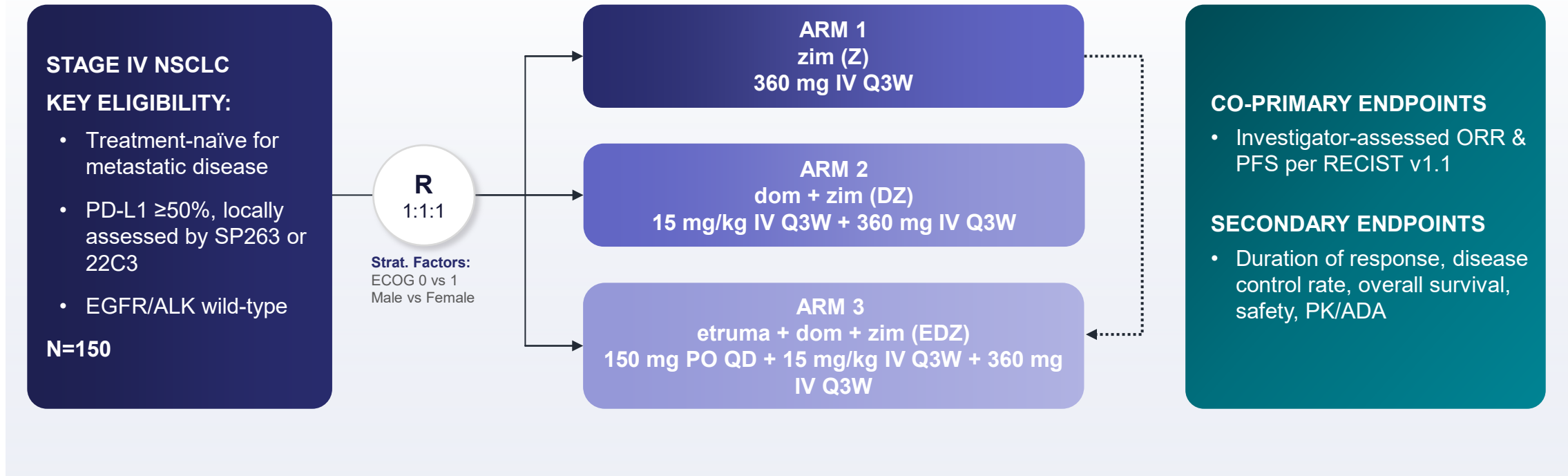
NCT #: NCT05568095

1L: first-line; chemo: chemotherapy; dom: domvanalimab; EAC: esophageal adenocarcinoma; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; nivo: nivolumab; ITT: intent to treat; OS: overall survival; PFS: progression-free survival; PI: principal investigator; RECIST: Response Evaluation Criteria in Solid Tumors; TAP: tumor area positivity; R: randomized; zim: zimberelimab

# Summary of ARC-7 Results and Domvanalimab Plus Zimberelimab Clinical Program in Non-Small Cell Lung Cancer

Data presented at the 2023 ASCO Annual Meeting, based on data cut-off of Feb. 7, 2023.

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



Participants randomized to Arm 1 had the option to crossover to separate, 2L EDZ cohort upon radiographically confirmed disease progression (PD)

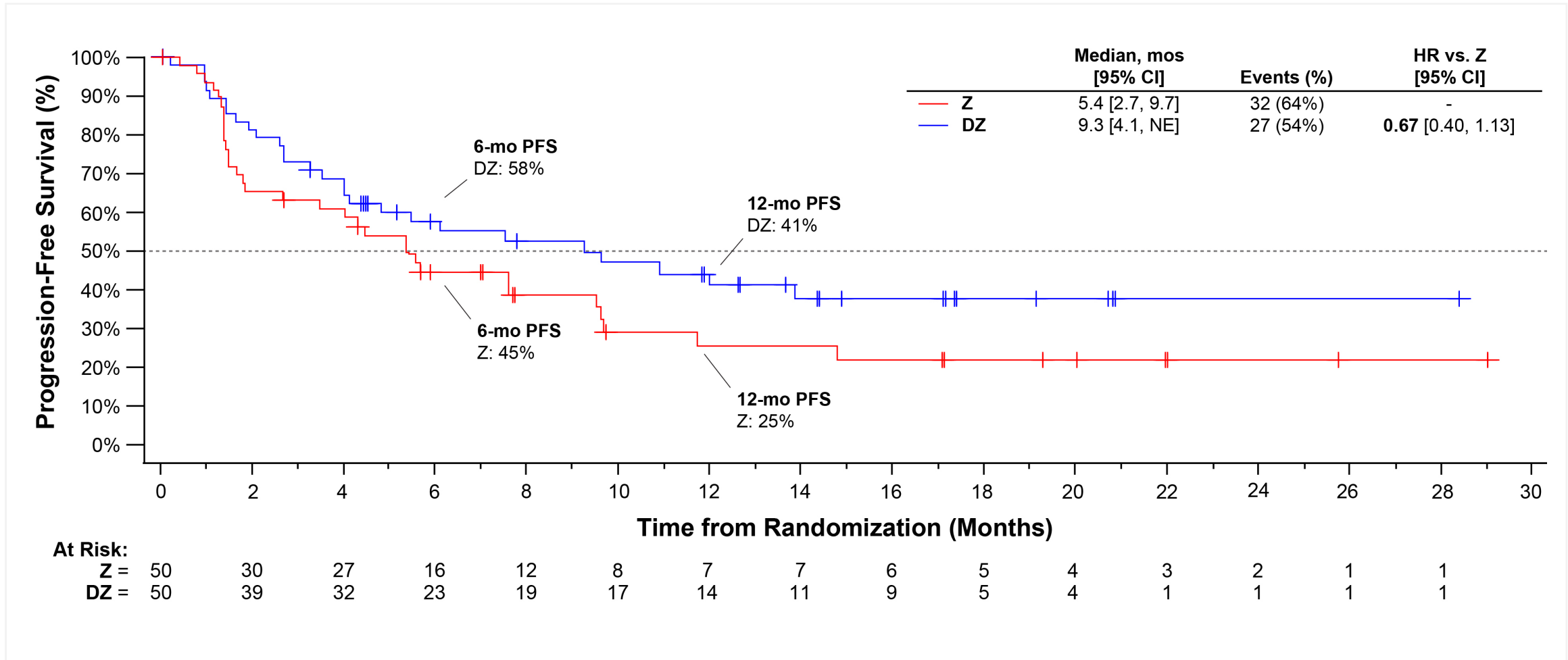
- As of the clinical cut-off date (Feb. 7, 2023), a total of 150 patients were randomized, with a median follow-up of 18.5 months

ADA: anti-drug antibody; D/dom: domvanalimab; ECOG: Eastern Cooperative Oncology Group; E/etruma: etrumadenant; IV: intravenous; NSCLC: non-small cell lung cancer; ORR: overall response rate; Ph: phase; PFS: progression-free survival; PK: pharmacokinetics; PO: orally; R: randomized; RECIST: Response Evaluation Criteria in Solid Tumors; Z/zim: zimberelimab; Q3W: every 3 weeks; QD: once-daily

Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

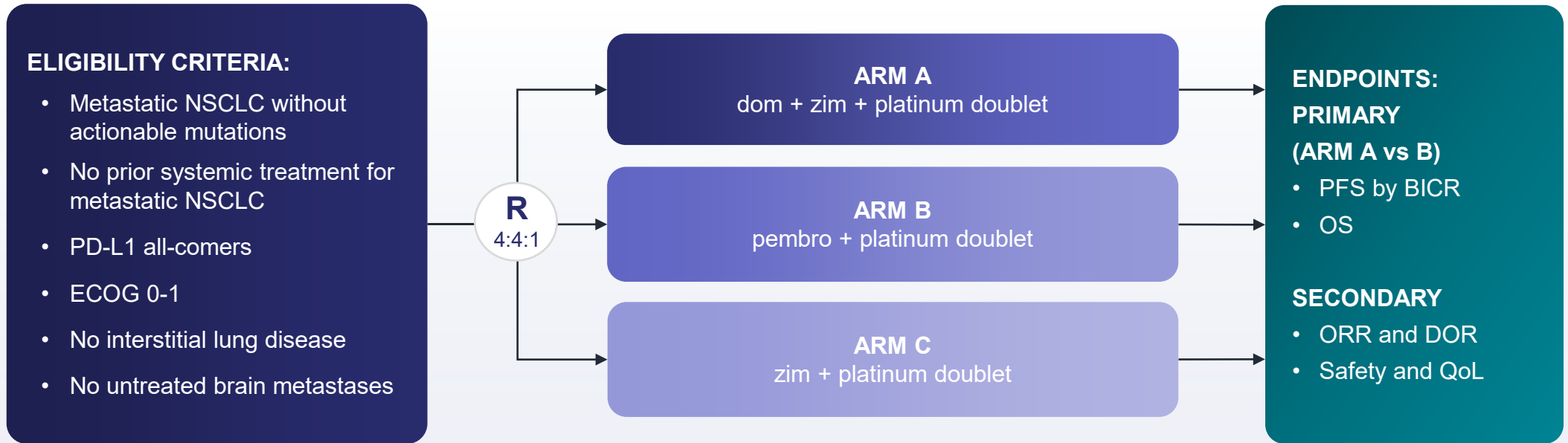


# Addition of Dom to Zim Resulted in a 33% Reduction in Risk of Progression or Death, Compared to Zim Monotherapy



# 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 ( $\geq 50\%$  vs. 1-49%)
- Geography (east Asia vs non-east Asia)
- Histology (Sq vs Non-sq)

 **ENROLLMENT COMPLETION  
EXPECTED YEAR END 2024**

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

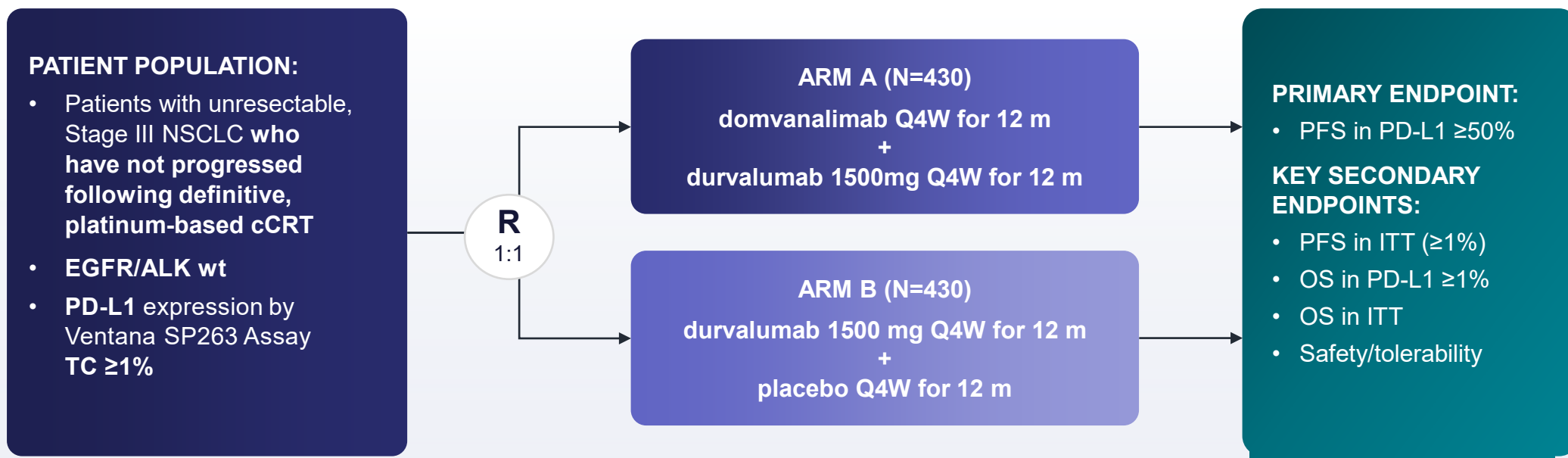
Gilead Sciences is operationalizing STAR-121

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)

# Casdatifan (HIF-2a) in ccRCC

# Casdatifan (AB521): A Potential Best-in-Class HIF-2a Inhibitor

## Efficacy

**Opportunity to reach greater intra-tumoral HIF-2a inhibition compared to the 120mg dose of belzutifan**

**Potential to result in:**

- Lower rate of primary progressive disease
- Higher ORR
- More durable responses
- Similar safety profile

## Novel Combinations in 1L and Post-IO Settings

**Opportunity to create potentially best-in-class and first-in-class combinations**

- Post-IO setting:
  - PEAK-1: Phase 3 study of cas plus cabozantinib (the current SOC in 2L RCC) in anti-PD-1 experienced RCC expected to initiate in 1H25
  - STELLAR-09: Phase 1b/2 trial of cas plus zanzalintinib, a next-generation TKI (ongoing)
- 1L setting:
  - In advanced stages of planning to evaluate cas in a potential first-in-class combination with a collaboration partner

## PH 1 DOSE ESCALATION

3+3 design with 21-day DLT window **Solid-tumor patients w/o SOC**

### KEY INCLUSION CRITERIA

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

### KEY EXCLUSION CRITERIA

- No prior HIF-2 $\alpha$  inhibitor (dose expansion only)



## EXPANSION COHORTS (2L+ ccRCC)

50 mg (n~30)

■ COMPLETED ENROLLMENT

100 mg (n~30)\*

■ COMPLETED ENROLLMENT

150 mg (n~30)

■ COMPLETED ENROLLMENT

cas + cabo (n~30)

■ ENROLLING

## CURRENT STATUS:

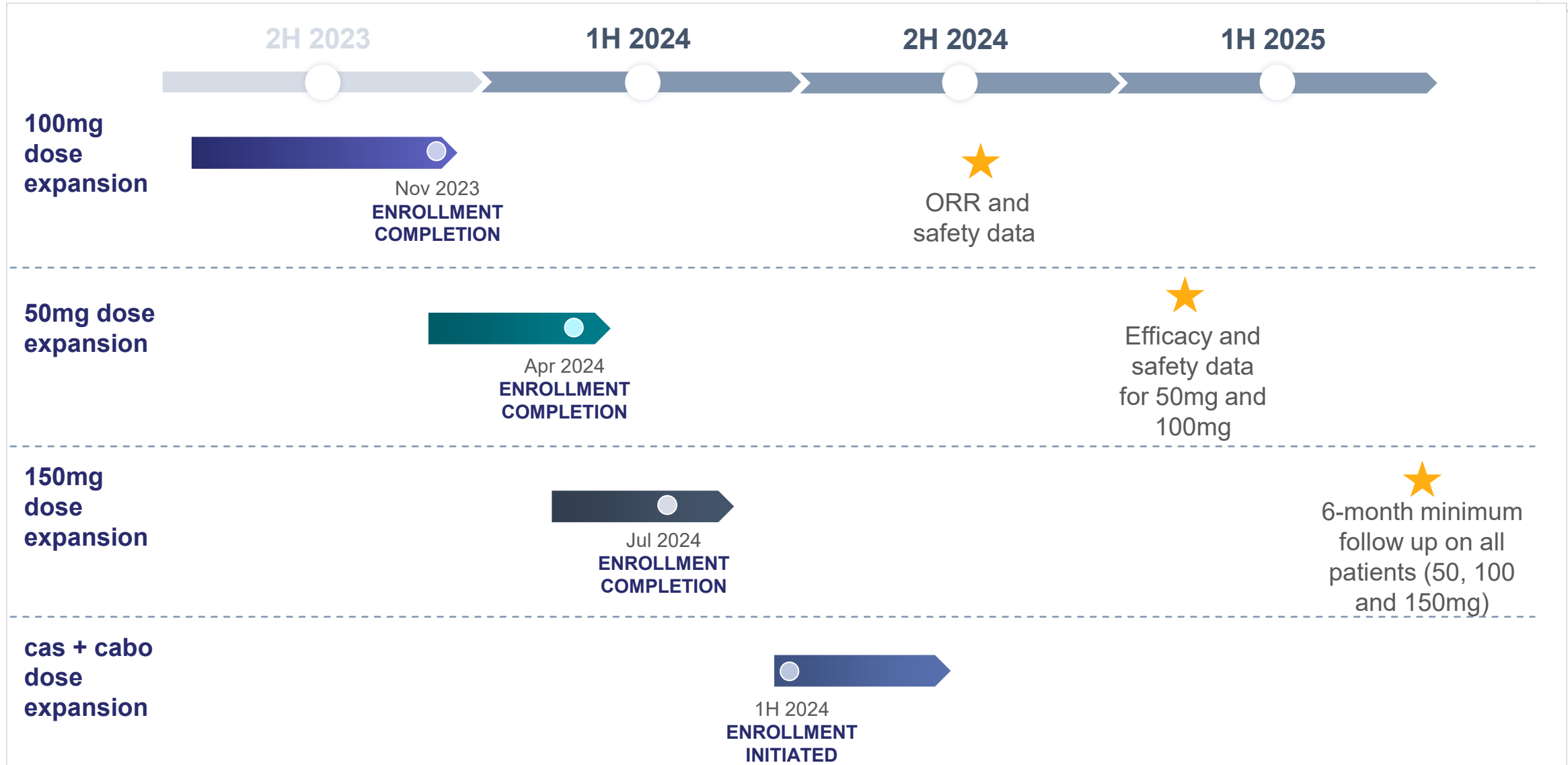
- Data from the dose expansion cohort evaluating the 100mg daily dose has been submitted for presentation at a medical meeting in Fall 2024

\*Opened enrollment to an additional 30 patients in the 100mg expansion cohort due to investigator interest

2L: second-line; 2H: second half; BID: twice daily; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DLT: dose limiting toxicities; PD: pharmacodynamics; Ph: phase; PK: pharmacokinetics; QD: once daily; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: standard of care



# Multiple Casdatifan Datasets from ARC-20 are Expected Over the Next 12 Months



# Trial Inclusion Criteria and ORR From Other 2L+ RCC Studies

STUDY DESCRIPTION	PHASE	INCLUSION CRITERIA	# OF LINES OF THERAPY	PRIOR TKI	PRIOR CPI	ORR
LITESPARK-001 <sup>1</sup>	Ph 1	<ul style="list-style-type: none"> <li>Locally advanced/metastatic ccRCC who previously received ≥1 therapy</li> </ul>	<ul style="list-style-type: none"> <li><b>Median 3 prior lines</b></li> </ul>	<ul style="list-style-type: none"> <li><b>91% had prior VEGF TKI</b></li> </ul>	<ul style="list-style-type: none"> <li>80% had prior CPI</li> </ul>	<ul style="list-style-type: none"> <li>20.5% (prior CPI and TKI, 41mo. f/u)</li> </ul>
LITESPARK-005 <sup>2</sup>	Ph 3	<ul style="list-style-type: none"> <li>Unresectable, locally advanced or metastatic ccRCC</li> <li>Disease progression after 1-3 prior systemic regimens, including ≥1 anti-PD-(L)1 and ≥1 VEGFR-TKI</li> </ul>	<ul style="list-style-type: none"> <li><b>1-3 prior lines for inclusion</b></li> <li><b>Mostly 2-3 prior lines</b></li> </ul>	<ul style="list-style-type: none"> <li><b>100% had prior TKI</b></li> </ul>	<ul style="list-style-type: none"> <li>100% had prior CPI</li> </ul>	<ul style="list-style-type: none"> <li>21.9% (prior CPI and TKI, 18.4mo. f/u)</li> </ul>
LITESPARK-013 <sup>3</sup>	Ph 2	<ul style="list-style-type: none"> <li>Histologically confirmed advanced/metastatic RCC with clear cell component</li> <li>Measurable disease per RECIST v1.1</li> <li>Received ≤3 prior systemic therapies for advanced/metastatic disease</li> <li>Received only 1 prior anti-PD-1/L1 therapy</li> </ul>	<ul style="list-style-type: none"> <li><b>Mostly 1-2 prior lines</b></li> </ul>	<ul style="list-style-type: none"> <li><b>71.4% had prior TKI</b></li> </ul>	<ul style="list-style-type: none"> <li>100% had prior CPI</li> </ul>	<ul style="list-style-type: none"> <li>19.1% (prior CPI and TKI, 20mo. f/u)</li> </ul>
ARC-20 <sup>4</sup>	Ph 1	<ul style="list-style-type: none"> <li>Histologically confirmed ccRCC</li> <li>Must have received prior treatment in the metastatic setting (either individually or in combination) with anti-PD-1 and a TKI</li> </ul>	<ul style="list-style-type: none"> <li><b>25% of patients had &gt;3 prior lines</b></li> <li><b>Median of 3 prior lines</b></li> </ul>	<ul style="list-style-type: none"> <li><b>100% had prior TKI</b></li> </ul>	<ul style="list-style-type: none"> <li>100% had prior CPI</li> </ul>	<ul style="list-style-type: none"> <li>Expected 2H24</li> </ul>

1. belzutifan in previously treated ccRCC (Dose Expansion Cohort) (NCT02974738); refs: Jonasch et al 2024; Choueiri et al 2021; ASCO GU 2021 273

2. belzutifan vs. everolimus in previously treated ccRCC (NCT04195750); ref: ESMO 2023 LBA88

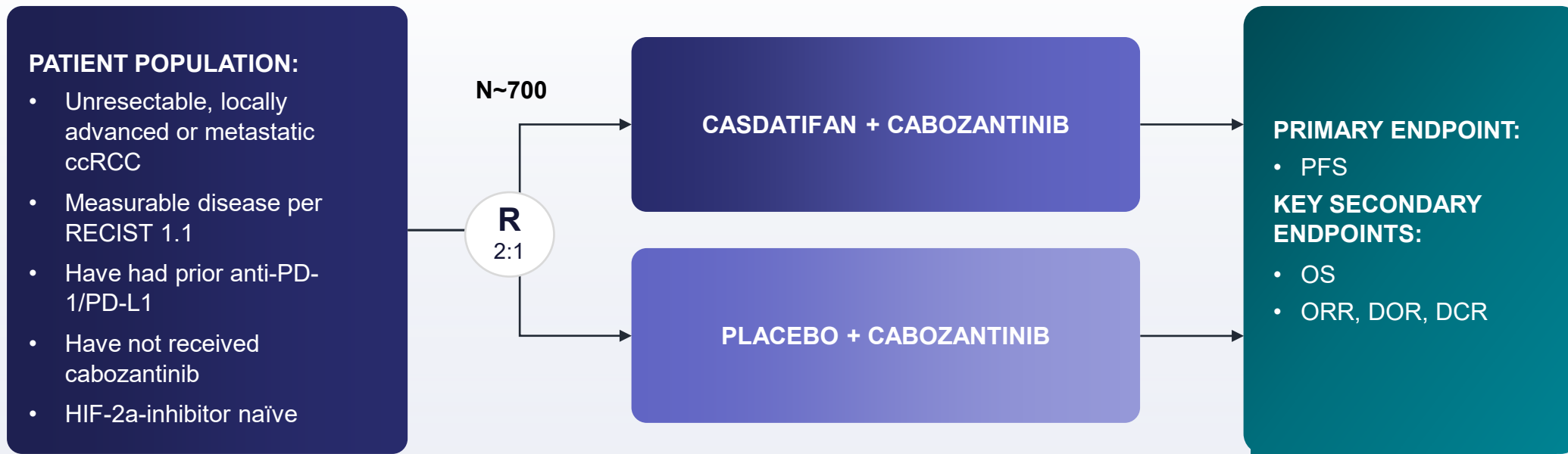
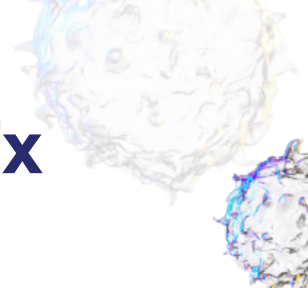
3. belzutifan 120mg and 200mg (pooled) in previously treated ccRCC (NCT04489771); ref: ASCO 2024 4534

4. casdatafan in previously treated ccRCC (NCT05536141); ref: ct.gov

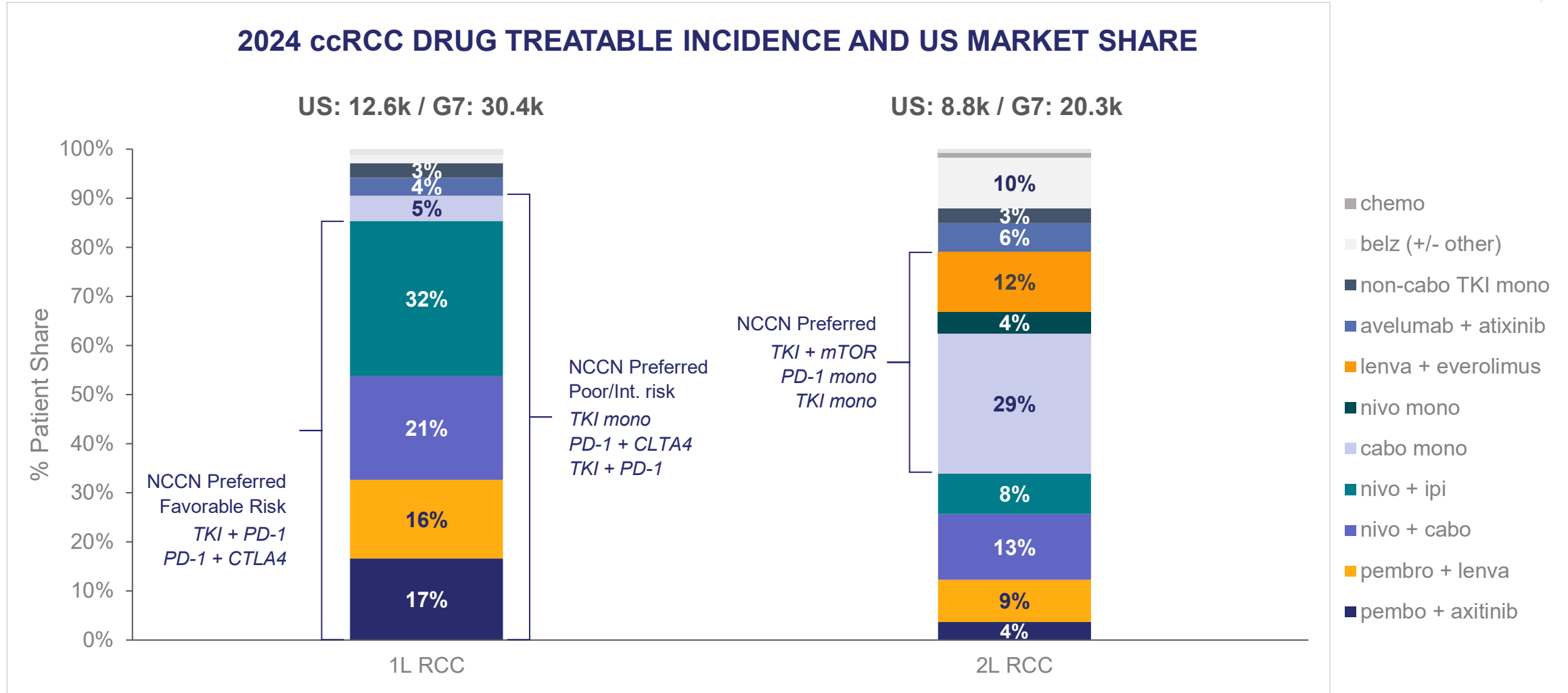
5. tivozanib vs. sorafenib in previously treated ccRCC (NCT02627963); ref: Rini et al 2020

2L: second line; ccRCC: clear-cell renal cell carcinoma; CPI: checkpoint inhibitor; f/u: follow up; KPS: Karnofsky Performance Status; mo: month; Ph: Phase; RECIST: Response Evaluation Criteria in Solid Tumors; VEGFR-TKI: Vascular endothelial growth factor receptor-tyrosine kinase inhibitor

# Proposed Phase 3 Study Evaluating Cas + Cabo in Advanced or Metastatic ccRCC, following prior PD-1 Tx



# RCC Treatment Landscape Favors Tailored Combination Therapies with Multiple TKIs



Sources - Epi: DRG, GlobalData | Share: Arcus primary research, US May 2024 (n=49)  
 Q1A: Please think of the metastatic clear cell renal cell carcinoma (ccRCC) patients that you have initiated on 1L treatment in the last 6 months. What percent (%) of patients were initiated on each of the following regimens:  
 Q2: Now please think of the metastatic clear cell renal cell carcinoma (ccRCC) patients that you have initiated on 2L treatment in the last 6 months. What percent (%) of patients were initiated on each of the following regimens:  
 1L: first line; 2L: second line; belz: belzutifan; cabo: cabozantinib; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; ipi: ipilimumab; lenva: lenvatinib; mono: monotherapy; NCCN: National Comprehensive Cancer Network; nivo: nivolumab; pembro: pembrolizumab; TKI: tyrosine kinase inhibitor

# RCC Patients Have Typically Cycled Through Multiple TKIs Due to Lack of Other Treatment Options

TKI	GLOBAL 2023 SALES (\$M) <sup>1</sup>	REGIMEN	PATIENT POPULATION	APPROVAL
cabozantinib	\$2,254	monotherapy	1L intermediate-/poor-risk	U.S. (Dec. 2017) E.U. (May 2018) Jp (Mar. 2020)
		nivolumab + cabozantinib	1L	U.S. (Jan. 2021) E.U. (Mar. 2021) Jp (Aug. 2021)
lenvatinib	\$2,199	pembrolizumab + lenvatinib	1L	U.S. (Aug. 2021) E.U. (Nov. 2021) Jp (Feb. 2022)
axitinib	\$1,036	pembrolizumab + axitinib	1L	U.S. (Apr. 2019) E.U. (Sep. 2019)
		avelumab + axitinib	1L	U.S. (May 2019) E.U. (Oct. 2019) Jp (Mar. 2020)
sunitinib	\$180	monotherapy	1L	U.S. (Feb. 2007) E.U. (Jan. 2007)
pazopanib	\$390	monotherapy	1L/2L	U.S. (Oct. 2009) E.U. (Jun. 2010)
tivozanib	~\$105 <sup>2</sup>	monotherapy	1L/2L	E.U. (Aug. 2017)

1) \$M USD, Globaldata

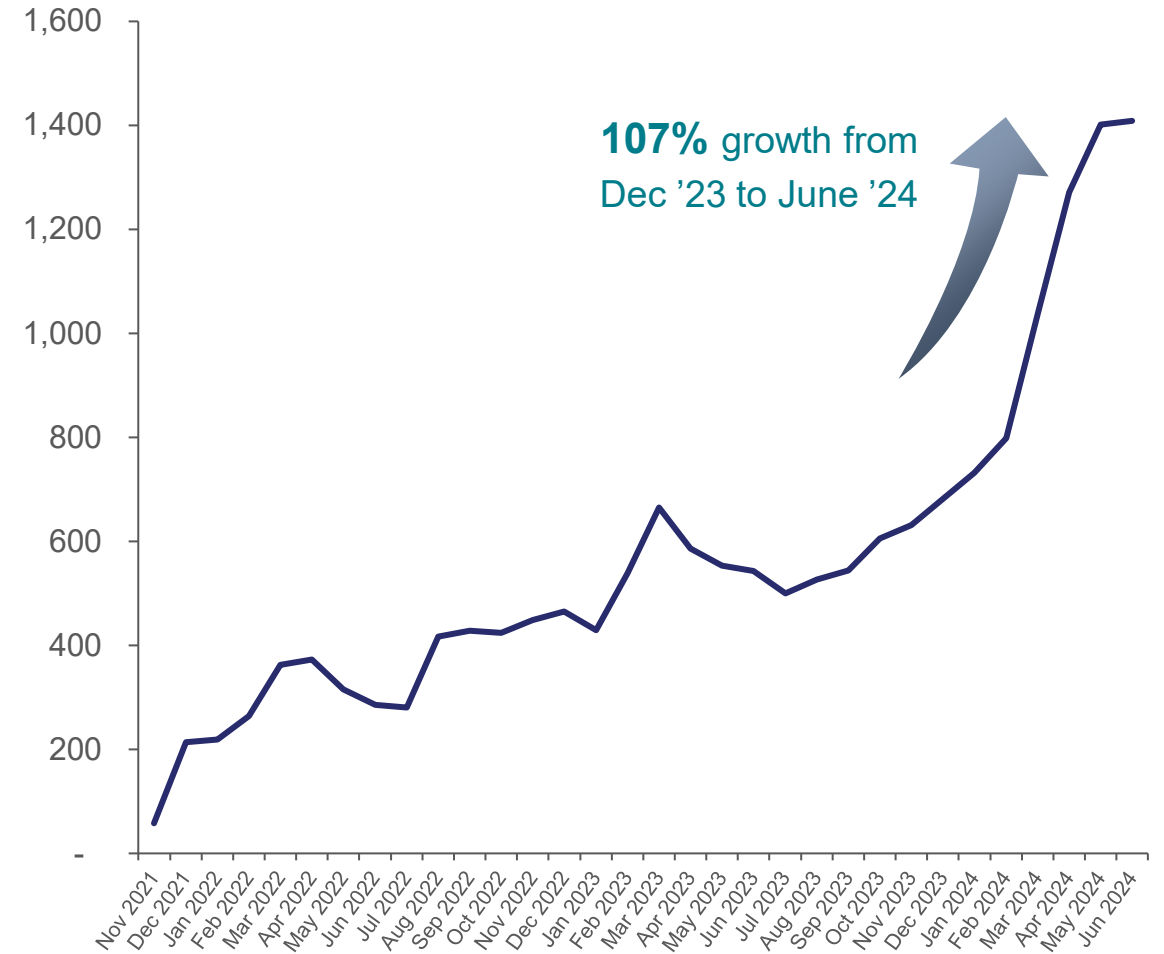
2) 2022, Aveo guidance per Fierce Pharma, <https://www.fiercepharma.com/pharma/lg-chem-picks-aveo-and-kidney-cancer-drug-fotivda-566m>

1L: first-line; 2L: second-line; E.U.: European Union; Jp: Japan; TKI: tyrosine kinase inhibitor; U.S.: United States

# Doubling of Belzutifan Scripts Since ccRCC Data Release in August 2023

- December 2023: Belzutifan received FDA approval for monotherapy in late-line ccRCC
- **Annualized Run-Rate Sales of >\$500M in the U.S.**
  - Increase in scripts driven by late-line monotherapy label only
- **Earlier stage settings, with HIF-2 $\alpha$ -based combinations, will unlock even greater opportunity**

MONTHLY BELZUTIFAN SCRIPTS





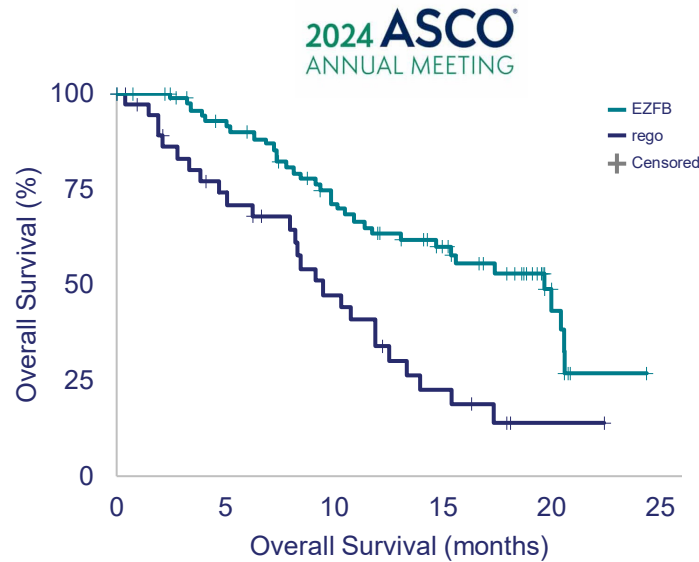
# CD73-Adenosine Axis Programs

# 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)

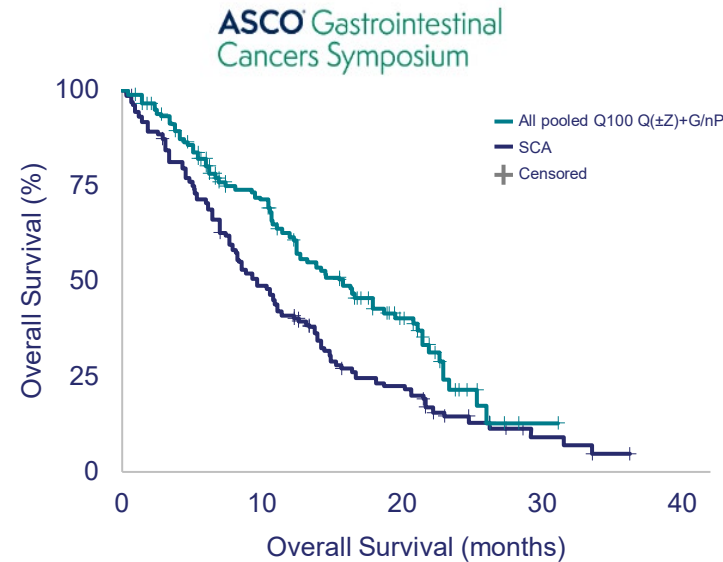
ARC-9



## 1L Metastatic PDAC

quemli ± zim + G/nP (n=122)

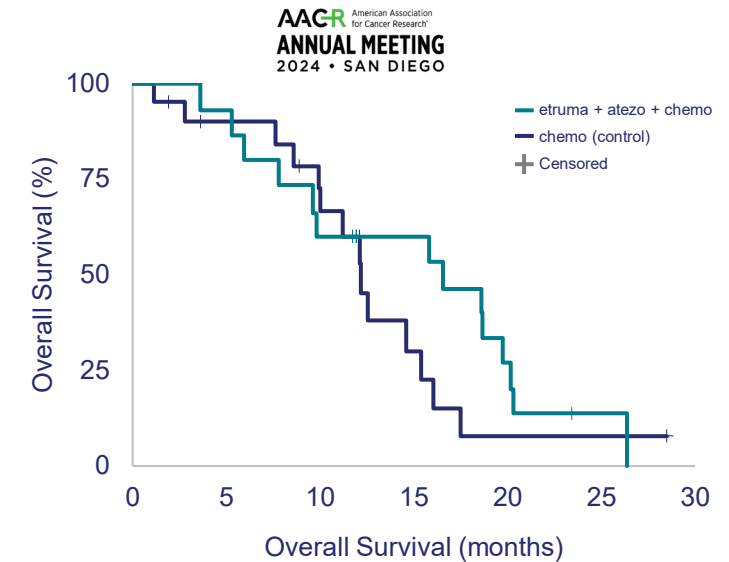
ARC-8



## 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/m<sup>2</sup> 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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ARCUS BIOSCIENCES



# Etrumadenant in Pancreatic and Colorectal Cancers

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

## ETRUMADENANT

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

## Etrumadenant has an ideal profile

- ✓ Retains potency in physiologically relevant conditions
  - IC<sub>50</sub> = 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

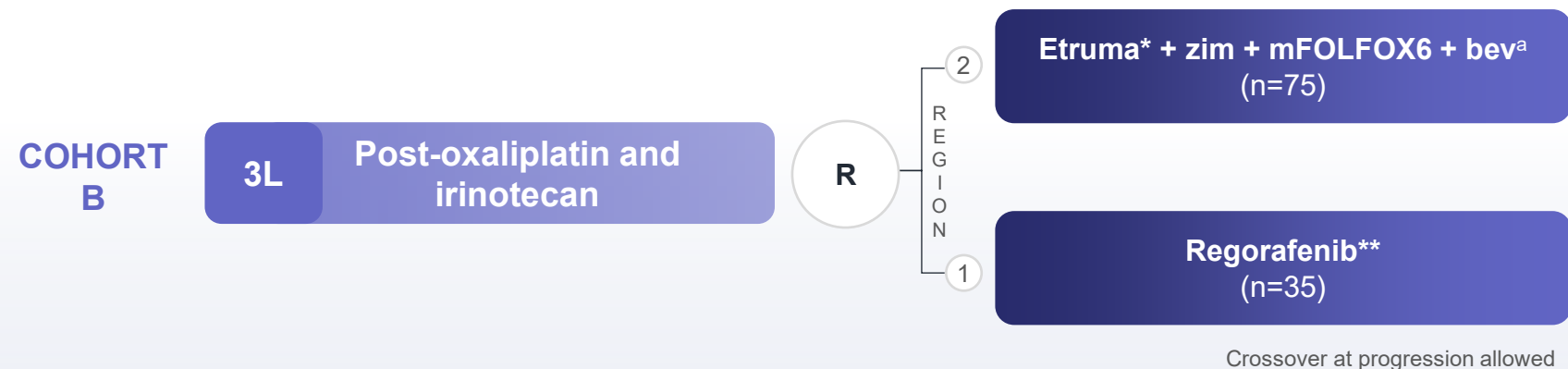
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# Summary of ARC-9 Results

Data presented at 2024 ASCO Annual Meeting, based on data cut off of November 13, 2023.

# ARC-9 Cohort B: Etruma + Zim + mFOLFOX6 + Bev<sup>a</sup> (EZFB) vs Regorafenib (Rego) in 3L mCRC



## PRIMARY ENDPOINTS:

- PFS (investigator assessed)

## KEY SECONDARY ENDPOINTS:

- OS
- ORR (investigator assessed)
- Safety

Sample size of approximately 105 participants was estimated in a 2:1 ratio randomization to detect an improvement of HR of 0.5 in PFS using a log-rank test in order to achieve 80% power at a two-sided significance level of 0.05

## KEY INCLUSION CRITERIA

- Histologically confirmed unresectable mCRC
- Measurable disease per RECIST v1.1
- ECOG PS of 0 or 1
- Disease progression on or after treatment with oxaliplatin and irinotecan containing chemotherapy in combination with anti-VEGF(R) or anti-EGFR

## KEY EXCLUSION CRITERIA

- Prior treatment with immune checkpoint blockade therapies
- Mutation in the BRAF oncogene; patients with unknown BRAF status will be required to undergo testing at a local laboratory and provide results at screening

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023

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

\*100 mg, IV, every 2 weeks (Days 1 and 15 of 28-day cycle)

\*\*Dose ramp up starting at 80mg PO QD week 1, 120mg PO QD Week 2 and 160mg PO QD week 3 for the first cycle, followed by 160mg QD for 21 days out of 28-day cycle thereafter

3L: third line; bev: bevacizumab; CRC: colorectal cancer; etruma: etrumadenant; irino: irinotecan; mCRC: metastatic CRC; ORR: objective response rate; OS: overall survival; oxali: oxaliplatin; R: randomized; zim: zimberelimab.

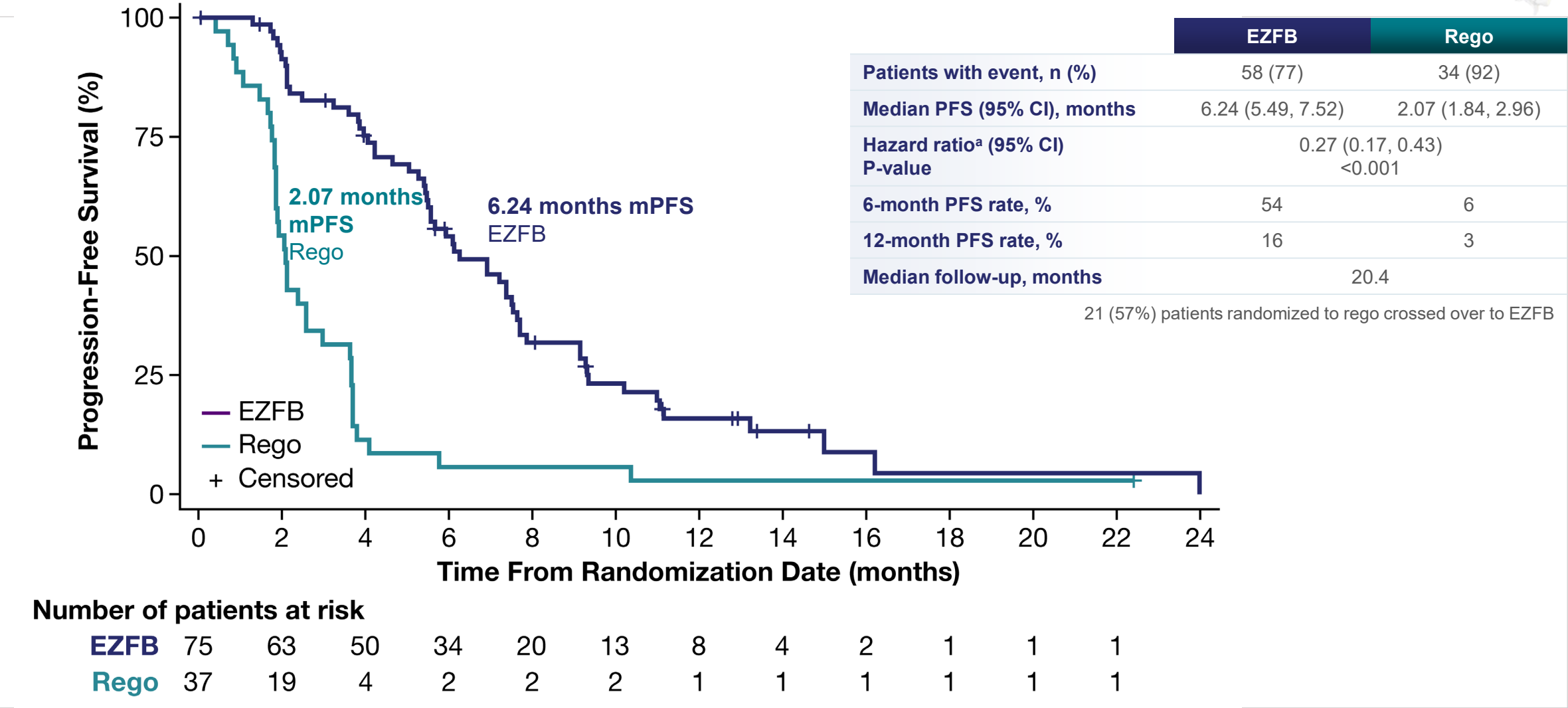


# Prior Performance on FOLFOX Is Consistent With Historical 1L Data

- Patients previously performed in-line with expectations for FOLFOX + bev in prior lines
- Prior performance in FOLFOX was well-balanced between arms

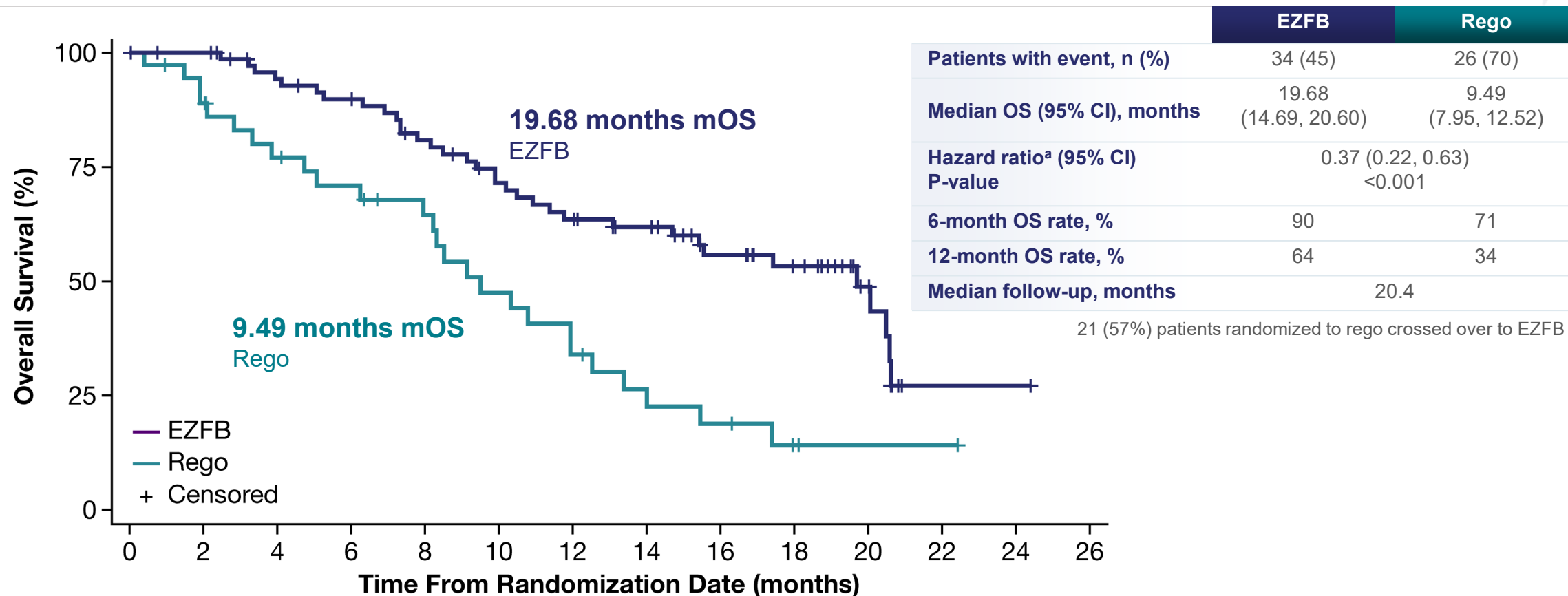
	EZFB (N=75)	REGO (N=37)
<b>Time from first oxaliplatin dose date to progression/discontinuation date of the last prior oxali-containing regimen, n (%)</b>	74 (98.7)	36 (97.3)
Median, months	9.0	9.8
Min, Max, months	0.7, 57.2	0.9, 33.7
<b>Prior BOR of last oxaliplatin regimen under metastatic setting, n (%)</b>	63 (84.0)	31 (83.8)
CR	2 (3.2)	2 (6.5)
PR	29 (46.0)	12 (38.7)
SD	15 (23.8)	9 (29.0)
PD	10 (15.9)	2 (6.5)
Unknown/Missing	7 (11.1)	6 (19.4)

# EZFB Demonstrated Statistically Significant Improvement in PFS vs Rego



ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023  
Progression free survival is defined as the first occurrence of progressive disease per RECIST v1.1 or death, whichever occurs first. Patients without documented disease progression at the time of analysis were censored on the date of their last adequate tumor assessment. If no tumor assessment was performed after the start of study treatment, PFS will be censored on the date of first dose of study treatment with duration of 1 day.  
<sup>a</sup> Hazard ratio and 95% confidence interval based on stratified (geographic region) Cox model. Study was not designed as a powered study to control for alpha in multiplicity testing.  
EZFB, etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; PFS, progression-free survival; rego, regorafenib.

# EZFB Demonstrated Significant Improvement in OS vs Rego



## Number of patients at risk

<b>EZFB</b>	75	73	65	61	53	45	40	35	26	20	10	1	1
<b>Rego</b>	37	32	26	23	19	14	10	6	5	2	1	1	0

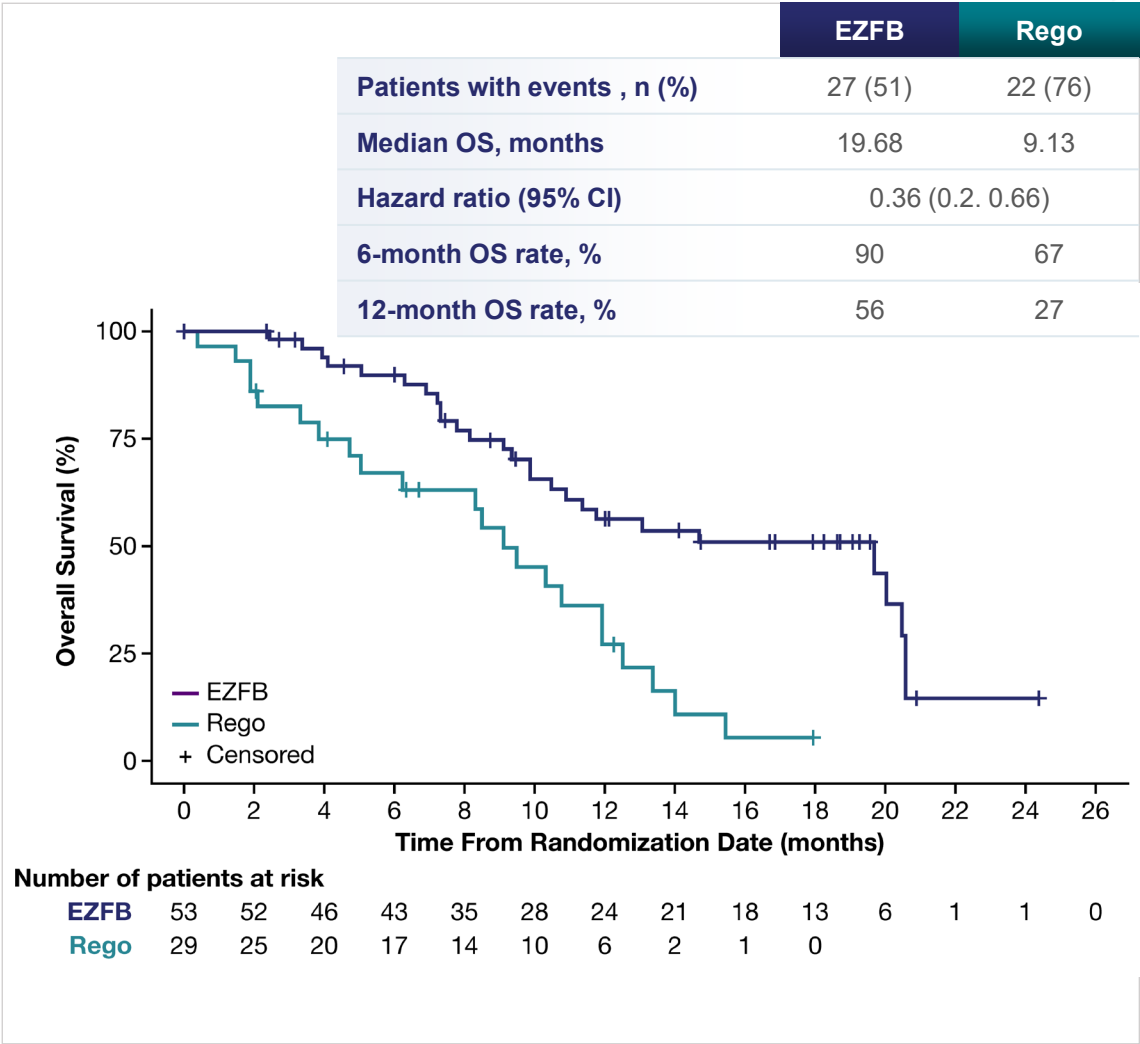
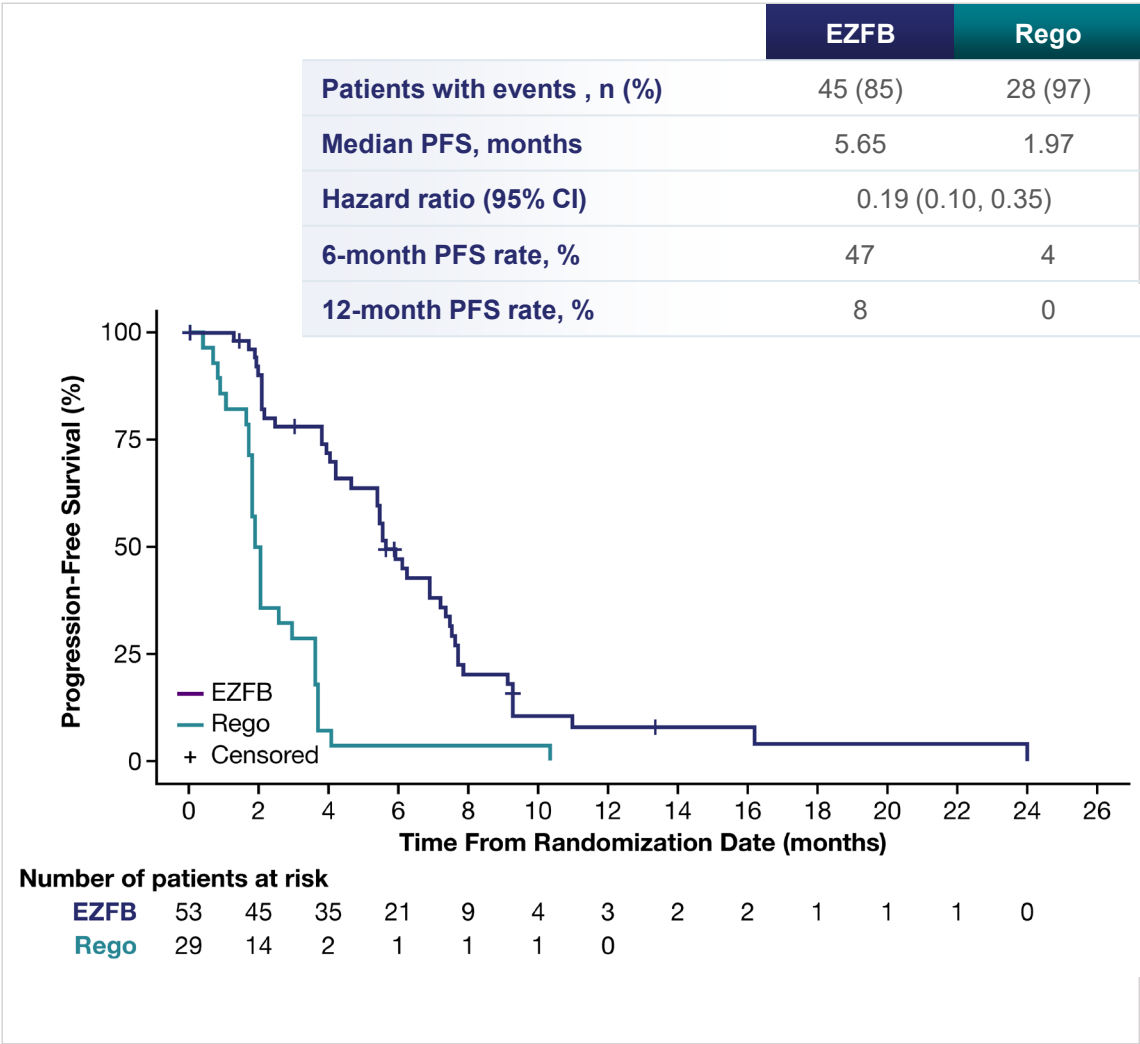
ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023.

Overall survival is defined as time (months) from randomization until death from any cause. Patients who did not die while on study are censored at the last known date they were alive.

<sup>a</sup> Hazard ratio and 95% confidence interval based on stratified (geographic region) Cox model. Study was not designed as a powered study to control for alpha in multiplicity testing.

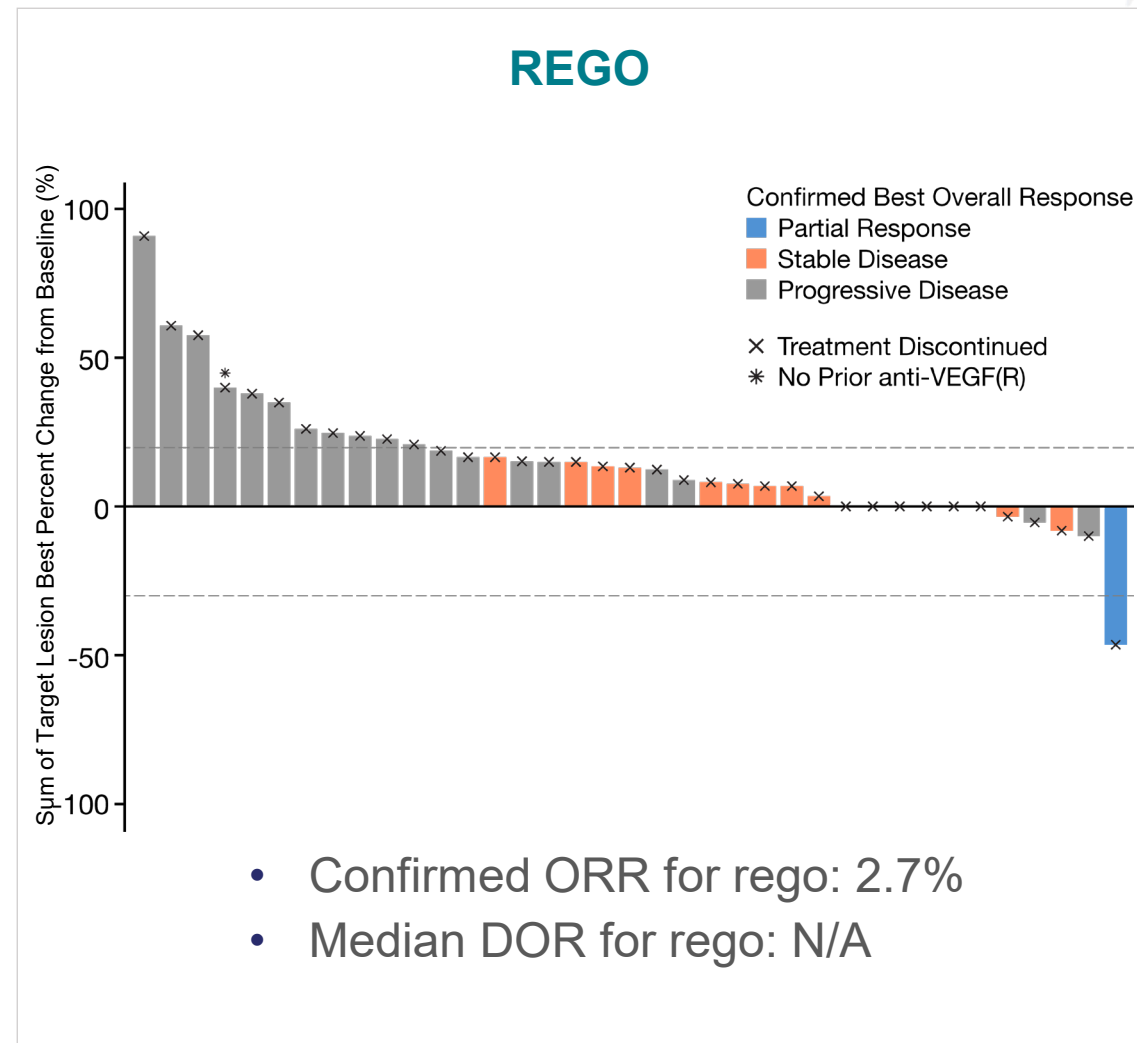
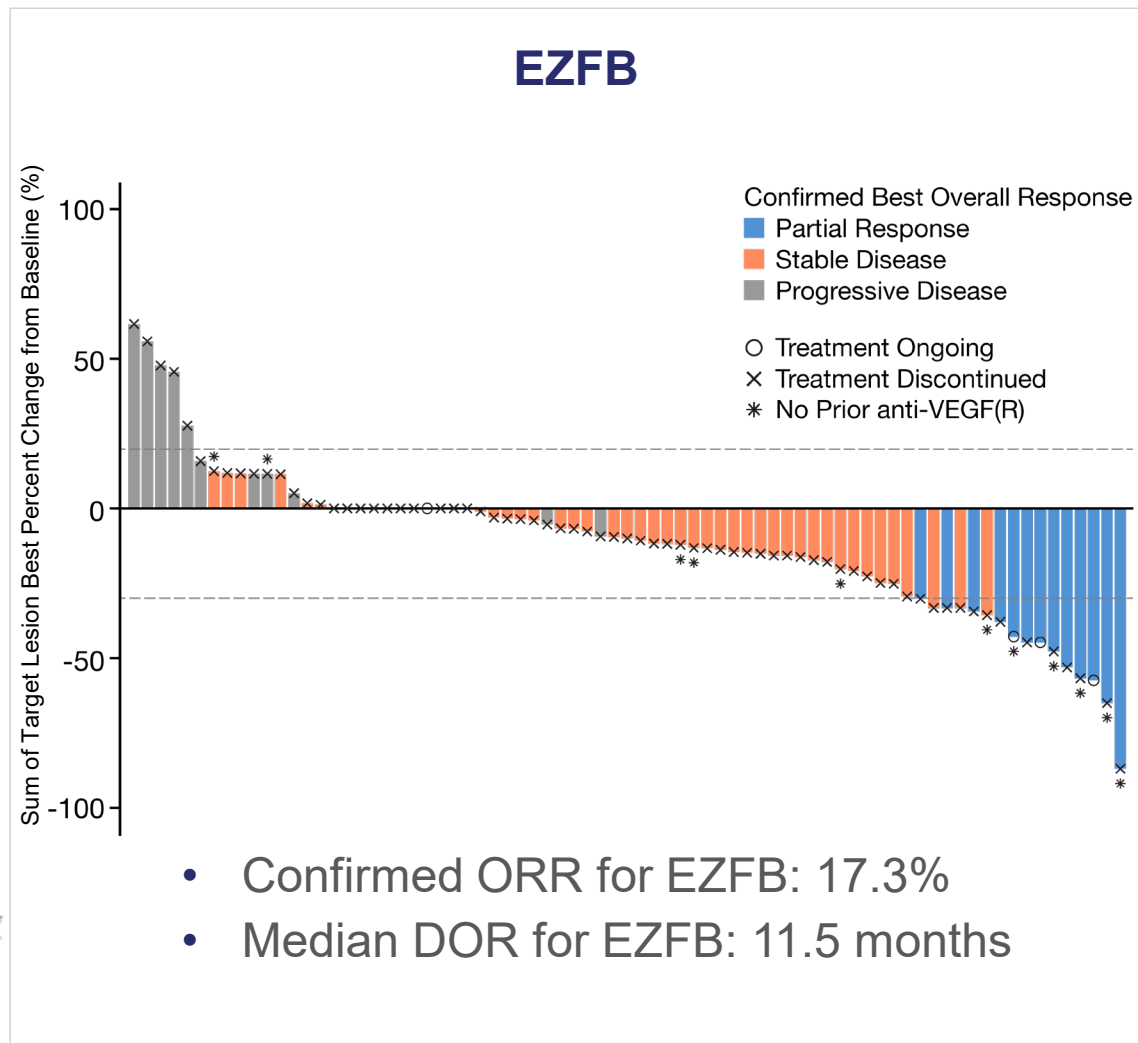
EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; OS: overall survival; rego: regorafenib

# 5.7 Month Median PFS and 20 Month Median OS for EZFB in Patients With Liver Metastasis



ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023  
Progression free survival is defined as the first occurrence of progressive disease per RECIST v1.1 or death, whichever occurs first. Patients without documented disease progression at the time of analysis were censored on the date of their last adequate tumor assessment. If no tumor assessment was performed after the start of study treatment, PFS will be censored on the date of first dose of study treatment with duration of 1 day. Overall survival is defined as time (months) from randomization until death from any cause. Patients who did not die while on study are censored at the last known date they were alive.  
CI: confidence interval; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; OS: overall survival; PFS: progression-free survival; rego: regorafenib

# Two-Thirds (66%) of Patients on EZFB Experienced Tumor Reduction



# EZFB Had an Acceptable Safety Profile, Consistent With Known Toxicity Profile of FOLFOX/bev in Combination With Anti-PD-1

n (%)	EZFB (N=74)	Rego (N=35)
Median treatment duration, weeks	26	7
Any TEAEs	73 (99)	31 (89)
Serious TEAEs	37 (50)	9 (26)
Grade ≥3 TEAEs	61 (82)	17 (49)
Any TEAEs leading to discontinuation of study drug	44 (59)	7 (20)
Leading to oxaliplatin discontinuation <sup>a</sup>	39 (53) <sup>a</sup>	-
Any TEAE leading to discontinuation of all study drugs	4 (5)	6 (17)
Any TEAEs leading to death	0	0
Any TEAEs that are immune-mediated reactions (per sponsor) <sup>b</sup>	12 (16)	2 (6)
≥3 event	4 (5)	0

Note: All-cause Grade 3+ AE rate for mFOLFOX6 + bev alone in 1L CRC of 67%; Serious AE rate for mFOLFOX6 + bev alone of 33%<sup>1</sup>. Grade 3+ TEAE rate for TAS-102 (Lonsurf) + bev was 72.4% in the SUNLIGHT Trial<sup>2</sup>.

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023

Safety-evaluable population includes all enrolled patients who received any amount of any study treatment. TEAEs are any AEs that start on or after the study treatment start date/time and within 90 days of the last dose date for all zim arms (30 days for non-zim arms), excluding any AEs occurring after initiation of new anti-cancer therapy. Treatment related corresponds to any adverse event marked as related to etruma or zim or FOLFOX or bev or rego on the case report form.

<sup>a</sup> AEs leading to oxaliplatin discontinuation included: neuropathy, neutropenia, thrombocytopenia, and infusion reactions.  
<sup>b</sup> Immune-mediated reactions programmatically identified via sponsor-defined preferred terms.

1. Schmoll et al 2012., Ph2/3 HORIZON III; 2. SUNLIGHT Ph3 Prager et al, Lancet 2023

AE: adverse event; etruma: etrumadenant; EZFB: etruma + zimberelimab + mFOLFOX6 + bevacizumab; rego: regorafenib; TEAE: treatment-emergent AE; zim: zimberelimab.



# Conclusions

**This is the first randomized, Phase 2, proof-of-concept study showing EZFB significantly improves PFS and OS compared with standard of care in microsatellite-stable 3L mCRC**

- **Longest OS reported for a randomized clinical trial in 3L mCRC**
- **Meaningful improvement shown across all subgroups, including 20-month median OS in patients with liver metastasis**
- **Tumor reduction was observed in two-thirds of patients**, with a clinically meaningful ORR and DOR for this latter line of treatment

**Safety was consistent with the individual study drugs and manageable with no treatment related deaths**

- Immune-mediated AE profile was consistent with that of anti-PD-1 antibodies

**These encouraging results support further development of EZFB in CRC, including both late-line and early line settings**



# Quemliclustat in Pancreatic Cancer

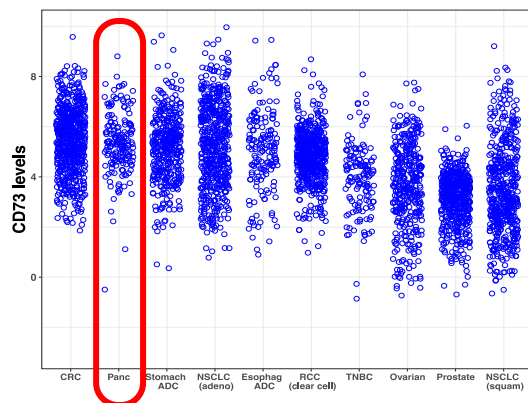
# Quemliclustat (quemli): A Unique, Highly Potent and Selective Small Molecule CD73 Inhibitor with Several Key Advantages

## 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<sup>1</sup>

- ✓ 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

# Final Overall Survival Analysis for Quemliclustat and Zimberelimab in Pancreatic Cancer (ARC-8)

Data presented at ASCO GI, January 19, 2024, based on a data cutoff of June 19, 2023.

# Highlights from the ARC-8, a Phase 1b Study in 1L PDAC

**Median overall survival (mOS) was 15.7 months** for patients treated with a quemliclustat-based regimen, which exceeds the historical benchmark data for chemotherapy alone (8.5 – 11.7 months)<sup>1,2</sup>

**A 37% reduction in risk of death and a 5.9-month improvement in mOS was observed** for patients treated with the quemli-based regimen when compared to a synthetic control arm of patients treated with G/nP alone<sup>1</sup> in a post-hoc analysis

**The quemli-based regimen was well-tolerated**, with no new safety signals or significant added toxicity compared to chemotherapy alone<sup>1</sup>

**Phase 3 study initiation expected by early 2025**

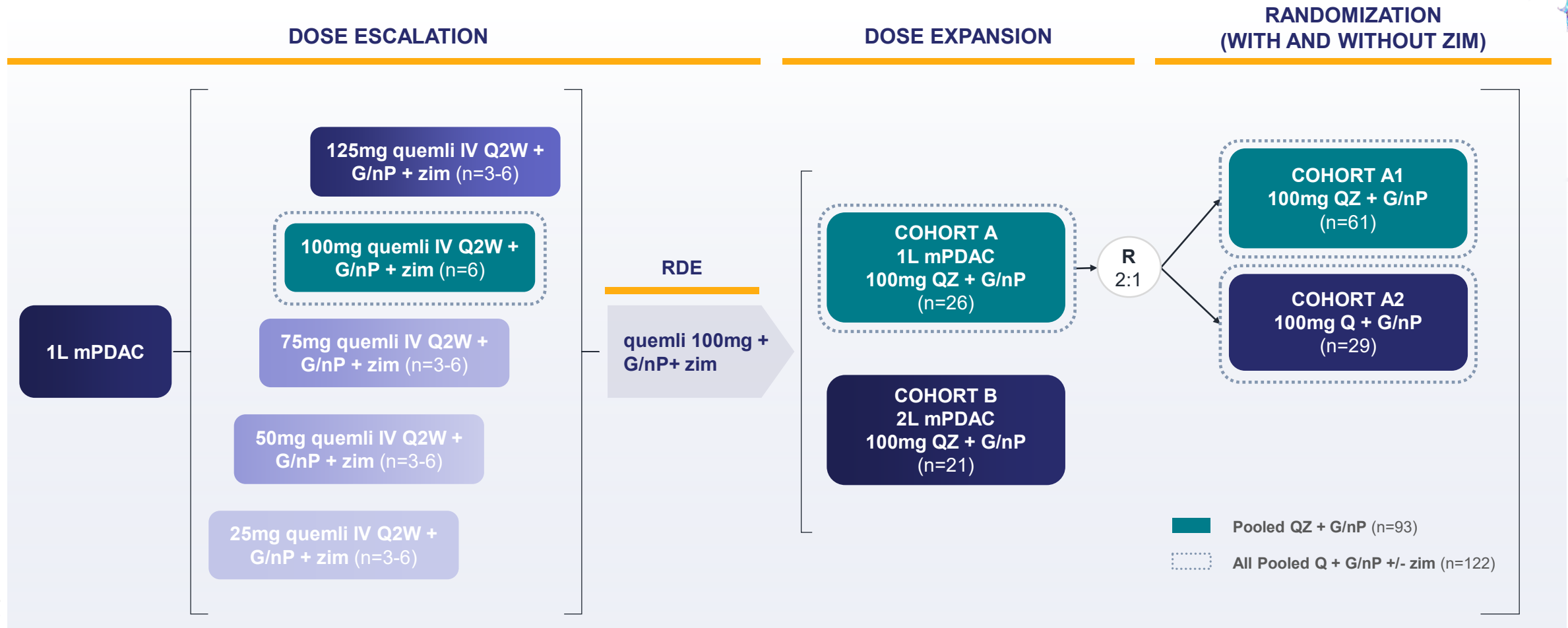
1L first-line; G/nP: gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat

1. Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

2. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

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# ARC-8 Study Design Included Dose Escalation, Expansion and Randomized Portions



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

1L: first-line; 2L: second-line; IV: intravenously; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; PDAC: pancreatic ductal adenocarcinoma; Q2W: every 2 weeks; Q/quemli: quemliclustat; R: randomization; RDE: recommended dose for expansion; Z/zim: zimberelimab  
NCT #: NCT04104672

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# Dataset Includes Four Groups of Patients Treated with 100 mg of Quemli

Cohort	Quemli Dose	Combination	Participants Dosed	>18m OS f/u?	Population
Dose escalation	25mg	Q + Z + G/nP (quad)	4	Yes	1L mPDAC
Dose escalation	50mg	Q + Z + G/nP (quad)	6	Yes	1L mPDAC
Dose escalation	75mg	Q + Z + G/nP (quad)	3	Yes	1L mPDAC
<b>Dose escalation</b>	<b>100mg</b>	<b>Q + Z + G/nP (quad)</b>	6	Yes	1L mPDAC
<b>Cohort A</b>	<b>100mg</b>	<b>Q + Z + G/nP (quad)</b>	26*	Yes (except for 3)*	1L mPDAC
<b>Cohort A1 (randomized)</b>	<b>100mg</b>	<b>Q + Z + G/nP (quad)</b>	<b>61</b>	Yes	1L mPDAC
<b>Cohort A2 (randomized)</b>	<b>100mg</b>	<b>Q + G/nP (triplet)</b>	<b>29</b>	Yes	1L mPDAC
Dose escalation	125mg	Q + Z + G/nP (quad)	3	Yes	1L mPDAC

**93**  
Pooled  
Q100 quad

**122**  
Pooled  
Q100 All

1L: first-line; f/u: follow up; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; OS: overall survival; Q/quemli: quemliclustat; Z/zim: zimberelimab

3 additional patients enrolled as contemporaneous control for Cohort C

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

# Demographics And Baseline Characteristics Are Well Balanced Across Arms & Efficacy-evaluated Populations

% ECOG 1 (65%-69%) Was Higher than Historical G/nP Studies (42-57%); % Liver Mets (59%-69%) Was Slightly Lower than Historical G/nP Studies (78-85%)

% (n)		A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q (±Z) +G/nP (n=122)
Median Age (IQR)		65.0 (61, 70)	66.0 (58, 72)	66.0 (58, 72)	65.5 (59, 72)
Age ≥65		55 (16)	59 (36)	58.1 (54)	57.4 (70)
Female		48 (14)	49 (30)	47 (44)	48 (58)
Race	White	83 (24)	74 (45)	74 (69)	76 (93)
	Asian	6.9 (2)	8.2 (5)	8.6 (8)	8.2 (10)
	Black	3.4 (1)	6.6 (4)	5.4 (5)	4.9 (6)
	Other/NR	6.9 (2)	11 (7)	12 (11)	11 (13)
ECOG 0		31 (9)	30 (18)	34 (32)	34 (41)
ECOG 1		69 (20)	69 (42)	65 (60)	66 (80)
ECOG Missing		-	1.6 (1)	1.1 (1)	0.8 (1)
Liver Metastasis at Baseline <sup>1</sup>		58.6 (17)	68.9 (42)	66.7 (62)	64.8 (79)

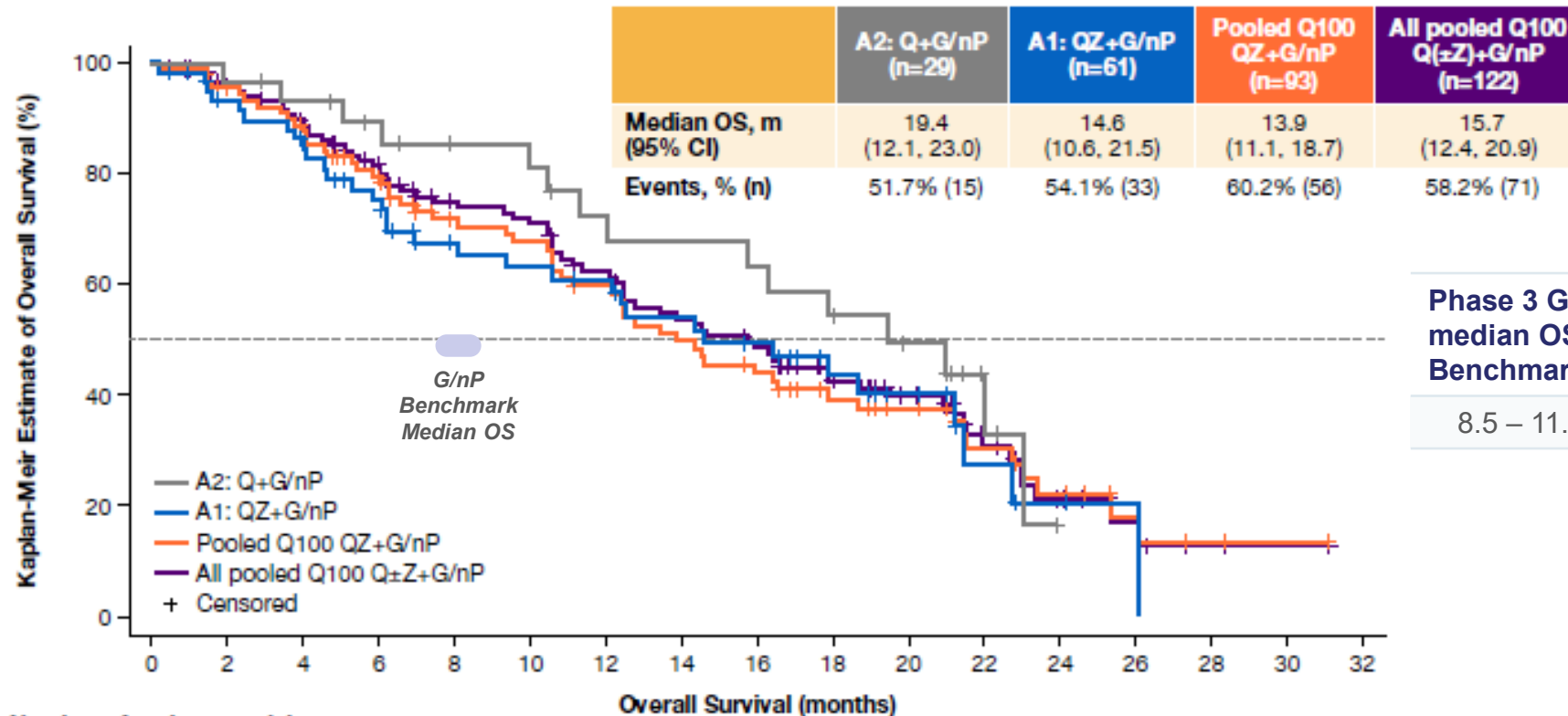
ECOG: Eastern Cooperative Oncology Group; G/nP: gemcitabine/nab-paclitaxel; IQR: interquartile range; NR: not reported; Q: quemiclustat; Z: zimberelimab

1. Derived from baseline tumor assessment data

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# With 21-month Median Follow-up, OS Results Exceed Ph3 Benchmarks for G/nP



Phase 3 G/nP  
median OS  
Benchmarks<sup>1,2</sup>

8.5 – 11.1 months

Number of patients at risk		Overall Survival (months)															
		0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30
A2: Q+G/nP	29	28	26	23	20	19	16	15	14	12	9	3	0	0	0	0	0
A1: QZ+G/nP	61	53	48	40	31	29	27	23	20	13	9	4	2	1	0	0	0
Pooled Q100 QZ+G/nP	93	84	77	66	53	50	43	35	30	22	18	12	8	4	2	1	0
All pooled Q100 Q(±Z)+G/nP	122	112	103	89	73	69	59	50	44	34	27	15	8	4	2	1	0

NE, not estimable; OS, overall survival; Q, quamiclustat; Z, zimberelimab.

CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; Ph3: Phase 3

1. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

2. Von Hoff et al. N Engl J Med 2013;369:1691-703.

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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# Favorable OS for Patients With & Without Liver Metastasis

- Because ARC-8 had a lower incidence of liver mets than historical studies, we analyzed the OS for ARC-8 patients with and without liver mets as shown below
- When adjusting for the lower incidence of liver mets in the triplet arm, mOS for the triplet and quad arms looked almost identical at approx. 12 months
- **When evaluating just those patients with liver mets, median OS still exceeded historical benchmarks AND meaningfully outperformed the OS for patients with liver mets treated with G/nP in NAPOLI-3 (the most contemporary phase 3 in 1L pancreatic) -- 12.1 mos for ARC-8 vs. 8.6 mos for NAPOLI-3**

Liver Mets at Baseline	A2: Q + G/nP (n=17)	A1: QZ + G/nP (n=42)	Pooled Q100 QZ + G/nP (n=62)	All Pooled Q100 Q(±Z) + G/nP (n=79)	NAPOLI-3 (n=309)
Events (%)	11 (64.7)	26 (61.9)	40 (64.5)	51 (64.6)	242 (78.3)
Median OS, months	12.1	12.2	11.1	12.1	8.6
95% CI	10.0, 20.9	6.2, 17.9	8.1, 14.5	10.0, 15.7	
No Liver Mets at Baseline	A2: Q + G/nP (n=12)	A1: QZ + G/nP (n=19)	Pooled Q100 QZ + G/nP (n=31)	All Pooled Q100 Q(±Z) + G/nP (n=43)	NAPOLI-3 (n=78)
Events (%)	4 (33.3)	7 (36.8)	16 (51.6)	20 (46.5)	43 (55.1)
Median OS, months	22.0	21.2	21.2	21.5	13.8
95% CI	17.9, NE	14.6, NE	13.9, 25.4	17.9, 25.4	

BL: Baseline; CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; mets: metastasis; mOS: median overall survival; mos: months; NE: not estimable; OS: overall survival; Q: quemiclustat  
 NAPOLI-3: Wainberg, et al. *The Lancet*. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1).  
 Data shown is for the G/nP arm only

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

# Safety Profile Similar to G/nP with Regards to Overall TEAEs

%	A2: Q + G/nP (n=29)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q (±Z)+G/nP (n=122)	NAPOLI-3 G/nP Benchmark <sup>4</sup> (n=379)
Any TEAE	100	100	100	99
Any TRAE	100	98.9	99.2	93
Grade 3-5 TEAE	89.7	83.9	85.2	86
Grade 3-5 TRAE	75.9	72.0	73.0	68
Serious TEAE	51.7	53.8	53.3	52
Serious TRAE	34.5	25.8	27.9	19
Grade 5 TEAE	0	5.4	4.1	6
Grade 5 TRAE	0	0	0	2
AE leading to mod <sup>1</sup>	58.6	51.6	53.3	54
AE leading to dose delay	75.9	75.3	75.4	NR
AE leading to discon <sup>2</sup>	24.1	22.6	23.0	23
IRR <sup>2</sup>	10.3	6.5	7.4	N/A
Immune related AE <sup>3</sup>	6.9	10.8	9.8	N/A

AE: adverse event; G/nP: gemcitabine/nab-paclitaxel; IRR: infusion-related reaction; NA: not applicable; NR: not reported; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event

1. AE leading to dose reduction; 2. Discontinuation of any study drug; 3. As reported by investigator; 4. Wainberg, et al. The Lancet. Sept 2023. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1)

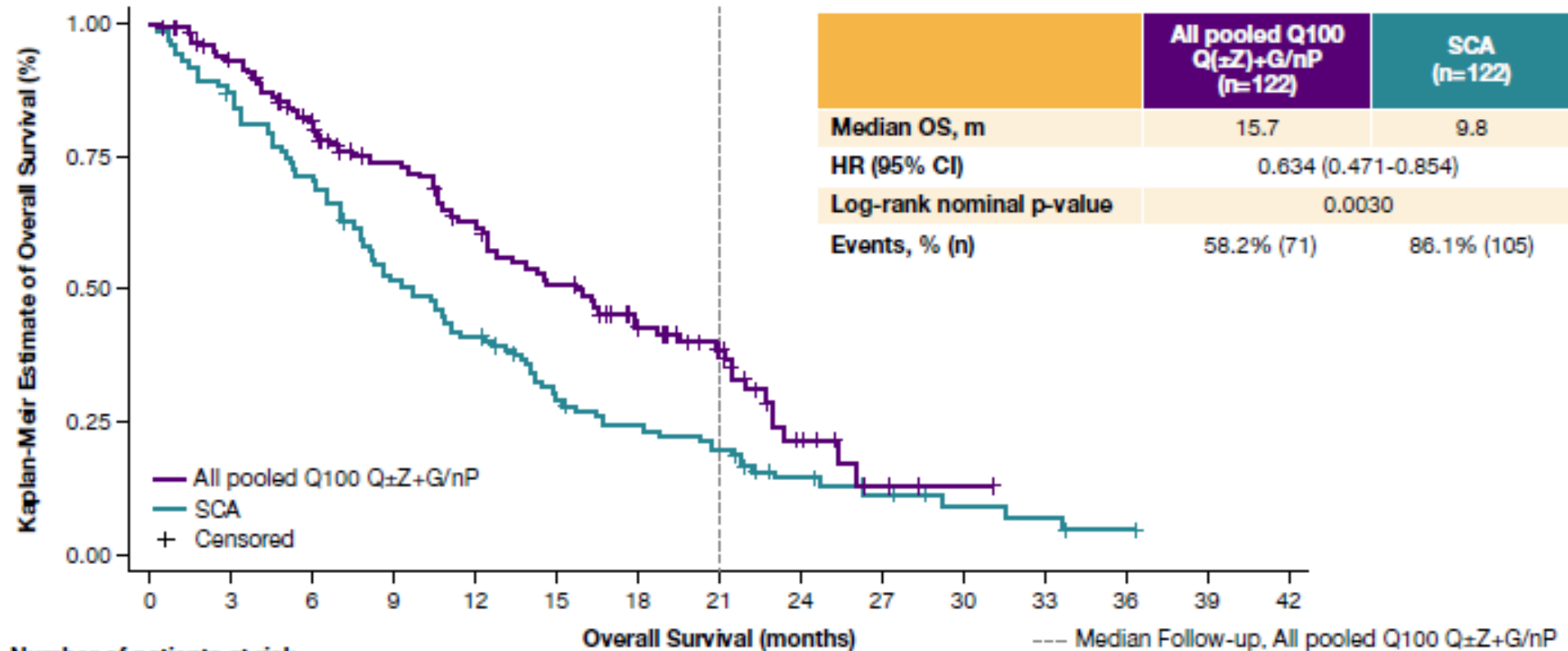
Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

# Arcus & Medidata AI Synthetic Control Arm (SCA) Project

- Developed in collaboration with Medidata, the industry's leading provider of electronic data capture for clinical trials
- Constructed SCA using historical data from patients treated with G/nP alone and balanced to the patient baseline characteristics of ARC-8
  - Contemporaneous global randomized Phase 2 and 3 clinical trials that meet key ARC-8 entry criteria
  - 515 eligible external patients identified for further matching
  - SCA matched to All Pooled Q100 Q±Z+G/nP (n=122) using propensity score statistical method including exact matching on baseline liver metastasis
- Assessed the treatment effects on OS, PFS, and objective response rate in the SCA patients and compared these to the matched ARC-8 patients
- **SCA analyses were conducted versus all four analysis groups and showed consistent results**; for simplicity, only the SCA for the All Pooled Q100 group was reported

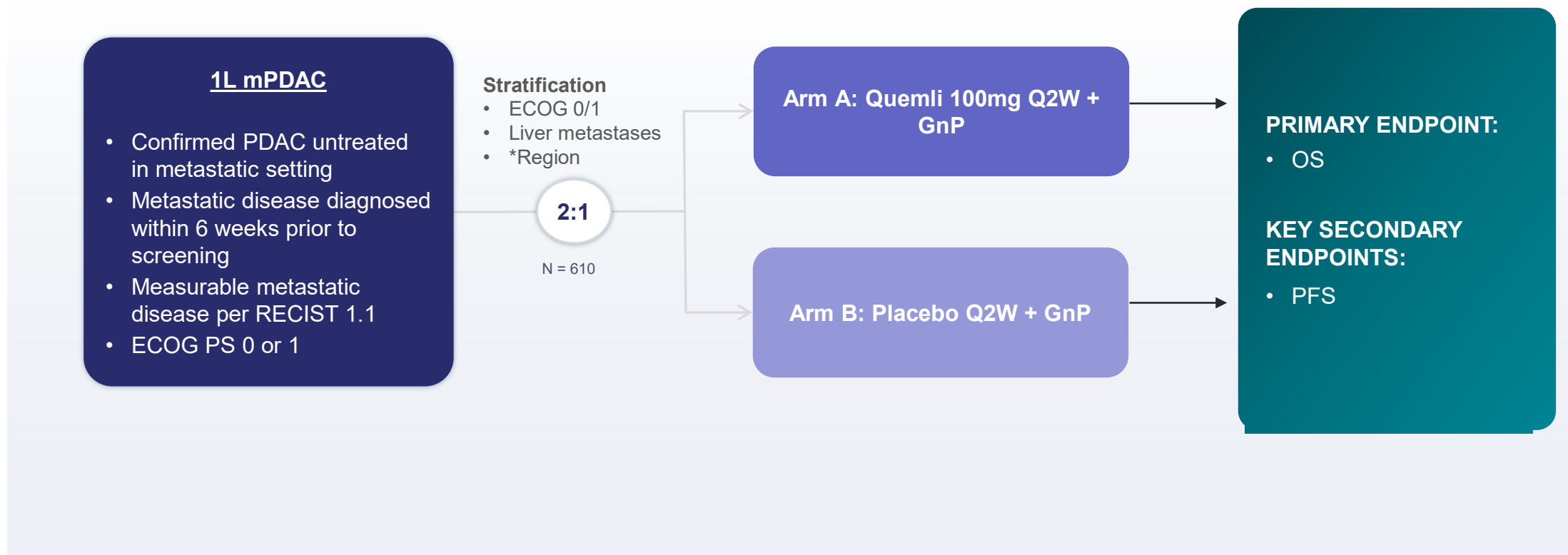


# Quemli-based Regimen Reduced Risk of Death by 37% and increased mOS by 5.9 months Compared to SCA



G/nP, gemcitabine/nab-paclitaxel; OS, overall survival; Q, quemliclustat; SCA, synthetic control arm; Z, zimmerliab.

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



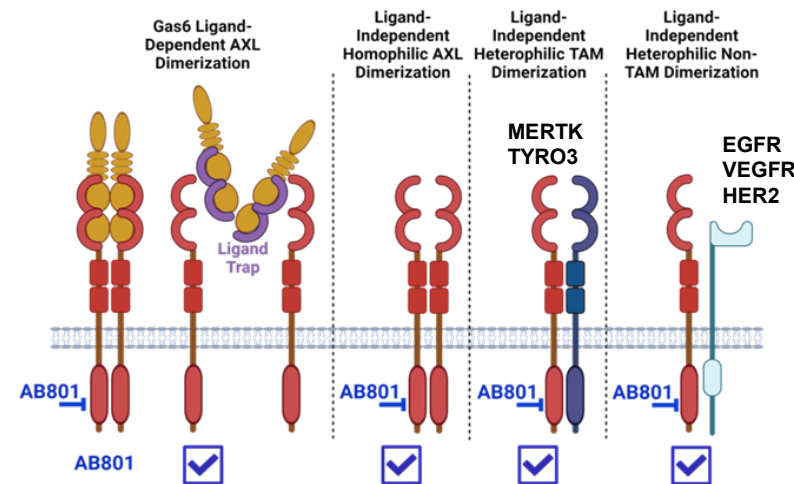
# AXL Program

# AB801 is a Potent, Selective AXL Inhibitor

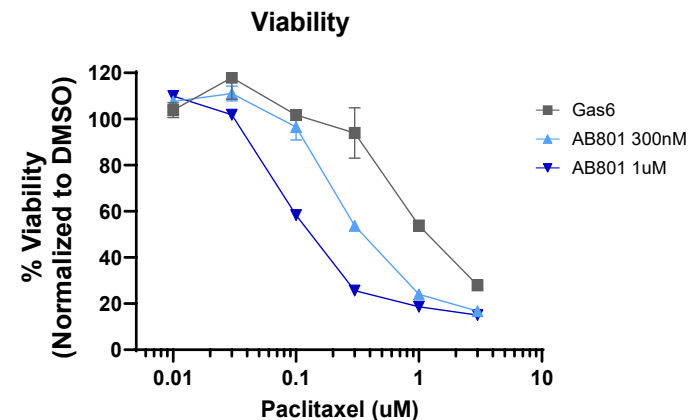
AB801 is a highly potent and selective AXL inhibitor

	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 than 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



# 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 first 3 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 underway; **expansion cohort planned in 2L+ NSCLC early 2025**

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

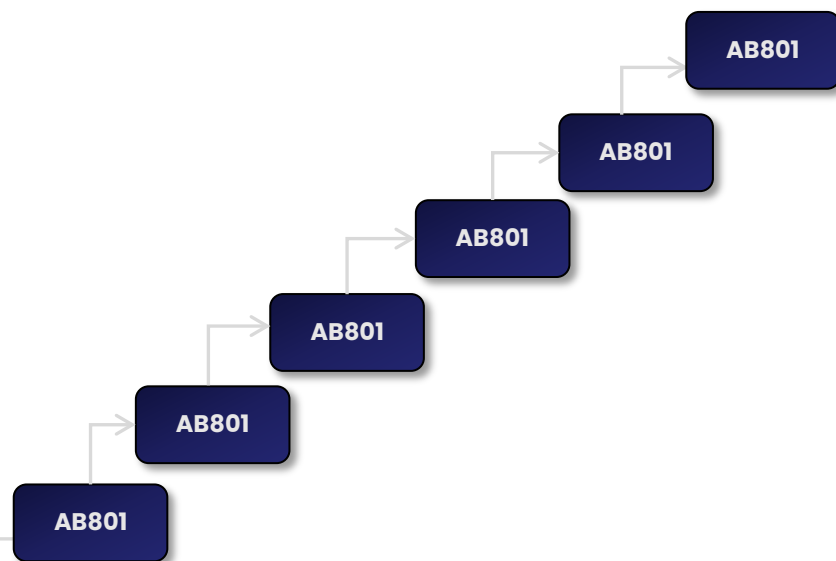
PRE-SCREENING / SCREENING

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  $\alpha$ -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

# APPENDIX



# Expansive Development Plan with Multiple Phase 3 Studies Ongoing or Planned



Program	Disease	Study	Line & Regimen	Ph 1/1b	Ph 2	Ph 3	Upcoming Milestones
Dom + Zim (Fc-silent anti-TIGIT + anti-PD-1)	NSCLC	STAR-121	1L, PD-L1 all-comers, metastatic dom + zim + chemo vs pembro + chemo				• 2024: Enrollment completion
		STAR-137	Perioperative lung cancer	IN PLANNING			
		PACIFIC8	Stage 3: durva ± dom				
		EDGE-Lung	1L / 2L, all-comers: dom ± zim ± quemli ± chemo				
		VELOCITY-Lung	1L/2L NSCLC: dom ± zim ± etruma ± SG				• 2024: Update expected
	Upper GI	STAR-221	1L Upper GI Malignancies dom + zim + chemo vs. nivo + chemo				✓ 2024: Enrollment completed
		EDGE-Gastric	1L / 2L Upper GI Malignancies dom ± zim ± quemli ± FOLFOX				✓ 1H24: ASCO presentation
Cas (HIF-2α inhibitor)	ccRCC	PEAK-1	2L ccRCC: cas + cabo vs cabo	IN PLANNING			• 1H25: Ph 3 initiation
		STELLAR <sup>009</sup>	2L ccRCC: cas + zanza				
		ARC-20	all-comer cancer; 2L+ ccRCC cas monotherapy and cas + cabo				✓ Early 2024: Dose escalation data • 2H24: Dose expansion data (30 pts, 7m+ follow-up)
ADENOSINE	PDAC	PRISM-1	1L quemli + G/nP vs. GnP	IN PLANNING			• Early 2025: Ph 3 initiation
		ARC-8	1L: quemli + zim + G/nP vs quemli + G/nP				✓ Jan 2024: ASCO GI poster; mature OS
	CRC	ARC-9	2L: etruma + zim + FOLFOX* vs FOLFOX* 3L: etruma + zim + FOLFOX* vs rego				✓ 1H24: MORPHEUS-PDAC (etruma); mature PFS/OS ✓ 1H24: ASCO presentation; PFS/OS data in 3L
AB801 (Axl inhibitor)	NSCLC	ARC-27	2L+: AB801 ± chemo				
AB598 (anti-CD39)	GI	ARC-25	1L: AB598 ± zim + chemo				

1L: first line; 2L: second line; 3L: third line; cabo: cabozantinib; cas: casatitan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; durva: durvalumab; etruma: etrumadenant; GI: gastrointestinal; G/nP: gemcitabine/nab-paclitaxel; NSCLC: non-small cell lung cancer; PD: pharmacodynamic; pembro: pembrolizumab; PFS: progression-free survival; Ph: phase; PK: pharmacokinetic; OS: overall survival; rego: regorafenib; SG: Sacituzumab govitecan-hziy; quemli: quemliclustat zanza/zanzalintinib; zim: zimberelimab

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

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