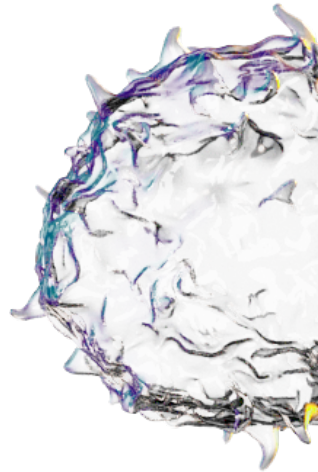
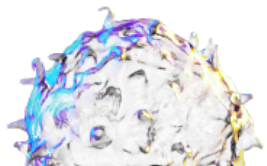
ARC-20 Data: Cas+Cabo

Phase 1b Study of Casdatifan + Cabozantinib in ccRCC

Data presented at ASCO 2025, June 1, 2025, based on data cutoff of March 14, 2025.





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Cas: casdatifan; dom: domvanalimab; quemli: quemliclustat

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Agenda

TOPIC	PRESENTER(S)
Casdatifan Value Proposition	**Dr. Terry Rosen** CEO, Arcus Biosciences
ARC-20 Cas + Cabo Cohort Data	**Dr. Richard Markus** CMO, Arcus Biosciences
Casdatifan Development Plan	**Dr. Richard Markus** CMO, Arcus Biosciences
Opportunity for Casdatifan	**Jennifer Jarrett** COO, Arcus Biosciences
Closing Remarks	**Dr. Terry Rosen** CEO, Arcus Biosciences
Q&A	**All**

Cabo: cabozantinib; cas: casdatifan

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Initial Data from the Cas + Cabo Cohort Were Presented in an Oral Presentation at ASCO 2025

2025 ASCO ANNUAL MEETING

Combination Casdatifan Plus Cabozantinib in Previously Treated Patients With Clear Cell Renal Cell Carcinoma: Results From the Expansion Cohort of the Phase 1 ARC-20 Study

Toni K Choueiri, MD, FASCO[1]; Moshe Ornstein, MD, MA[2]; Pedro Barata, MD, FACP[3]; Marc Matrana, MD, FACP[4]; Jamie Merchan, MD[5]; Craig Gedye, MBChB, FRACP, PhD[6]; Clara Hwang, MD[7]; Rohit Kumar, MD[8]; Jae Lyun Lee, MD, PhD[9]; Yinghui Guan, MS, PhD[10]; Mohammad Ghasemi, PhD[10]; Syed Quadri, MD[10]; Chris Negro, MS[10]; Jianfen Chen, MS[10]; Paul Foster, PhD[10]; Deepti Warad, MBBS[10]; Bradley A McGregor, MD[1]; Sun Young Rha, MD, PhD[11]; Alexandra Drakaki, MD, PhD[12]

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2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Toni K Choueiri, MD, FASCO

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

ASCO: American Society of Clinical Oncology; Cabo: cabozantinib; cas: casdatifan

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Arcus is Capitalized to Advance its Broad Portfolio of Late-Stage Programs Through Phase 3 Readouts

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

Validated mechanism and compelling market opportunity

ARC-20
cas + cabo oral at ASCO

PEAK-1
Phase 3 initiation expected in 2Q25

DOMVANALIMAB: THREE PHASE 3 STUDIES

STAR-221
1L Gastric
Approaching Ph 3 Data

STAR-121
1L NSCLC (all comers)
Ongoing

PACIFIC-8
Stage 3 NSCLC
Ongoing

$1 BILLION IN CASH*

Funded through initial pivotal readouts for dom, quemli and cas, which include PEAK-1**

WORLD-CLASS DRUG DISCOVERY

Small molecules focused on oncology and I&I

1H25: first half of 2025; 1L: first-line; 2Q25: second quarter of 2025; ASCO: American Society of Clinical Oncology; cabo: cabozantinib; cas: casdatifan; dom: domvanalimab; I&I: immunology & inflammation; NSCLC: non-small cell lung cancer; Ph: phase; quemli: quemliclustat; R&D: research & development

* cash, cash equivalents and marketable securities as of March 31, 2025

** runway estimate based on cash, cash equivalents, marketable securities, and available facilities

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Casdatifan Value Proposition

Dr. Terry Rosen
CEO, Arcus Biosciences

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Initial Cas + Cabo Data Substantially De-Risk PEAK-1

ROBUST EFFICACY

- The 46% ORR for cas + cabo **exceeds benchmarks for either agent alone[1] and the Phase 2 LITESPARK-003 benchmark for belz + cabo[2]**

RESPONSES ALREADY APPEAR DURABLE

- **All responses to date have confirmed** and all 11 responders remain on treatment as of today
- Majority of patients with best response of SD also remain on treatment, indicating that even SD patients are experiencing meaningful benefit

NO SIGNS OF OVERLAPPING TOXICITY

- **AE profile for cas + cabo is consistent with that expected for either agent alone**
- No cas-related TEAEs > grade 3

HIGH DOSE INTENSITY OF BOTH DRUGS

- **88-95% dose intensity achieved for both cas and cabo** enabling optimization of efficacy for the combination
- As of the DCO, only 5% of safety evaluable patients discontinued a drug due to an AE and no patients have discontinued both drugs

Belz: belzutifan; cabo: cabozantinib; cas: casdatifan; DCO: data cutoff date; IO: immunotherapy; ORR: overall response rate; SD: stable disease; TEAE: treatment-emergent adverse event

1. For cabo monotherapy - Phase 3, CONTACT-03 , Pal et al 2023; Phase 3 METEOR, Choueiri et al 2015; cas monotherapy: Arcus ENA 2024 presentation
2. Choueiri et al. 2023, Lancet Oncology

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Two Datasets Now Demonstrate Casdatifan's Potential to be the Best-in-Class HIF-2α Inhibitor for ccRCC



100mg Cas + 60mg cabo in IO-experienced ccRCC[a] (n=24)



Cas mono in 2L+ ccRCC[b]
(n=89 across 3 cohorts)

	cas + cabo (ARC-20) 5m follow-up	belz + cabo (LS-003)[1] 24m follow-up	cas (ARC-20) 5-15m follow-up	belz (LS-005)[2] 26m follow-up
HIGH cORR:	**46%**	31%	**25-33%**	21%
LOW RATE OF PRIMARY PROGRESSION:	**5%**	6%	**<20%**	34%
MEDIAN PFS:	**TBD**	13.7m	**9.7-12m+**	5.6m

Despite limited follow-up, key efficacy measures exceed those for the Phase 2 LITESPARK-003 study (belzutifan + cabozantinib)

All three cohorts demonstrated improvement on every efficacy endpoint evaluated relative to the Phase 3 LITESPARK-005 study

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.

2L: second-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; cORR: confirmed overall response rate; IO: immunotherapy; m: month; PFS: progression-free survival; TBD: to be determined

a. Data cutoff date: March 14, 2025 b. Data cutoff date: January 3, 2025 1. Choueiri et al. 2023, Lancet Oncology 2. Albiges L. et al. Abstract LBA88, ESMO 2023

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Casdatifan has an Optimal Pharmacological Profile Relative to That of the Competitor Belzutifan

GREATER INHIBITION OF HIF-2α / PD EFFECT

- Belzutifan achieves its maximal PD effect (approx. 63% EPO suppression) at 120mg, its approved dose; dose reductions to 80mg or 40mg could result in a loss of efficacy
- **Casdatifan achieves this same effect on EPO at only 20mg, one-fifth the "going forward" dose** of 100mg
- Casdatifan's effect on EPO is highly durable over multiple months, while belzutifan appears to lose its PD effect within 3 months

LINEAR, DOSE PROPORTIONAL PK

- Belzutifan does not achieve meaningfully higher drug exposure at doses above 120mg and, therefore, cannot achieve a more robust PD effect
- **Casdatifan has linear, dose-proportional pharmacokinetics**

OPTIMAL HALF-LIFE AND FORMULATION

- **Belzutifan's half-life is only ~14h, versus ~24h for casdatifan**
- Belzutifan is dosed as three pills once-daily (40mg x 3) vs a planned 100mg tablet once-daily for casdatifan

EPO: erythropoietin; h: hours; PD: pharmacodynamic; PK: pharmacokinetic

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The HIF-2α Market is a 2-Horse Race and Cas is Poised to Become the HIF-2α Treatment of Choice in ccRCC

EFFICACY & SAFETY DATA BASED ON ARC-20 (CAS) AND LITESPARK-005 (BELZ), EACH FROM MONOTHERAPY COHORTS IN "LATE-LINE" PATIENTS	casdatifan 	belzutifan[1] 
Primary progressive disease	**<20%**	34%
cORR ("post anti-PD-1/TKI")	**25-33%**	21%
mPFS ("post anti-PD-1/TKI")	**9.7-12m+**	5.6m
Grade 3 Hypoxia	**High single digits**	Low teens
TKI combo partner in post-IO setting	**+ cabo**	+ lenva (data in 2027) + zanza (data in ??)
1L strategy	**+ anti-PD-1/CTLA-4 *(volru; TKI-free)***	+ pembro (anti-PD-1) + lenva (TKI)
Pill burden	**1 (+1 for cabo)**	3 (+2 for lenva)

1L: first-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; cORR: confirmed overall response rate; IO: immunotherapy; lenva: lenvatinib; mPFS: median progression free survival; m: months; pembro: pembrolizumab; volru: volrustomig; zanza: zanzalintinib

1. Clinical data from LITESPARK-005. Sources: Albiges L. et al. Abstract LBA88, ESMO 2023; Choueiri et al. 2024.

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eVOLVE-RCC02 is Targeting the 1L Setting with the First HIF-2α-Containing TKI-Free Regimen

AstraZeneca

- Clinical collaboration between Arcus and AZ where both parties retain all economics / rights to their respective molecules
- Evaluating casdatifan in combination with AZ's volrustomig (anti-CTLA-4/anti-PD-1 bispecific)
- AZ to sponsor the study and study costs to be shared
- **Enables Arcus to target the 1L setting in a cost- and resource-efficient manner**

eVOLVE RCC02

cas + volrustomig
(anti-CTLA-4/anti-PD-1 bispecific)

- **Utilizing a seamless Phase 1b/3 design**
- Potential first-in-class, TKI-sparing combination
- Volru has demonstrated exciting preliminary data in 1L ccRCC

1L: first-line; AZ: AstraZeneca; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; volru: volrustomig

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Casdatifan Has the Potential to Change the Treatment Paradigm in ccRCC and Displace TKIs in Early Lines

	CURRENT SOC	POTENTIAL PARADIGM SHIFT
1L Favorable Risk	**Watch and Wait** **anti-PD-1 + TKI** **TKI mono**	**HIF-2α mono** cas
1L all-comers	**anti-PD-1 + anti-CTLA-4**	**HIF-2α + anti-PD-1/CTLA-4** cas +volrustomig
	anti-PD-1 + TKI	**HIF-2α + anti-PD-1** cas + zim
2L (Post-IO)	**TKI mono**	**HIF-2α + TKI** cas + cabo **HIF-2α mono** cas
3L+ (Post-IO & TKI)	**mTOR** **HIF-2α** (belz)	**TKI mono** **mTOR** **HIF-2α** (belz)

1L: first-line; 2L: second-line; 3L: third-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; zim: zimberelimab

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ARC-20 Cas + Cabo Cohort

Dr. Richard Markus
CMO, Arcus Biosciences

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Data Presented at ASCO Were From the Cas + Cabo Cohort of the ARC-20 Expansion Cohorts

- To date, over 200 patients have received casdatifan across all cohorts of ARC-20

DOSE ESCALATION

Patients with advanced solid tumors
Casdatifan monotherapy



DOSE EXPANSION

N = ~30 per cohort, except cas + cabo (n=45)

2L+ ccRCC
Casdatifan mono 50mg BID capsule

2L+ ccRCC
Casdatifan mono 50mg QD capsule

2L+ ccRCC
Casdatifan mono 100mg QD tablet

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

2L+ ccRCC
Casdatifan mono 150mg QD

Favorable-risk 1L ccRCC
Casdatifan mono 100mg QD

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

Post-IO ccRCC
Casdatifan mono 100mg QD

At the March 14 data cutoff:

- **42 patients were evaluable for safety** (had received at least one dose of cas and had at least one month follow-up)
- **24 patients were evaluable for efficacy** (had reached at least 12 weeks follow-up)

1L: first-line; 2L: second-line; ASCO GU: American Society of Clinical Oncology Genitourinary Cancers; BID: twice daily; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; ORR: overall response rate; PFS: progression-free survival; Q3W: every three weeks; QD: once daily

Data presented at ASCO GU, February 2025
Data presented at ASCO, June 1, 2025

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Patient Characteristics in the Casdatifan Plus Cabozantinib Expansion Cohort

CHARACTERISTIC	SAFETY POPULATION[a] (N = 42)
Age, years, median (range)	63 (43–81)
Sex, female/male, n (%)	9 (21%) / 33 (79%)
ECOG PS 0/1, n (%)	29 (69%) / 13 (31%)
IMDC risk score, n (%)	
Favorable	9 (21%)
Intermediate	29 (69%)
Poor	4 (10%)
Number of prior regimens, n (%)	
1	35 (83%)
2+	7 (17%)
Prior treatment, n (%)	
VEGFR-TKI plus IO	17 (40%)
IO only	25 (60%)

Patients were enrolled at 15 sites across 3 countries

ECOG PS: Eastern Cooperative Oncology Group Performance Status; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; IO: immunotherapy;

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff: March 14, 2025.

[a]Safety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cutoff date.

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Confirmed ORR of 46% in Patients Eligible for a Minimum of 12 Weeks Follow-Up

- To date, all responses have confirmed and all responders remain on treatment

	EFFICACY-EVALUABLE POPULATION (n = 24)[a]
Follow-up, months, median (range)	5.3 (2.8–9.1)
Confirmed ORR[b], % (n)	**46% (11)**
(95% CI)	**(26%, 67%)**
Best Overall Response, n (%)	
CR	1 (4%)
PR[b]	10 (42%)
SD	12 (50%)
PD	1 (4%)

AE: adverse event; CR: complete response; ORR: overall response rate; PD: progressive disease; PR: partial response; SD: stable disease

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff date: March 14, 2025.

[a]All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.

[b]Inclusive of one patient who had confirmed PR after March 14, 2025.

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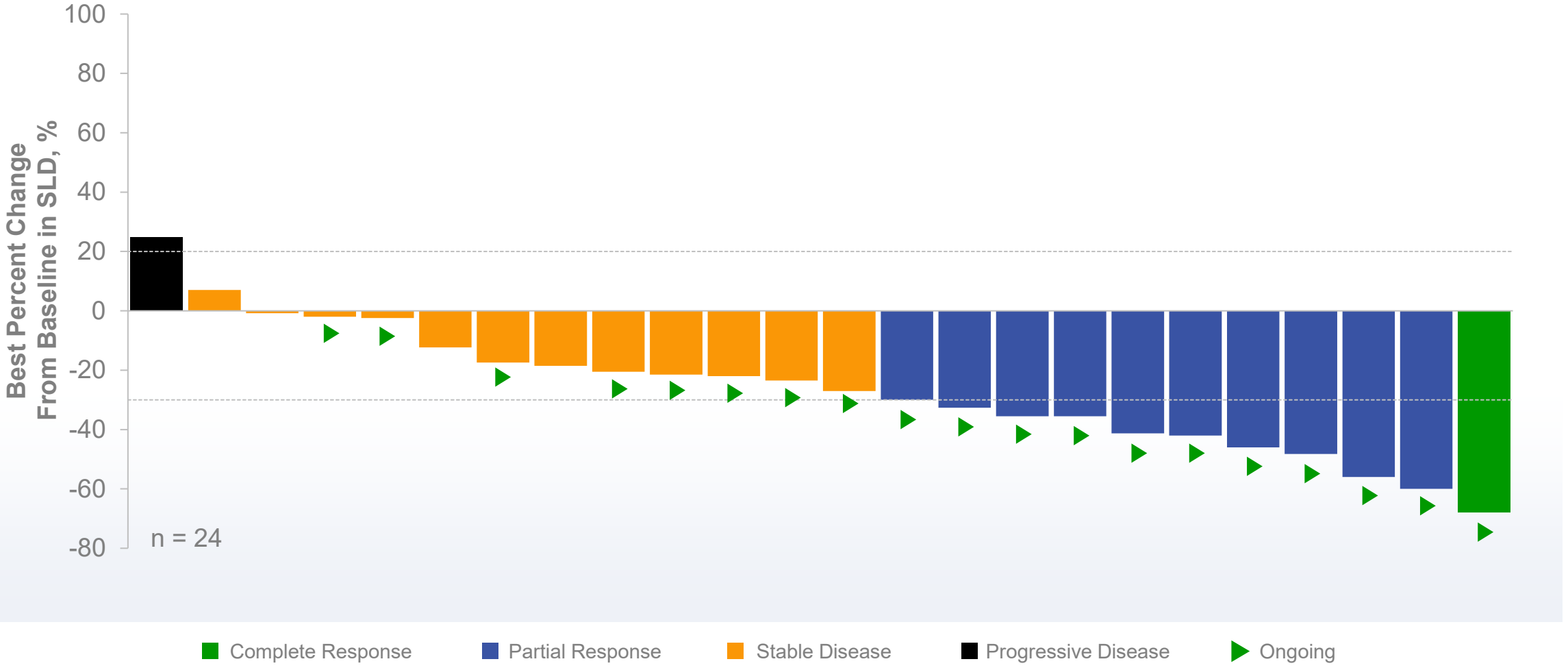
Almost All Patients Achieved Tumor Reduction[a,b]



SLD: sum of lesion diameter; ORR: overall response rate
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[a]All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.
[b]Inclusive of one patient who had confirmed PR after March 14, 2025.

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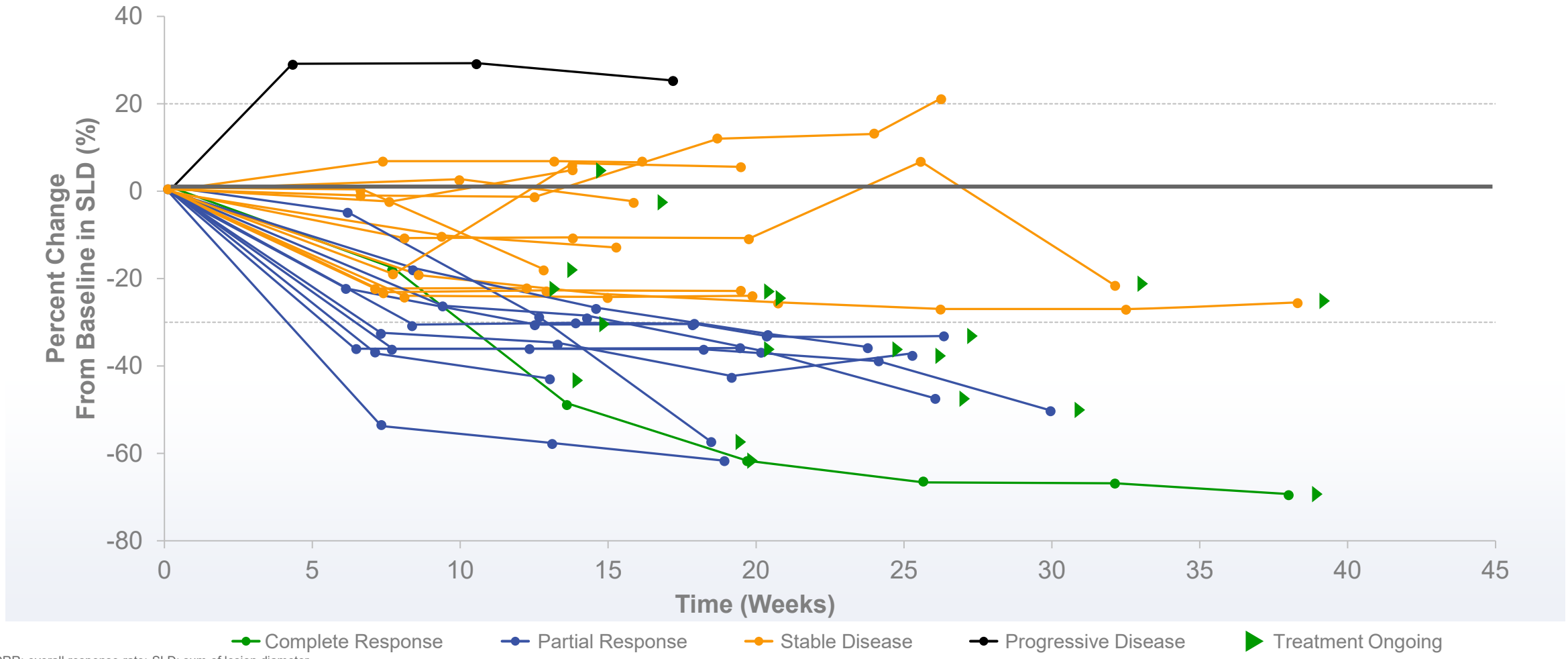
Tumor Reduction Has Deepened Over Time and Responses Already Appear Very Durable



ORR: overall response rate; SLD: sum of lesion diameter
Data cutoff date: March 14, 2025.
All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.

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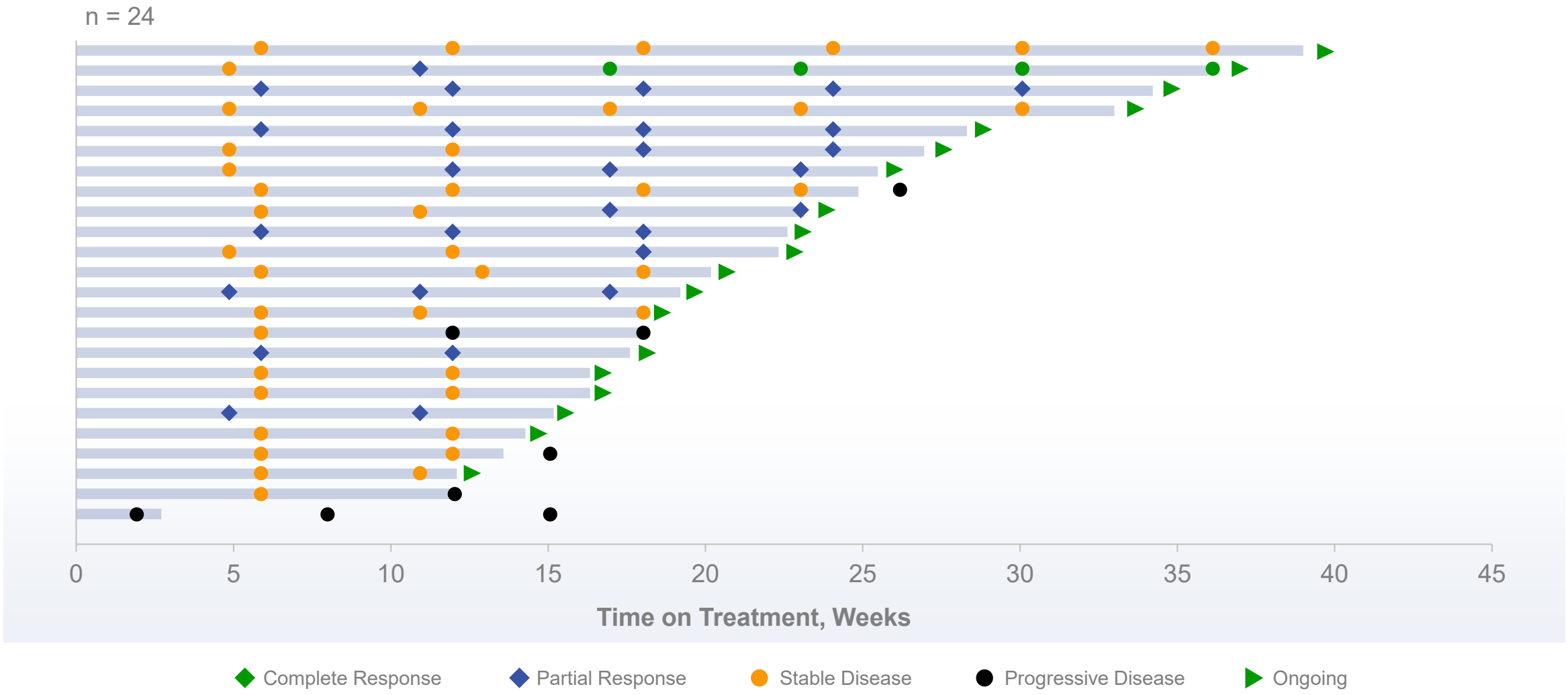
Most Patients Remain on Treatment[a,b]



Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff date: March 14, 2025.

[a]All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.

[b]Inclusive of one patient who had confirmed PR after March 14, 2025.

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Casdatifan Dose Intensity was Consistently 95%+, Driving Efficacy and Durability

	CAS 100MG QD + CABO 60MG QD* N=27	CAS 100MG QD* N=29	CAS 50MG QD* N=31	CAS 50MG BID* N=33
Median duration of follow-up, months	3.7	5.1	12.3	15.5
Median Tx duration, months	3.0	4.1	10.6	7.1
Cas relative dose intensity, median	**94.9%**	**98.6%**	**100.0%**	**98.6%**
Cabo relative dose intensity, median	**88.0%**	NA	NA	NA

BID: twice daily; cabo: cabozantinib; cas: casdatifan; NA: not applicable; QD: once daily; tx: therapy
*Data cutoff date: January 3, 2025

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TRAEs (Any Grade): Safety Profile was Consistent with Expectations for Cas and Cabo

	SAFETY POPULATION,[a] n (%) (N = 42)		
	AE RELATED TO:		
	casdatifan	cabozantinib	Any study drug
Follow-up, months, median (range)		3.7 (1.1–9.1)	
Patients with any treatment-related AE[b], n (%)	41 (98%)	39 (93%)	41 (98%)
Anemia	29 (69%)	18 (43%)	29 (69%)
Fatigue	20 (48%)	23 (55%)	23 (55%)
Alanine aminotransferase increased	8 (19%)	16 (38%)	16 (38%)
Diarrhea	6 (14%)	15 (36%)	15 (36%)
Aspartate aminotransferase increased	6 (14%)	14 (33%)	14 (33%)
Platelet count decreased	5 (12%)	12 (29%)	12 (29%)
Nausea	5 (12%)	10 (24%)	10 (24%)
Dizziness	7 (17%)	6 (14%)	8 (19%)

- Most cases of anemia and fatigue did not require a dose change and resolved

Cabo: cabozantinib, cas: casdatifan; TRAE: treatment related adverse event

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff: March 14, 2025.

[a]Safety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cutoff date.

[b]Treatment-emergent adverse events (any grade) related to casdatifan, cabozantinib, or any study drug reported in ≥ 15% of patients in any treatment arm.

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Very Few Grade 3 or Higher Treatment Related AEs

	SAFETY POPULATION,[a] n (%) (N = 42)		
	GRADE 3 OR HIGHER AE RELATED TO:		
	casdatifan	cabozantinib	any study drug
Patients with any treatment-related ≥ grade 3 AE[b]	13 (31%)	16 (38%)	20 (48%)
Anemia	10 (24%)	6 (14%)	10 (24%)
Hyponatremia	0	3 (7%)	3 (7%)
Hypoxia	3 (7%)	0	3 (7%)
Hypertension	0	2 (5%)	2 (5%)
Neutrophil count decreased	1 (2%)	2 (5%)	2 (5%)

- No casdatifan-related grade 4 or 5 AEs were observed

AE: adverse event

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[a]Safety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cutoff date.

[b]Treatment-emergent adverse events (grade 3 or higher) related to casdatifan, cabozantinib, or any study drug reported in ≥ 3% of patients in any treatment arm.

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AEs Were Manageable with Dose Reductions, Leading to Very Few Discontinuations

	SAFETY POPULATION,[a] n (%) (N = 42)		
	LEADING TO REDUCTION IN:		
	casdatifan	cabozantinib	any study drug
Patients with any AE leading to dose reduction[b]	10 (24%)	16 (38%)	22 (52%)
Fatigue	1 (2%)	5 (12%)	6 (14%)
Anemia	4 (10%)	1 (2%)	4 (10%)
Hypoxia	4 (10%)	0	4(10%)
Palmar-plantar erythrodysesthesia	0	2 (5%)	2 (5%)
Stomatitis	0	2 (5%)	2 (5%)

- Only 2 patients (of 42 safety evaluable) discontinued a treatment due to a TEAE (hypoxia and drug hypersensitivity), and no patients discontinued both treatments due to a TEAE

TEAE: treatment-emergent adverse event

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[a]Safety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cutoff date.

[b]Treatment-emergent adverse events (any grade) leading to dose reduction in casdatifan, cabozantinib, or any study drug reported in ≥ 3% of patients in any treatment arm.

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Key Takeaways from the Cas + Cabo Cohort

- **ORR for cas + cabo already exceeds that of belzutifan + cabo in LITESPARK-003**
- **Vast majority of patients experience some tumor reduction and clinical benefit**
- **While follow-up is limited, responses already appear very durable**
- **Safety profile of the combination appears very manageable, and consistent with the individual agents**
  - Dose intensity of cas in the combination is very high and similar to monotherapy
- **Very low rate of discontinuations and "short" dose interruptions ensure that drug is "on board" almost continuously**

Cabo: cabozantinib; cas: casdatifan; ORR: overall response rate

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8 Cohorts of ARC-20 Study Enable A Steady Cadence of Data Over the Next ~18 Months

TIMING	ARC-20 COHORTS	EVENT
Early 2025	• 50mg BID • 50mg QD • 100mg QD	✓ Updated data from 50mg BID, 50mg QD (ORR, PFS) ✓ Initial data from 100mg QD tablet (ORR) mono cohort
June 2025	• cas + cabo (post-IO)	✓ Safety and initial efficacy data for the cas + cabo cohort oral presentation at ASCO
Fall 2025	• 50mg BID • 50mg QD • 100mg QD • 150mg QD	• More mature safety and efficacy data for monotherapy cohorts (ORR, PFS)
2026	• cas + cabo • cas mono (1L favorable risk) • cas +zim (1L) • cas mono (post-IO)	• More mature data on cas + cabo combination • Data from new ARC-20 cohorts in earlier line settings

1L: first-line; ASCO: American Society of Clinical Oncology; BID: twice daily; cabo: cabozantinib; cas: casdatifan; IO: immunotherapy; mono: monotherapy; ORR: overall response rate; PFS: progression-free survival; QD: once daily; zim: zimberelimab

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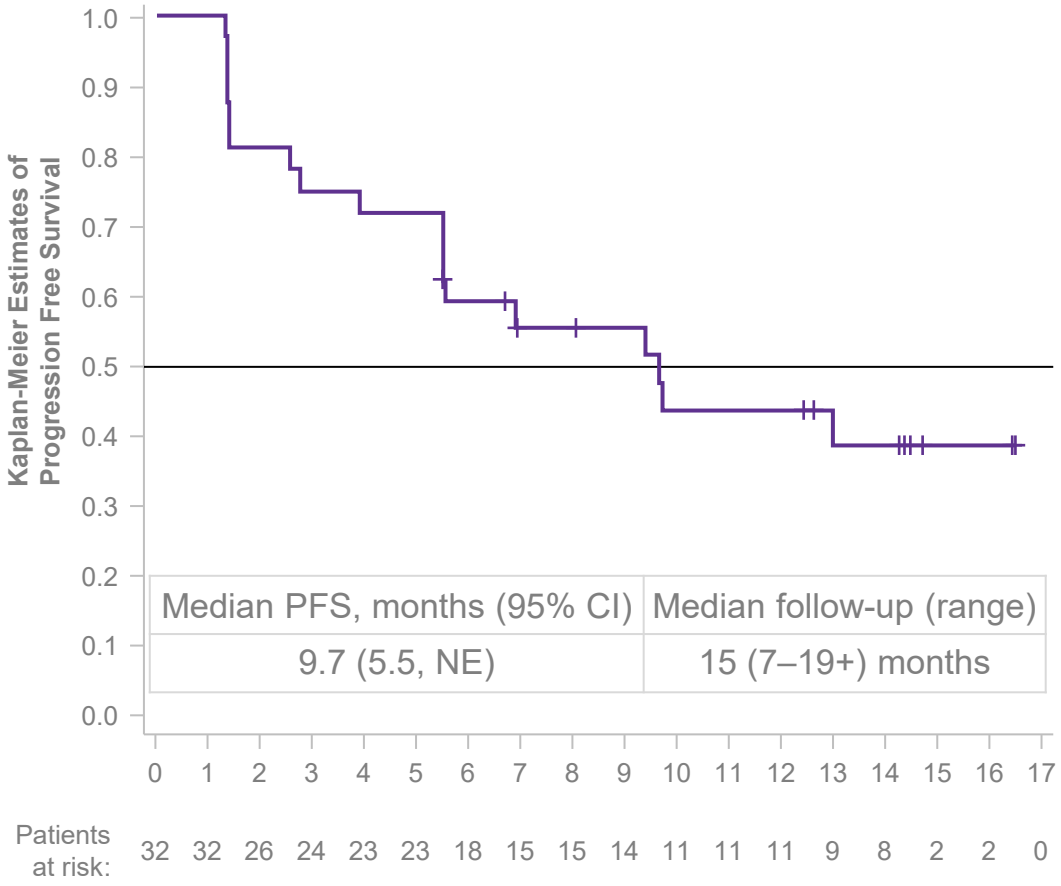
PFS Kaplan-Meier Curves Shown at ASCO GU Bode Well for Updated PFS for Cas Mono Cohorts Later this Year

50mg BID Cohort (n=32)

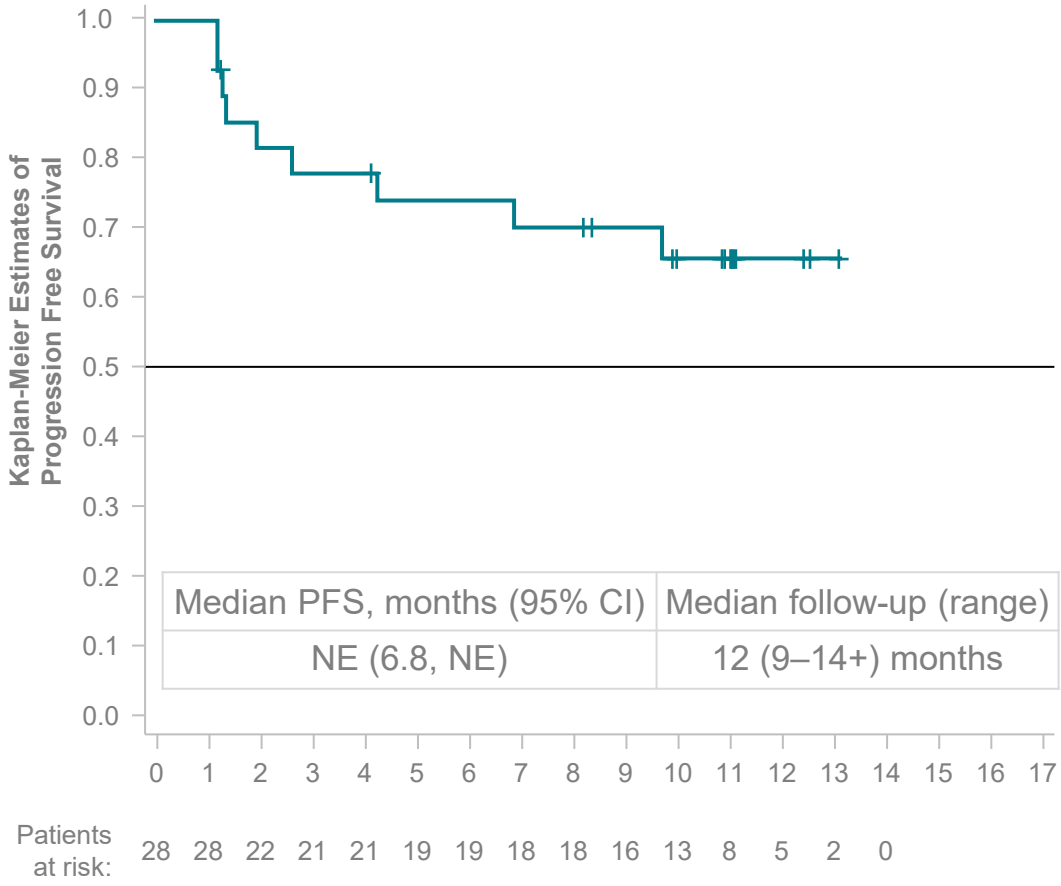
Median follow-up of 15 months



Median PFS, months (95% CI)	Median follow-up (range)
9.7 (5.5, NE)	15 (7–19+) months

50mg QD Cohort (n=28)

Median follow-up of 12 months



Median PFS, months (95% CI)	Median follow-up (range)
NE (6.8, NE)	12 (9–14+) months

+ Censored

- mPFS for belzutifan in Phase 3 LITESPARK-003 was 5.6 months with 18 months median follow-up

ASCO GU: American Society of Clinical Oncology Genitourinary Cancers Symposium; BID: twice daily; CI: confidence interval; DCO: data cutoff; mPFS: median progression-free survival; NE: not estimable; QD: once daily

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.
Data cutoff date: January 3, 2025

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Casdatifan Development Plan

Dr. Richard Markus
CMO, Arcus Biosciences

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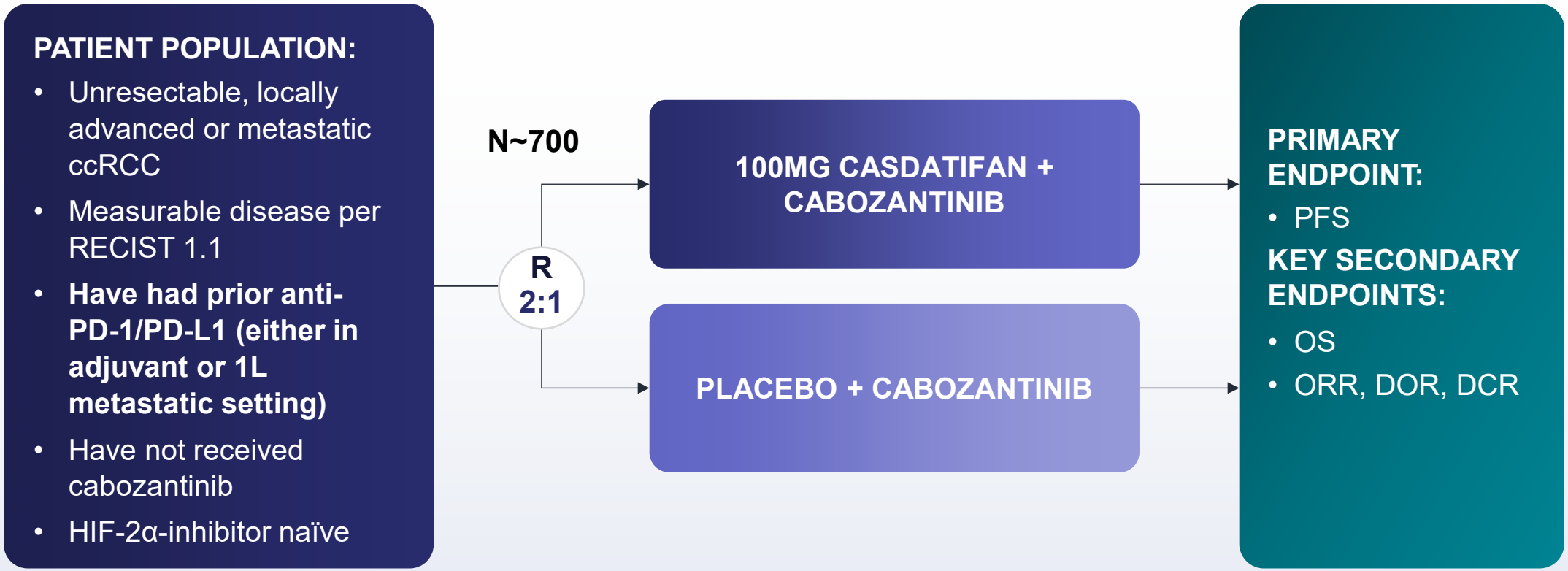
First Phase 3 Study for Cas Has a Simple Design that Utilizes the Preferred SOC in Post-IO ccRCC



PEAK-1 is Expected to Initiate Imminently

1L: first-line; cabo: cabozantinib: cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; IO: immunotherapy; ORR: objective response rate; OS: overall survival; PFS: progression free survival; R: randomized; RCC: renal cell carcinoma; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: standard of care

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New Cohorts Added to ARC-20 to Evaluate New Opportunities to Displace TKIs

EXPANSION COHORTS		
2L+ ccRCC casdatifan mono 50mg BID capsule	Data presented at ASCO GU 2025	Satisfies Project Optimus and confirmed 100mg QD tablet as the "going forward" dose and formulation
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	Data presented at ASCO 2025	Generated data to support the Phase 3 PEAK-1 study
Favorable-risk 1L ccRCC casdatifan mono 100mg QD	**New cohorts added and currently enrolling; Designed to inform the potential of cas in early-line settings**	
1L ccRCC casdatifan 100mg QD + zimberelimab 360mg Q3W		
Post-IO ccRCC casdatifan mono 100mg QD		

1L: first-line; 2L: second-line; ASCO: American Society of Clinical Oncology Genitourinary Cancers; BID: twice daily; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; Q3W: every three weeks; QD: once daily

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Opportunity for Casdatifan

Jennifer Jarrett
COO, Arcus Biosciences

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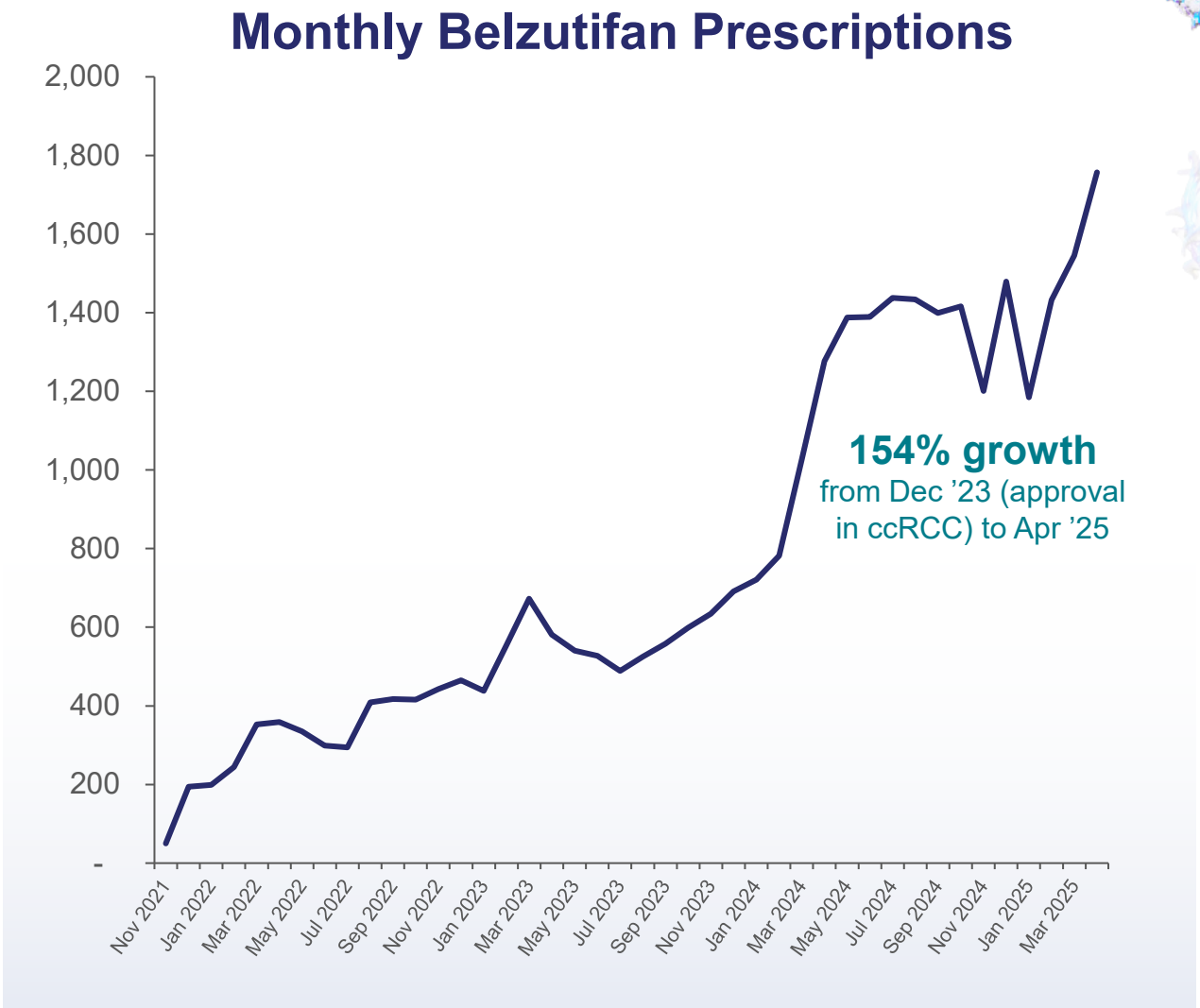
Belzutifan Sales Have Grown Exponentially Despite its Usage Being Limited to Late-line ccRCC

- **Belzutifan has rapidly established itself as the SOC in the 3L+ ccRCC setting**
  - High rate of primary progression likely limits use in earlier line settings
- **LTM Sales of >$560M in the U.S.; Run rate sales based on April Rx's are now $720M+**
- **Cas has the potential to meaningfully exceed this based on an improved efficacy profile and superior combination strategy in earlier lines**



3L: third-line; Apr: April; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; Dec: December; LTM: last twelve months; Rx: prescriptions; SOC: standard of care
Source: IQVIA, Merck Q1 2025 Earnings

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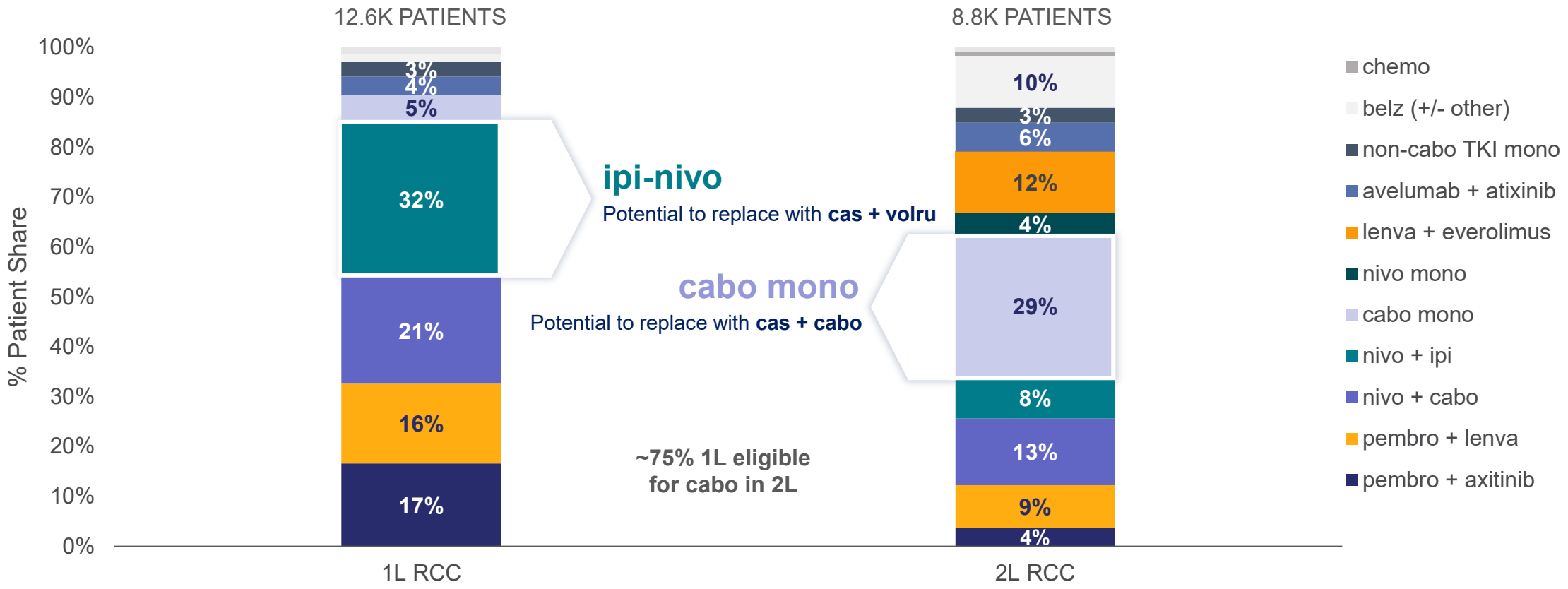
Initial Cas Development Plan Targets the Largest Market Segments and Could Expand Share Within These Segments

2024 ccRCC | US Market Share



1L: first-line; 2L: second-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; ipi: ipilimumab; lenva: lenvatinib; mono: monotherapy; nivo: nivolumab; pembro: pembrolizumab; volru: volrustomig

Sources - Epi: DRG, GlobalData | Share: Arcus primary research, US May 2024 (n=49)

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Cas + Cabo Has the Potential to Establish a New SOC in IO-Experienced ccRCC

Cas 100mg
(1 x 100mg)



Cabo 20-60mg
(1 x Xmg)



Establishing Cas + Cabo as the HIF-2α + TKI Combination of Choice

- Cabo is the preferred TKI in IO-experienced ccRCC due to a perceived better safety profile and simpler titration
- **Cas is the only HIF-2α inhibitor being developed in Phase 3 with cabo**
- Cas + cabo has the potential to displace TKI monotherapy by prolonging PFS without significant additional toxicity
- 2-drug regimen enables continued treatment on at least one therapy and optimal management of TKI-related toxicities
- With LITESPARK-011 readout delayed, the gap between this study and PEAK-1 has significantly narrowed

Cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; PFS: progression-free survival; SOC: standard of care

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Avoiding Overlapping Toxicity is Key to Maintaining Patients on Therapy and Positions HIF-2α as the Ideal Backbone

Casdatifan





100mg coated tablet



25mg coated tablet

- Anemia
- Hypoxia
- Fatigue

TKIs



- Diarrhea
- Rash
- Hepatotoxicity
- Hypothyroidism
- Hypertension
- Fatigue
- PPE

anti-PD-1



- Diarrhea
- Rash
- Hepatotoxicity
- Hypothyroidism
- Pneumonitis

anti-PD-1/CTLA-4



- Diarrhea
- Rash
- Hepatotoxicity
- Hypothyroidism
- Fatigue
- Pneumonitis
- Pyrexia

PPE: palmar-plantar erythrodysesthesia

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Our Initial Focus Is on the IO-naive and Post-IO Settings, Both Multi-Billion Dollar Market Opportunities

	CURRENT SOC	POTENTIAL FUTURE TREATMENT	MARKET SIZE (MAJOR MARKETS[1,2])
IO-naive metastatic	**Anti-PD-1 + CTLA4**	AstraZeneca eVOLVE RCC02 cas + volru	21k patients **~$3B OPPORTUNITY**
Post-IO metastatic	**TKI mono**	PEAK-1 cas + cabo	19k patients **~$2B OPPORTUNITY**
Post-IO & post-TKI	**mTOR, TKI, HIF-2α**		12k patients

CAS FUTURE DEVELOPMENT

New cohorts added to ARC-20:

- 1L (cas + zim)
- 1L favorable risk (cas mono)
- 1L/2L Post-IO/ TKI-naive (cas mono)

New tumor types

1L: first-line; 2L: second-line; B: billion; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; mTOR: mechanistic target of rapamycin; SOC: standard of care; volru: volrustomig; zim: zimberelimab

1. Drug Treatable Addressable Populations (Major Markets, 2024); Decision Resources Group, Arcus analysis
2. Major Markets (US, EU5, JP) - total projected 2034

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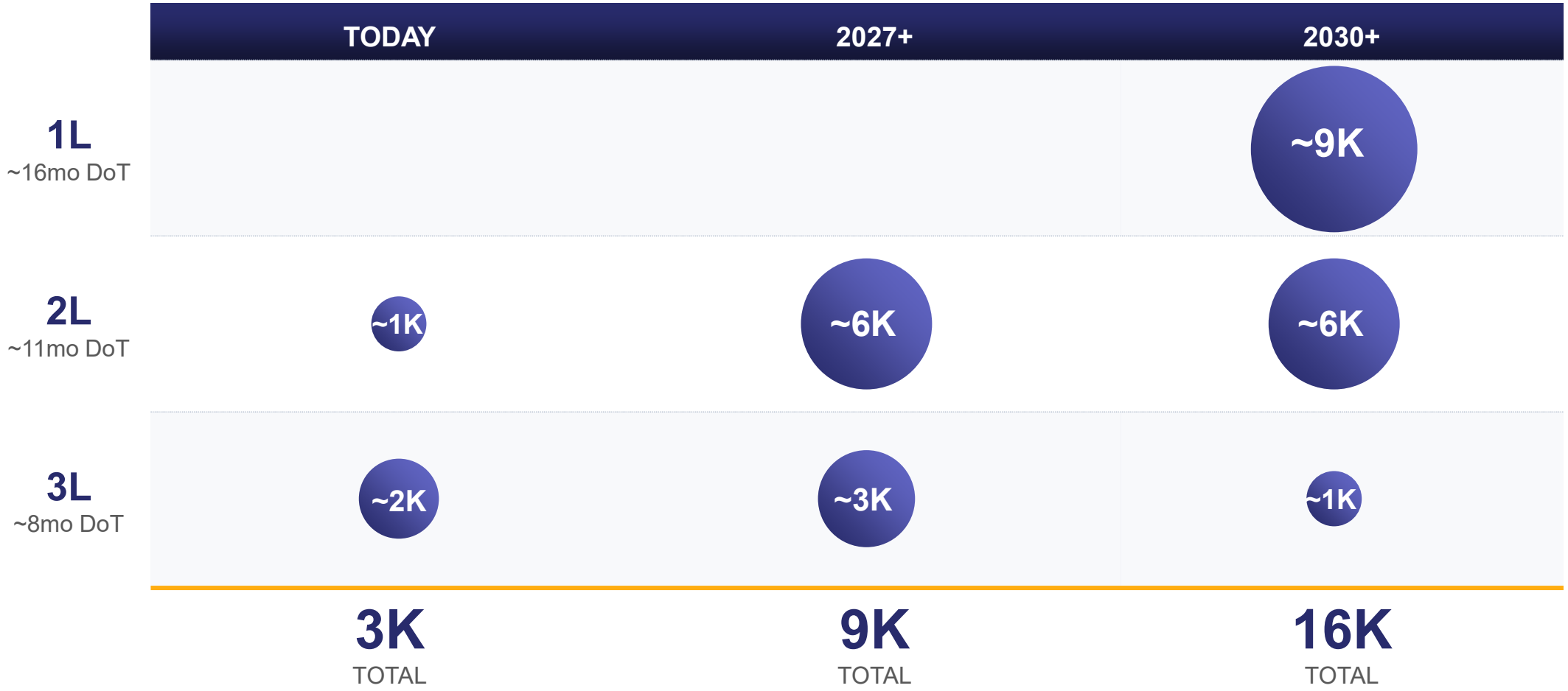
As Casdatifan Moves Up in the Treatment Paradigm, the U.S. Market Opportunity Will Grow Substantially

Potential ccRCC Patients on HIF-2α Inhibitors over Time (US, Annual)



1L: first-line; 2L: second-line; 3L: third-line; ccRCC: clear cell renal cell carcinoma; DoT: duration of therapy; mo: months

Source: Primary market research. DRG epi projections.

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Closing Remarks

Dr. Terry Rosen
CEO, Arcus Biosciences

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Rapid Advancement and Expansion of the Cas Program Is Our Priority over the Next Year

Cas is Poised to Be the HIF-2α Inhibitor of Choice for RCC

- HIF-2α inhibitors is expected to become another SOC in the $6B+ ccRCC market*, in addition to anti-PD-1's and TKIs
- HIF-2α market is currently a "2-horse" race between cas and belz
- Cas has a potential best-in-class profile, both as monotherapy and in combination with other agents
- We are pursuing a broad and differentiated development strategy to drive cas usage to earlier lines of therapy

Multiple Data Events Coming Over the Next ~18 Months

TIMING	SETTING	EVENT
Fall 2025	2L+ (Post-IO & TKI) ccRCC	• More mature data for cas mono from ARC-20
Throughout 2026	1L/2L ccRCC	• More mature cas + cabo data from ARC-20 • Data from three new cas cohorts added to ARC-20 (cas + zim in 1L, cas mono in 1L favorable risk, and cas mono in 1L/2L TKI-naive)

1L: first-line; 2L: second-line; belz: belzutifan; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; mPFS: median progression-free survival; ORR: overall response rate; PD: progressive disease; SOC: standard of care; zim: zimberelimab

*https://www.precedenceresearch.com/kidney-cancer-drugs-market

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Three Phase 3 Programs Targeting Substantial Market Opportunities and Unmet Medical Need

Designed to improve upon the current standard of care

	PEAK INVESMENT YEAR	PHASE 3 TRIAL NAME	STATUS	INDICATION	PATIENTS (MAJOR MARKETS[1,2])	MARKET POTENTIAL (MAJOR MARKETS[2])
CAS HIF-2α small molecule inhibitor	2027+	PEAK-1	To Begin Shortly	Post-IO ccRCC	19K	**~$2B**
		eVOLVE RCC02	To Begin Shortly	IO-naive ccRCC	21K	**~$3B**
DOM (+ ZIM) Fc-silent anti-TIGIT mAb + anti-PD-1 mAb	2025	STAR-221	Data Expected 2026 (event-driven)	1L Gastric/GEJ/EAC – all comers	105K	**~$3B**
		STAR-121	Ongoing	1L NSCLC – all comers	307K	**~$10B**
		PACIFIC-8	Ongoing	Stage 3 NSCLC, PD-L1>1%	35K[3]	**~$2B**
QUEMLI CD73 small molecule inhibitor	2025	PRISM-1	Ongoing	1L PDAC	109K	**>$4B**

1L: first-line; 2L: second-line; 3L: third-line; casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immunotherapy; 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
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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