



Arcus Biosciences Investor Event 2025

October 6, 2025

Agenda

TOPIC	PRESENTER(S)	TIME (ET)
Overview of Arcus	Dr. Terry Rosen	10:00-10:10
Overview of Casdatifan	Dr. Terry Rosen	10:10-10:20
New Casdatifan Monotherapy Data	Dr. Richard Markus	10:20-10:35
Treatment Paradigm in ccRCC	Dr. Rana McKay	10:35-10:55
Q&A		10:55-11:15
Role of HIF-2 α in ccRCC and Casdatifan Biomarker Data	Dr. Juan Jaen	11:15-11:25
Panel Conversation	Dr. Bill Kaelin, Dr. Juan Jaen	11:25-11:45
Break		11:45-12:00
Casdatifan Development Strategy	Dr. Richard Markus	12:00-12:10
Casdatifan Market Opportunity	Jennifer Jarrett	12:10-12:25
Our Emerging I&I Portfolio	Dr. Juan Jaen	12:25-12:40
Q&A		12:40-1:00
Closing Remarks	Dr. Terry Rosen	1:00-1:05

Forward-looking Statements/Safe Harbor

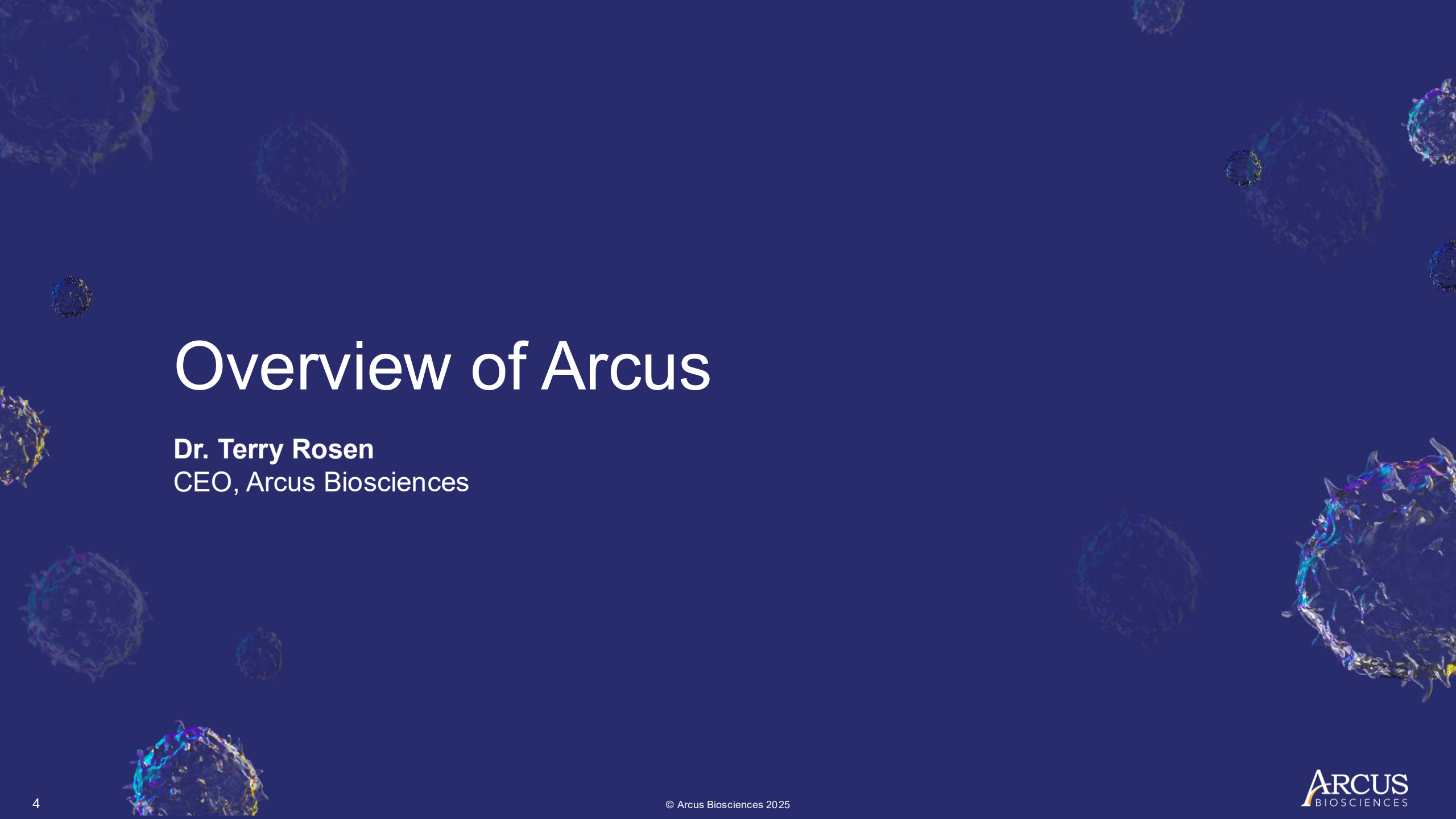
Forward Looking Statements Safe Harbor: This presentation contains forward-looking statements about Arcus Biosciences, Inc. (“we,” “Arcus” or the “Company”) made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements regarding events or results to occur in the future contained in this presentation are forward-looking statements, including statements about: our anticipated cash runway through the initial pivotal readouts for domvanalimab, quemliclustat and casdatifan, including PEAK-1; expected potential, advantages, efficacy or safety of casdatifan, including potential opportunities and benefits from our differentiated development strategy; estimates related to the market opportunities for our product candidates; and achievement and expected timing of clinical and developmental milestones, including the timing of additional data from the casdatifan program, timing of advancement into the clinic for Arcus’s inflammation and immunology programs and results from clinical studies. Forward-looking statements may be identified by words such as “anticipate,” “believe,” “expect,” “intend,” “may,” “should,” “plan,” “project,” “target,” “will,” and similar expressions, although not all forward-looking statements contain these identifying words.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions that may cause actual results to differ materially from those expressed or implied by any forward-looking statements, including, but not limited to: risks associated with interim clinical data not being replicated in other studies for casdatifan or other product candidates; the unexpected emergence of adverse events or other undesirable side effects; difficulties or delays in conducting or completing our clinical trials due to regulatory review, site activation, patient identification or enrollment, or manufacturing and supply of investigational or standard-of-care products for such clinical trials, all of which may be exacerbated by unfavorable global economic, political, public health and trade conditions; changes in the competitive landscape; our ability to successfully market and commercialize any investigational product that is approved; our ability to obtain and maintain intellectual property protection for our product candidates; our reliance on collaboration partners, including Gilead, and the timing and success of activities conducted by such partners; our ability to obtain additional funding as needed; 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 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 is described in our most recent periodic reports filed with the U.S. Securities and Exchange Commission, including our most recent Quarterly Report on Form 10-Q, and in other filings and reports we make with the SEC from time to time. 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 or completeness of the forward-looking statements. We undertake no obligation to update 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, except as required by law.

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No Regulatory Approval: All of Arcus’s molecules are investigational and Arcus (and Gilead for all of the molecules in each optioned program) has not received approval from any regulatory authority for any use globally, nor established the safety and efficacy of these investigational molecules.

Notice of Trademarks: The Arcus name and logo are the property of Arcus. All other trademarks used herein are the property of their respective owners and are used for reference purposes only. Such use should not be construed as an endorsement of Arcus.

The background is a solid dark blue. Scattered across the slide are several stylized, glowing 3D models of cells or molecular structures. These models are composed of thin, translucent lines in shades of blue, purple, and yellow, giving them a futuristic, high-tech appearance. They vary in size and are positioned at different depths, creating a sense of a microscopic or molecular environment.

Overview of Arcus

Dr. Terry Rosen
CEO, Arcus Biosciences

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

CASDATIFAN: COMMERCIALY-VALIDATED MECHANISM

ARC-20

Phase 1/1b in
ccRCC

eVOLVE
RCC02

Phase 1b/3 in 1L
ccRCC

PEAK-1

Phase 3 in 2L
ccRCC

\$927 MILLION IN CASH*

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

* cash, cash equivalents and marketable securities as of June 30, 2025
** runway estimate based on cash, cash equivalents, marketable securities,
available facilities, and current planned operations

DOMVANALIMAB: APPROACHING PHASE 3 DATA

STAR-221

1L Gastric
*Ph 3 Data expected
in 2026*

STAR-121

1L NSCLC
(PD-L1 all comer)

PACIFIC-8

Stage 3 NSCLC

WORLD-CLASS DRUG DISCOVERY

Small molecules, with focus
on oncology and I&I

QUEMLICLUSTAT: PHASE 3 FULLY ENROLLED

PRISM-1 1L Pancreatic

Today, We Will Focus on Our Casdatifan Program and Emerging Portfolio in I&I

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

- Data presented today are from a data cut-off of August 15th – analysis was conducted to support our first manuscript for ARC-20 (target timing early 2026)
- Includes ~120 late-line ccRCC patients treated with cas monotherapy, with ~8 months more follow-up since the last data presentation at ASCO GU
- Results clearly support cas's potential best-in-class efficacy profile
- **With our Phase 3 study, PEAK-1, and eVOLVE-RCC02 now enrolling, today's data provide another important "tailwind" for enrollment**

EMERGING PORTFOLIO IN IMMUNOLOGY AND INFLAMMATION (I&I)

- I&I discovery efforts have been ongoing at Arcus since its founding
- We now have 5 active research programs in I&I
- Data presented today will provide visibility into Arcus's next wave of programs and future clinical programs
- **First Phase 1 trial (for our MRGPRX2 program) is expected to begin in 2026**

Our Late-Stage Trial Experience Demonstrates Our Ability to Rapidly Enroll Large Studies, Which Should De-Risk PEAK-1 Execution



Study	Phase 3 trial for dom/zim	Phase 3 trial for quemli	Phase 1b trial for cas
Enrollment Period	Nov 2022 – June 2024	Jan 2025 – Sept 2025	June 2023 – Present
Time to enrollment completion	18 months	9 months	NA
# of countries	30	13	5
# of sites	212	135	30
Patients enrolled	1040 (enrollment completed)	649 (enrollment completed)	>240 (enrolling new cohorts)

The Majority of Our Phase 3 Studies Have Received Substantial External Support from Partners...

	PHASE 3 TRIAL NAME	STATUS	PARTNERSHIP FUNDING	ARCUS ECONOMIC & COMMERCIAL RIGHTS
CAS HIF-2α small molecule inhibitor	 PEAK-1	Enrolling	--	100% ¹ Economics WW Commercial Rights
	 eVOLVE *	Enrolling (Ph1b)	 AstraZeneca	
DOM (+ ZIM) Fc-silent anti-TIGIT mAb + anti-PD-1 mAb	 STAR-221	Data expected 2026 (event-driven)	 GILEAD  TAIHO TAIHO PHARMA	50% Profit / Co-Promote (US) Royalties (ex-US)
	 STAR-121	Enrolling		
	 PACIFIC-8 *	Enrolling	 GILEAD  AstraZeneca	50% Profit / Co-Promote (US) Royalties (ex-US)
QUEMLI CD73 small- molecule inhibitor	 PRISM-1	Enrollment completed	 TAIHO TAIHO PHARMA + equity investment from  GILEAD	50% Profit / Co-Promote (US) Royalties (ex-US)

1. Taiho Pharmaceutical has an option to license casdatifan rights in Japan and other Asian countries, excluding China

*Sponsored by AstraZeneca

cas: casdatifan; mm: million; R&D: research & development; volru: volrustomig

...Enabling Multiple Phase 3 Studies, Several of Which Are Approaching Readouts and Targeting Large Opportunities

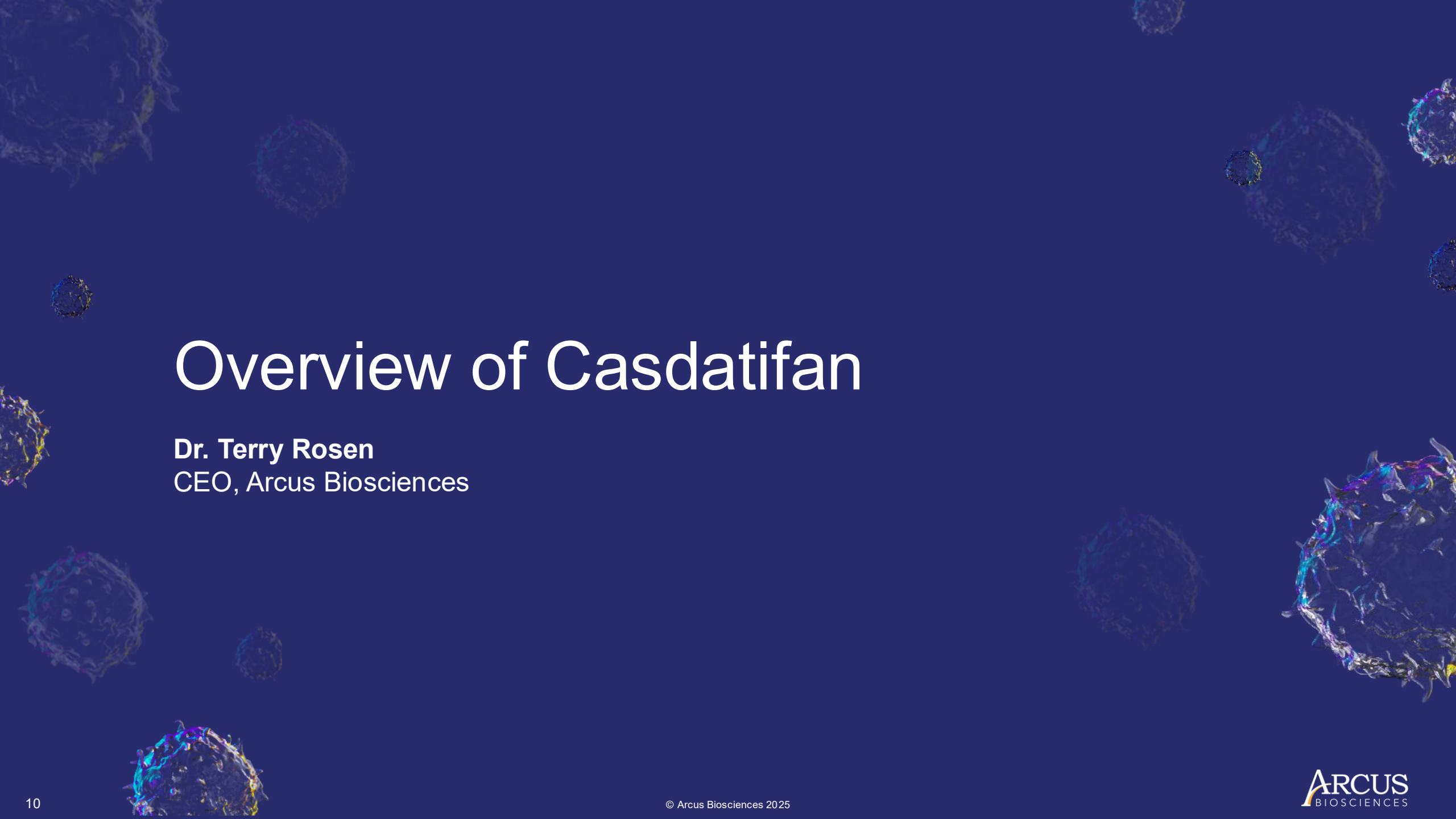
	PEAK CLINICAL INVESTMENT	PHASE 3 TRIAL NAME	STATUS	INDICATION	PATIENTS (MAJOR MARKETS ^{1,2})	MARKET POTENTIAL (MAJOR MARKETS ²)
CAS HIF-2α small molecule inhibitor	2026+	 PEAK-1	Enrolling	Post-IO ccRCC	21K	~\$2B
		 eVOLVE RCC02	Enrolling (Ph1b)	1L ccRCC	24K	~\$3B
DOM (+ ZIM) Fc-silent anti-TIGIT mAb + anti-PD-1 mAb	2025	 STAR-221	Data Expected 2026 (event-driven)	1L Gastric/GEJ/EAC	105K	~\$3B
		 STAR-121	Enrollment completing YE	1L NSCLC	307K	~\$10B
		 PACIFIC-8	Enrolling	Stage 3 NSCLC, PD- L1>1%	35K ³	~\$2B
QUEMLI CD73 small molecule inhibitor	2025	 PRISM-1	Enrollment completed	1L PDAC	109K	>\$4B

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 & HIF-2α opportunity

3. Post-cCRT consolidation

1L: first-line; 2L: second-line; 3L: third-line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; EAC: esophageal adenocarcinoma; EU5: France, Germany, Italy, Spain, and the United Kingdom; GEJ: gastroesophageal junction; IO: immunotherapy; mAb: monoclonal antibody; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; quemli: quemlidustat; zim: zimberelimab



Overview of Casdatifan

Dr. Terry Rosen
CEO, Arcus Biosciences

The Discovery of HIF-2 α and Therapeutic Intervention

Peter Ratcliffe, Gregg Semenza and Bill Kaelin elucidate the biology of hypoxia response

Kaelin, Ratcliffe and Semenza receive Nobel Prize in Physiology and Medicine

Peloton Therapeutics acquired by Merck pre-Phase 3 for \$1.05B upfront (\$2.2B total) for belzutifan

Belzutifan monoTx approved by FDA for advanced ccRCC

Casdatifan, the only competitor to belzutifan, enters Phase 3

1990's

Early 2000's

2010's

2019

2021

2023

2024

2025+

HIF-2 α shown to play a causal role in VHL-deficient kidney cancer; viewed as “non-druggable”

Druggable “pocket” on the HIF-2 α protein elucidated

Belzutifan approved by the FDA for VHL-deficient kidney cancer

Casdatifan, a potential best-in-class HIF-2 α inhibitor discovered at Arcus, enters the clinic for dose escalation

Casdatifan Is a Potential Best-in-Class HIF-2 α Inhibitor

- Casdatifan is an oral, small-molecule inhibitor of HIF-2 α , a target that has been **clinically and commercially validated by Merck's WELIREG[®]** (belzutifan)
- Cas's substantially better PK/PD profile has translated into greater clinical activity relative to that of belzutifan: **2x longer PFS, 50% higher ORR, 50% lower rate of PD***
 - >240 patients have been treated with casdatifan to date
- We are pursuing a differentiated development strategy with our Phase 3 program and targeting the two largest RCC market segments:
 - PEAK-1: cas + cabo in **IO-experienced ccRCC, a \$2B+ peak sales opportunity**
 - eVOLVE-RCC002 (AZ sponsoring, Phase 1b/3 study): cas + volrustomig in **1L ccRCC, a \$3B+ peak sales opportunity**
- The total RCC market is **\$9B+ today** (in G7 countries alone) **and growing**

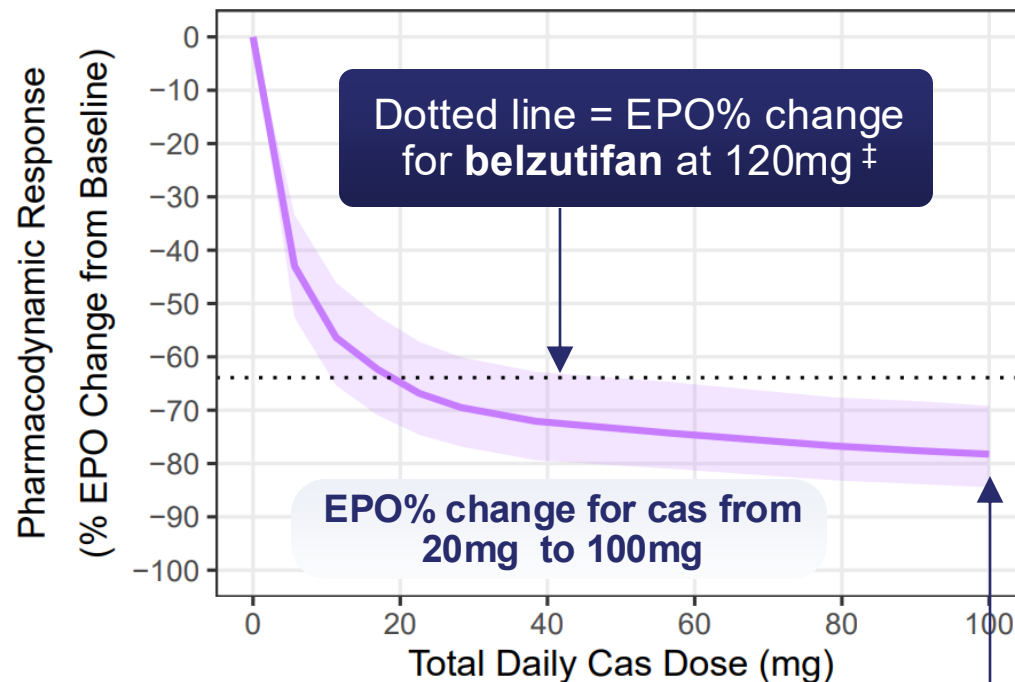
1L: first-line; AZ: AstraZeneca; cas: casdatifan; cabo: cabozantinib; ccRCC: clear cell renal cell carcinoma; EPO: erythropoietin; G7 countries: Canada, France, Germany, Italy, Japan, United Kingdom, United States; h: hours; IO: immunotherapy; ORR: overall response rate; PD: pharmacodynamic; PFS: progression-free survival; PK: pharmacokinetic

*Data 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.

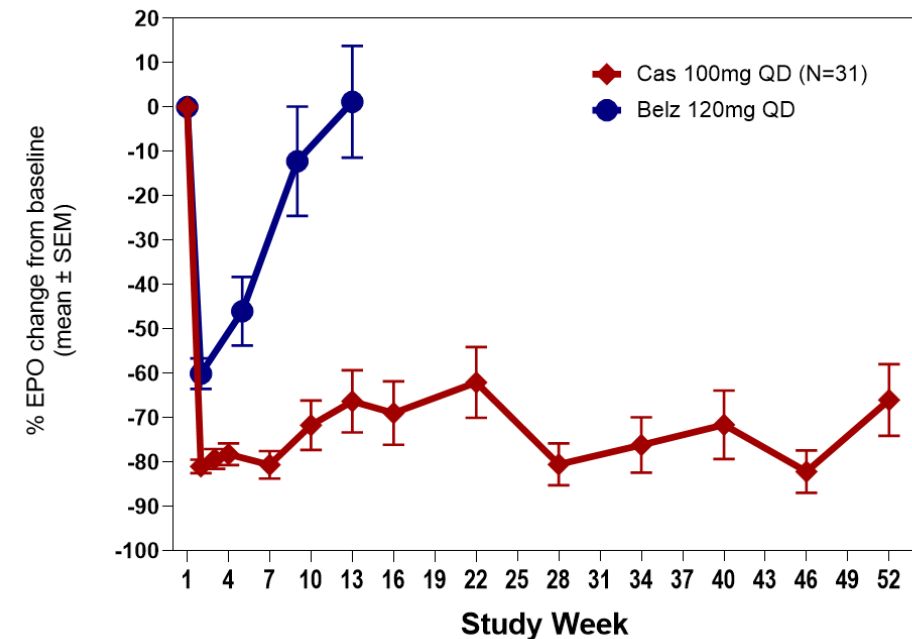
Casdatifan's Advantages Stem from an Improved PK / PD Profile, Enabling it to “Hit the Target Harder”

EPO Suppression: PD Biomarker for HIF-2α Inhibition

20mg of cas achieves the same EPO reduction as that of 120mg of belz, with significantly greater sustained suppression



20mg of cas is **one fifth** our going-forward dose of 100mg



100mg QD of cas results in substantial and **sustained** EPO suppression

Cas: median (solid purple line) and inter-quartile range (shaded area) of population PK/PD simulations using model developed from data.

[‡] Source: Marathe DD, J Clin Pharm 2024, Fig S20. Comparison not based on head-to-head studies.

Casdatifan (AB521) is an investigational molecule and its safety and efficacy have not been established. PK/PD data are from both escalation and expansion cohorts. belz: belzutifan; cas: casdatifan; EPO: erythropoietin; PD: pharmacodynamic; PK: pharmacokinetic; SEM: standard error of mean; QD: once daily

Three Oral Presentations at Major Medical Meetings in Less Than a Year Have Created Substantial Interest in Casdatifan



50mg BID (n=31)	11 MOS MED. FOLLOW-UP PD: 19% cORR: 25% mPFS: Not reached	15 MOS MED. FOLLOW-UP PD: 19% cORR: 25% mPFS: 9.7 mos	--
50mg QD (n=28)	8 MOS MED. FOLLOW-UP PD: 14% cORR: 21% mPFS: Not reached	12 MOS MED. FOLLOW-UP PD: 14% cORR: 32% mPFS: Not reached	--
100mg QD (n=27)	--	5 MOS MED. FOLLOW-UP PD: 15% cORR: 33% mPFS: Not reached	--
Cas + Cabo (n=24)	--	--	5 MOS MED. FOLLOW-UP PD: 4% cORR: 46% mPFS: Not reached

DCOs - ENA 2024: August 30, 2024; ASCO GU 2025: January 3, 2025; ASCO 2025: March 14, 2025

BID: twice daily; cabo: cabozantinib; cas: casdatifan; cORR: confirmed overall response rate; DCO: data cut-off; mos: months; mPFS: median progression-free survival; PD: pharmacodynamic; QD: once daily

And the Data Have Been Consistently Robust and Have Improved Over Time



Today

50mg BID (n=31)	11 MOS MED. FOLLOW-UP PD: 19% cORR: 25% mPFS: Not reached	15 MOS MED. FOLLOW-UP PD: 19% cORR: 25% mPFS: 9.7 mos	23 MOS MED. FOLLOW-UP PD: 19% cORR: 26% mPFS: 9.7 mos
50mg QD (n=28)	8 MOS MED. FOLLOW-UP PD: 14% cORR: 21% mPFS: Not reached	12 MOS MED. FOLLOW-UP PD: 14% cORR: 32% mPFS: Not reached	20 MOS MED. FOLLOW-UP PD: 14% cORR: 36% mPFS: 19.2 mos
100mg QD (n=31)	--	5 MOS MED. FOLLOW-UP PD: 15% cORR: 33% mPFS: Not reached	12 MOS MED. FOLLOW-UP PD: 16% cORR: 35% / uORR: 42%* mPFS: Not reached

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

With a Differentiated Efficacy Profile and Development Plan, Cas is Poised to Become the HIF-2 α Treatment of Choice

EFFICACY & SAFETY DATA BASED ON ARC-20 (CAS) AND LITESPARK-005 (BELZ), MONOTHERAPY DATA IS FOR PATIENTS THAT HAVE RECEIVED BOTH PRIOR ANTI-PD-1 AND TKI

	casdatifan 100mg QD	belzutifan¹
		
Primary PD for monotherapy	16%	34%
cORR for monotherapy	35% (42% uORR*)	22%
mPFS for monotherapy	12+ months	5.6 months
cORR in combination with cabo ("IO-experienced")	46%	31%
TKI combo partner in post-IO setting	+ cabo	+ lenva (data in 2026?) + 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)

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%. DCO for casdatifan data: August 15, 2025

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

Data 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.

1L: first-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; cORR: confirmed overall response rate; DCO: data cut-off; IO: immunotherapy; lenva: lenvatinib; mPFS: median progression free survival; m: months; pembro: pembrolizumab; QD: once daily; TKI: tyrosine kinase inhibitor; uORR: unconfirmed overall response rate; volru: volrustomig; zanza: zanzalintinib

Casdatifan Clinical Data: Monotherapy in Late-Line ccRCC

Dr. Richard Markus
CMO, Arcus Biosciences

The Data We Are Presenting Today Support Cas's Best-in-Class Profile

- For the first time, we are presenting data from all four late-line monotherapy cohorts from ARC-20, including PFS – a 121-patient dataset
- Across this dataset (n=121), we have observed*:
 - ✓ **Substantially higher ORR vs. that of belzutifan**
 - ✓ **~50% lower rate of primary progressive disease**
 - ✓ **~2x longer median PFS**
 - ✓ **Faster time to response**
- Responses observed have been highly durable with the vast majority of patients still on treatment
- We believe these data substantially de-risk PEAK-1 and demonstrate the potential for casdatifan to displace TKIs in earlier line settings

*Data 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.

Cas: casdatifan; ORR: overall response rate; PFS: progression-free survival; TKI: tyrosine kinase inhibitor

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Today's Data Focuses on the ARC-20 Cohorts Evaluating Cas Mono in anti-PD-1/TKI Experienced ccRCC

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 tablet

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

To date, over 240 patients have received casdatifan across all cohorts of ARC-20

We Are Focusing on LITESPARK-005 as the Benchmark, but Data from Multiple Belzutifan Studies Are Consistent

STUDY DESCRIPTION	# OF LINES OF THERAPY	PRIOR TKI	PRIOR CPI	ORR (PRIOR CPI <u>AND</u> TKI PTS ONLY)	MEDIAN PFS (PRIOR CPI <u>AND</u> TKI PTS ONLY)
LITESPARK-005¹	• 1-3 prior lines for inclusion • Mostly 2-3 prior lines	• 100% had prior TKI	• 100% had prior CPI	• 21.9%	5.6 months
LITESPARK-001²	• Median 3 prior lines	• 91% had prior VEGF TK	• 80% had prior CPI	• 20.5%	NA
LITESPARK-013³	• Mostly 1-2 prior lines	• 71.4% had prior TKI	• 100% had prior CPI	• 19.1%	7.3 months
KEYMAKER-U03B⁴	• Mostly ≥3 prior lines	• 100% had prior TKI	• 100% had prior CPI	• 19.4%	5.4 months

1. Phase 3; belzutifan vs. everolimus in previously treated ccRCC (NCT04195750); ref: ESMO 2023 LBA88.

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

3. Phase 2; belzutifan 120mg and 200mg (pooled) in previously treated ccRCC (NCT04489771); ref: ASCO 2024 4534.

4. Phase 2; belzutifan + pembrolizumab in PDx and VEGF TKI experienced ccRCC (NCT04626518); ref: ASCO GU 2025 440; note: IO rechallenge not known to be effective in post-IO ccRCC.

2L: second-line; ccRCC: clear cell renal cell carcinoma; CPI: checkpoint inhibitor; ORR: overall response rate; PFS: progression-free survival; Pts: patients; RECIST: Response Evaluation Criteria in Solid Tumors; TKI: tyrosine kinase inhibitor

Patients in ARC-20 Had Greater Number of Prior Therapies Relative to the Patients in LITESPARK-005

Safety-Evaluable Population ¹	Dose Expansion: 2L+ ccRCC					Belzutifan ³
	50mg BID (n = 33)	50mg QD (n = 31)	100mg QD (n = 32)	150mg QD (n = 31)	Pooled (n = 127)	120mg QD (n = 374)
Age, years, median (range)	62 (41–79)	65 (43–82)	60 (45–77)	65 (53–78)	62 (41–82)	66 (49–78)
Sex, Female/Male, n (%)	8 (24) / 25 (76)	10 (32) / 21 (68)	5 (16) / 27 (84)	8 (26) / 23 (74)	31 (24) / 96 (76)	77 (21) / 297 (79)
ECOG PS 0/1, n (%)	16 (48) / 17 (52)	18 (58) / 13 (42)	15 (47) / 17 (53)	13 (42) / 18 (58)	62 (49) / 65 (51)	NA
IMDC Risk Score, n (%) ²						
Favorable	10 (30)	8 (26)	7 (22)	9 (29)	34 (27)	79 (21)
Intermediate	21 (64)	17 (55)	20 (63)	19 (61)	77 (61)	249 (67)
Poor	2 (6)	5 (16)	3 (9)	3 (10)	13 (10)	46 (12)
Prior lines of therapy, n (%)						
1	2 (6)	5 (16)	5 (17)	7 (23)	21 (17)	46 (12)
2	14 (42)	9 (29)	7 (24)	6 (19)	39 (30)	157 (42)
3	8 (24)	8 (26)	10 (34)	7 (23)	33 (26)	171 (46)
4 or more	9 (27)	9 (29)	7 (24)	11 (36)	35 (28)	0 (0)

DCO date: August 15, 2025

1. The safety-evaluable population included all dose expansion enrolled patients who received any amount of study treatment.

2. One patient in the 50 mg QD group had an unknown IMDC risk score and one patient in the 100 mg QD group had a missing IMDC risk score.

3. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023; *2 or 3 prior VEGF-R TKI regimens; DCO date: August 30, 2024.; Baseline was defined as the last non-missing assessment prior to the first dosing of treatment.

Data 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; BID: twice daily; ccRCC: clear cell renal cell carcinoma; DCO: data cut-off; ECOG PS: Eastern Cooperative Oncology Group Performance Status; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; QD: once daily; VEGFR-TKI: vascular endothelial growth factor receptor tyrosine kinase inhibitor

Confirmed ORR for the “Pooled” Cohort (n=121) is >30%

Belzutifan²

Dose Expansion: 2L+ ccRCC

Efficacy-Evaluable Population ¹	50mg BID (n = 31)	50mg QD (n = 28)	100mg QD (n=31)	150mg QD (n = 31)	All Pooled (n = 121)	120mg QD (n = 374)
Median Follow-Up, mos (range)	22.8 (14.4, 26.0)	19.7 (15.9, 21.3)	12.4 (6.3, 13.5)	14.4 (12.5, 15.5)	15.2 (6.3, 26.0)	18.4 (9.4–31.7)
Median Time to Response, mos	2.7	4.1	2.6	2.7	2.8	3.8
Confirmed ORR (95% CI)	26% (12, 45)	36% (19, 56)	35% (19, 55)	29% (14, 48)	31% (23, 40)	22% (18, 27)
Complete Response, % (n)	0% (0)	4% (1)	0% (0)	0% (0)	1% (1)	3% (10)
Partial Response, % (n)	26% (8)	32% (9)	35% (11)	29% (9)	31% (37)	19% (72)
Stable Disease, % (n)	55% (17)	50% (14)	48% (15)	45% (14)	50% (60)	39% (147)
Progressive Disease, % (n)	19% (6)	14% (4)	16% (5) ³	26% (8)	19% (23) ³	34% (126)
ORR, including responses pending confirmation (95% CI)*	26% (12, 45)	36% (19, 56)	42% (25, 61)	29% (14, 48)	33% (25, 42)	NA

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

DCO date: August 15, 2025

1. Efficacy-evaluable population for this expansion cohort is defined as all eligible participants who received any study treatment and have at least one post-baseline efficacy assessment, or who discontinued study treatment due to progressive disease or death, regardless of whether they had a scan.

2. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023; *2 or 3 prior VEGF-R TKI regimens; DCO date: August 30, 2024; Baseline was defined as the last non-missing assessment prior to the first dosing of treatment.

3. Includes three patients with radiological progressive disease and two patients who had clinical progression before the first scan, which have been included by do not meet criteria for progressive disease per RECIST.

Data 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; BID: twice daily; ccRCC: clear cell renal cell carcinoma; CI: confidence interval; cORR: confirmed overall response rate; DCO: data cut-off; ECOG PS: Eastern Cooperative Oncology Group Performance Status; IMDC: International Metastatic Renal Cell

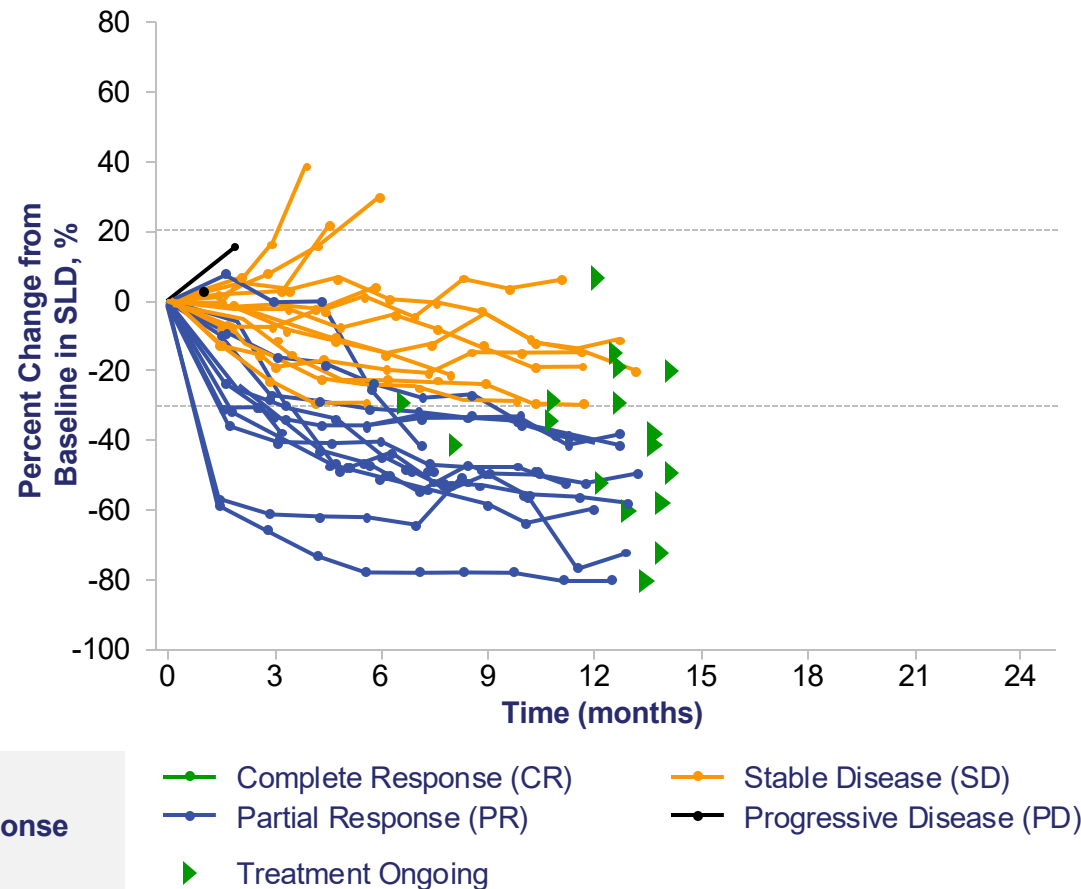
Carcinoma Database Consortium; NA: not applicable; ORR: overall response rate; QD: once daily; u: unconfirmed; VEGFR-TKI: vascular endothelial growth factor receptor tyrosine kinase inhibitor

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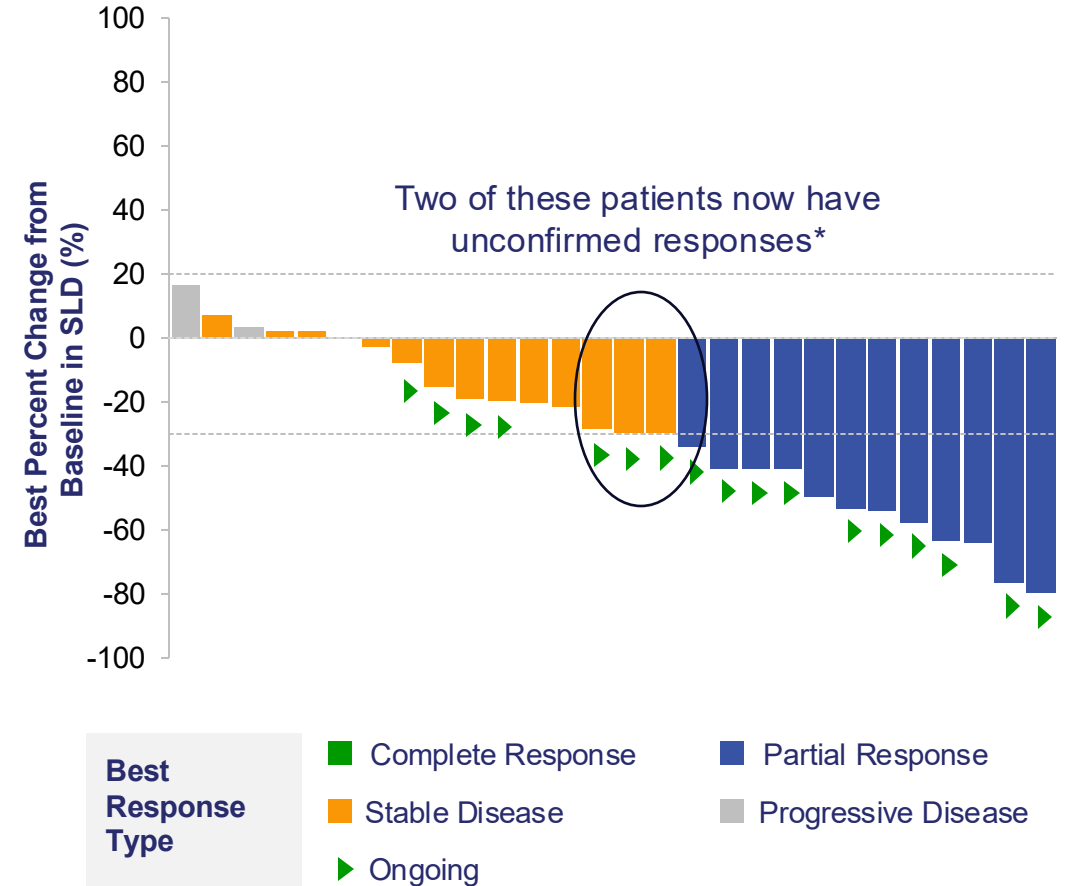
Vast Majority of Patients Have Achieved Meaningful Clinical Benefit

Majority of patients remain on treatment, even with 12+ months median follow-up

Spider Plot (100mg QD)



Waterfall Plot (100mg QD)



*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

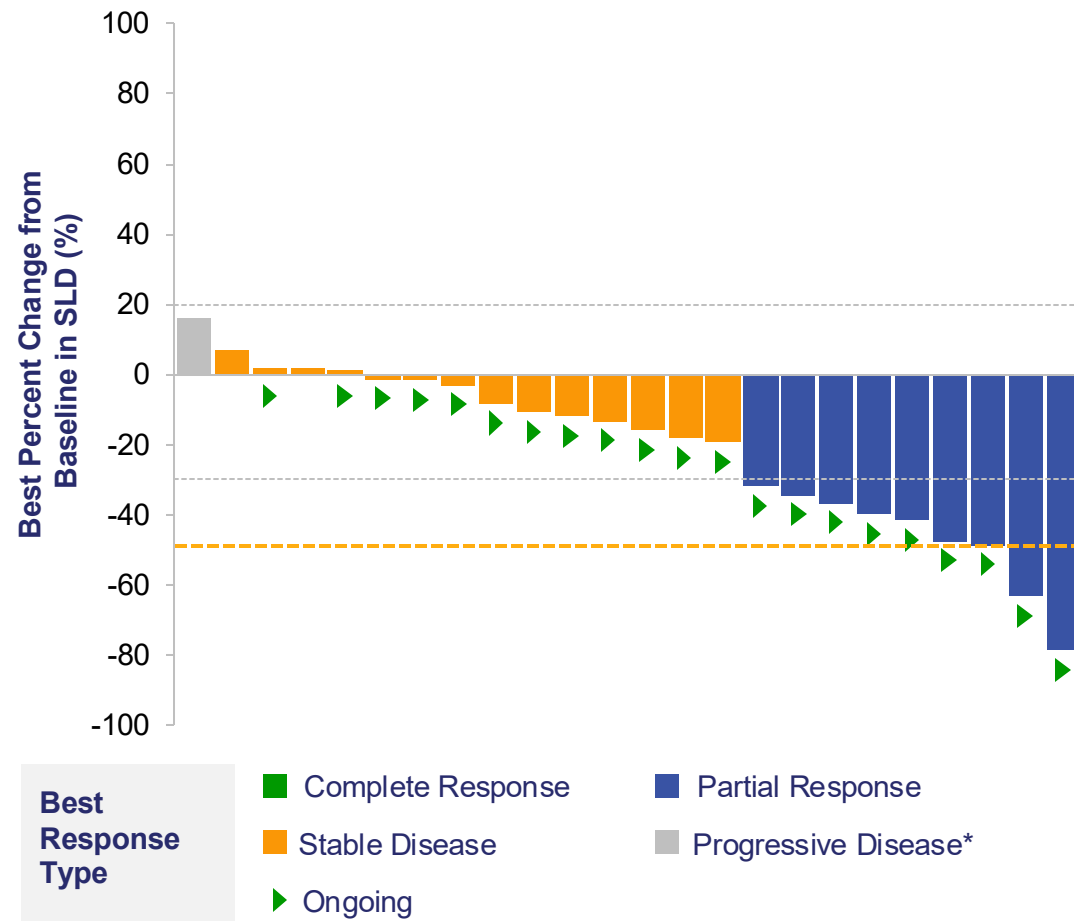
DCO date: August 15, 2025

DCO: data cut-off; QD: once daily; SD: stable disease; SLD: sum of lesion diameter

Tumor Reduction Has Deepened with Longer Follow-up

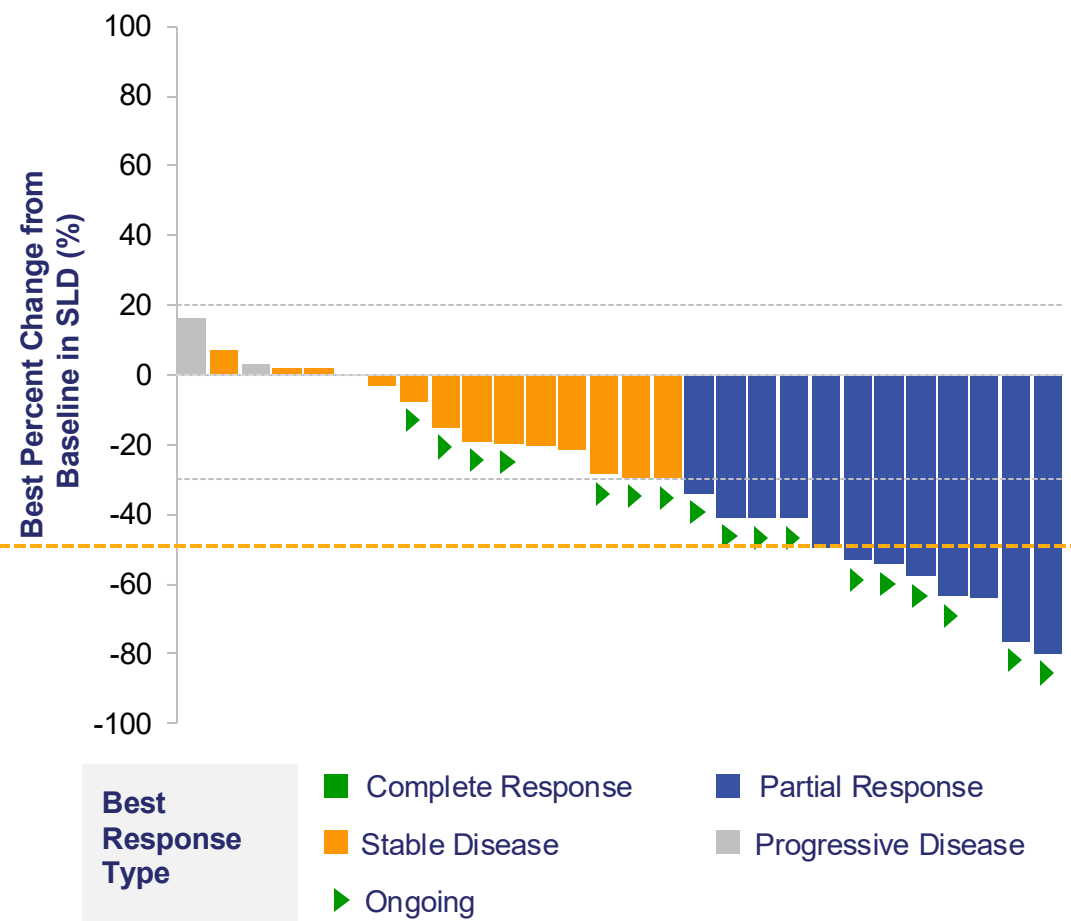
5 Months Median Follow-up: 100mg QD Cohort¹

n = 27, cORR: 33%



12 Months Median Follow-up: 100mg QD Cohort²

n = 31, cORR: 35% / uORR: 42%*



*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

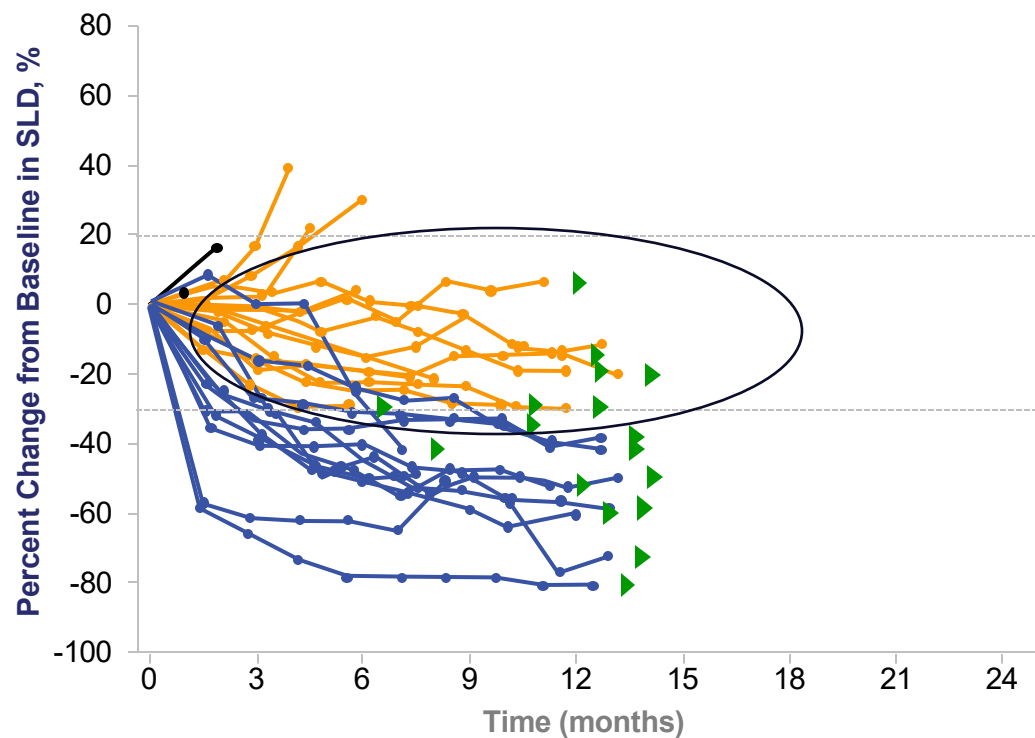
1.DCO: January 3, 2025 as presented at ASCO GU 2025.

2. DCO: August 15, 2025.

cORR: confirmed response rate; QD: once daily; SLD: sum of lesion diameter; u: unconfirmed

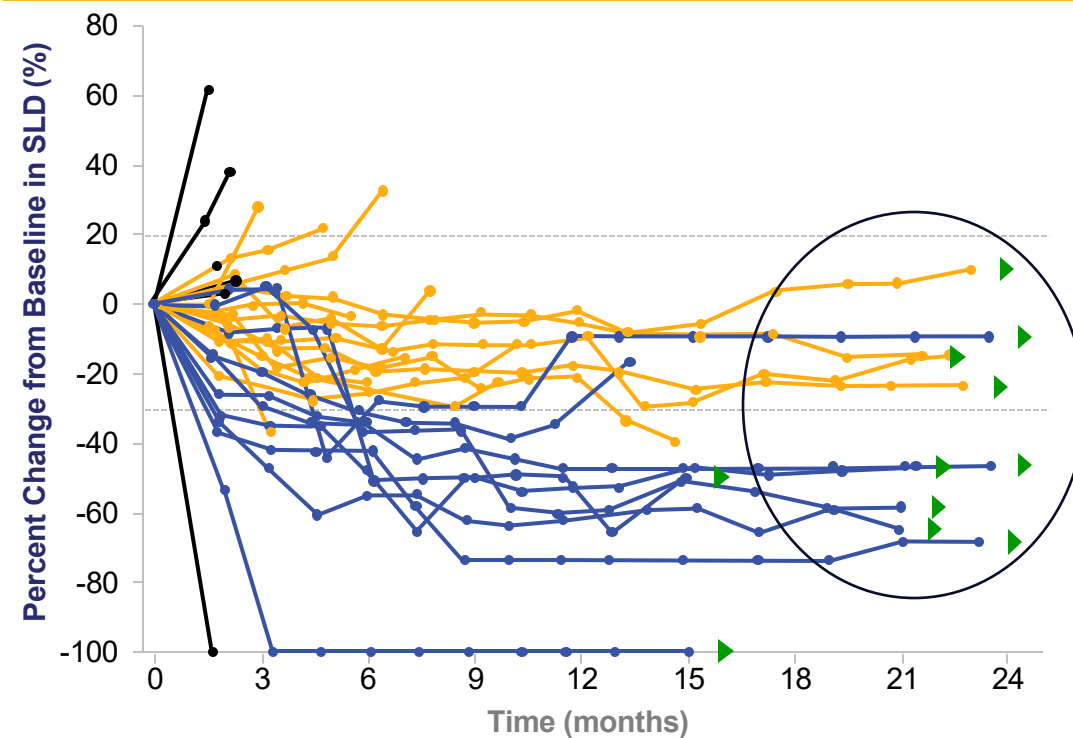
Stable Disease Patients Have Also Benefited Meaningfully from Treatment, With Many on Treatment >12 Months

100mg QD Cohort



Go-forward Dose for Phase 3

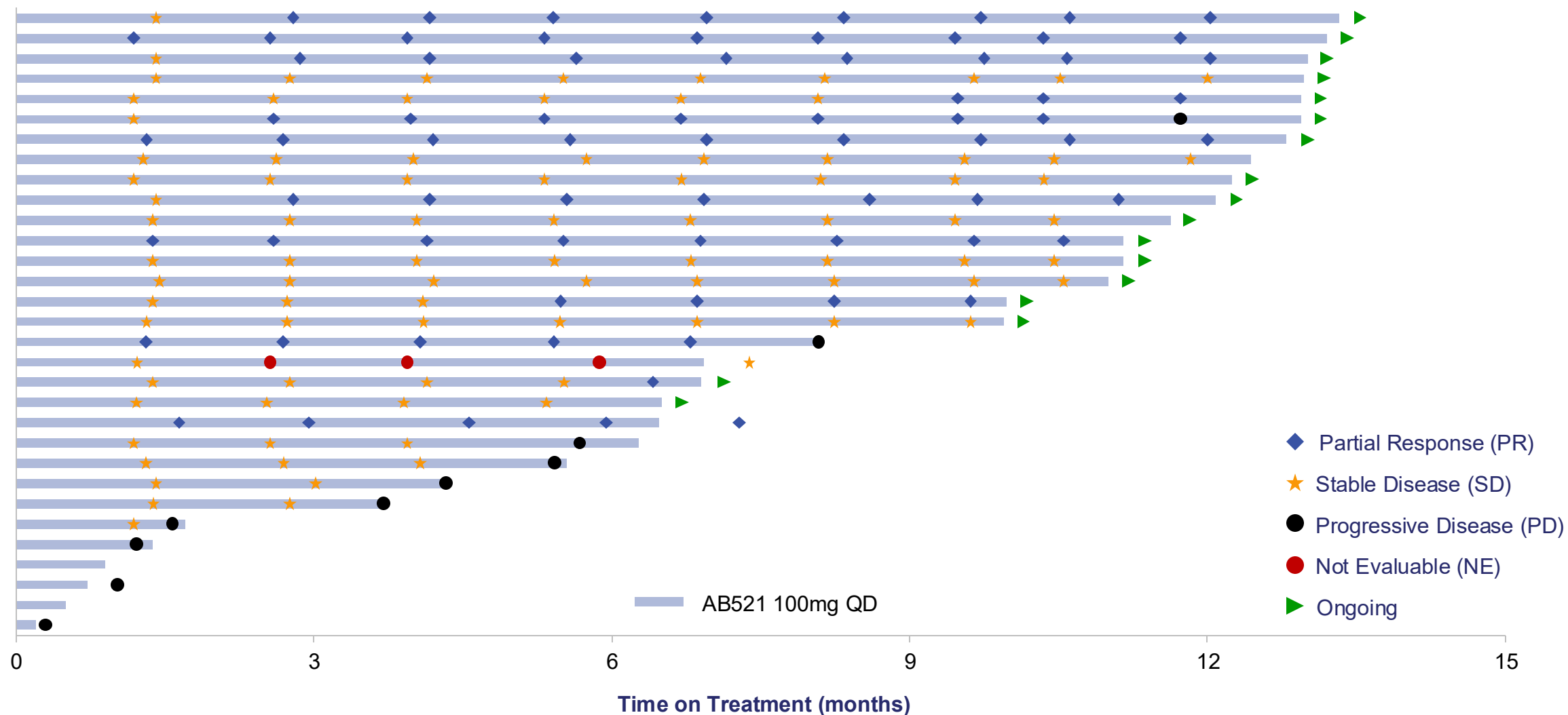
50mg BID Cohort



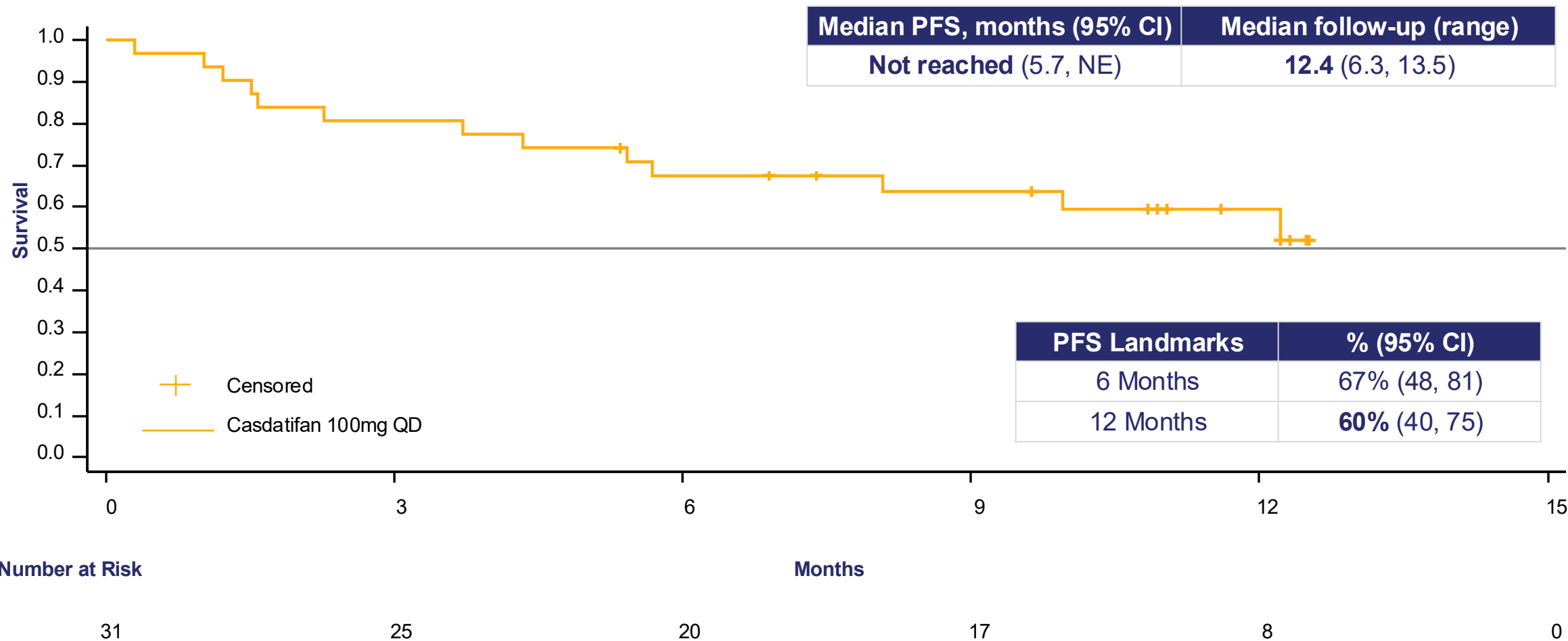
Cohort with Longest Follow-up

—●— Complete Response (CR) —●— Partial Response (PR) —●— Stable Disease (SD) —●— Progressive Disease (PD) ▶ Treatment Ongoing

Most Patients Remain on Treatment, Including Almost All of the Responders in the 100mg QD Cohort



Median PFS for the 100mg QD Cohort Has Still Not Been Reached with >12 Months Follow-Up



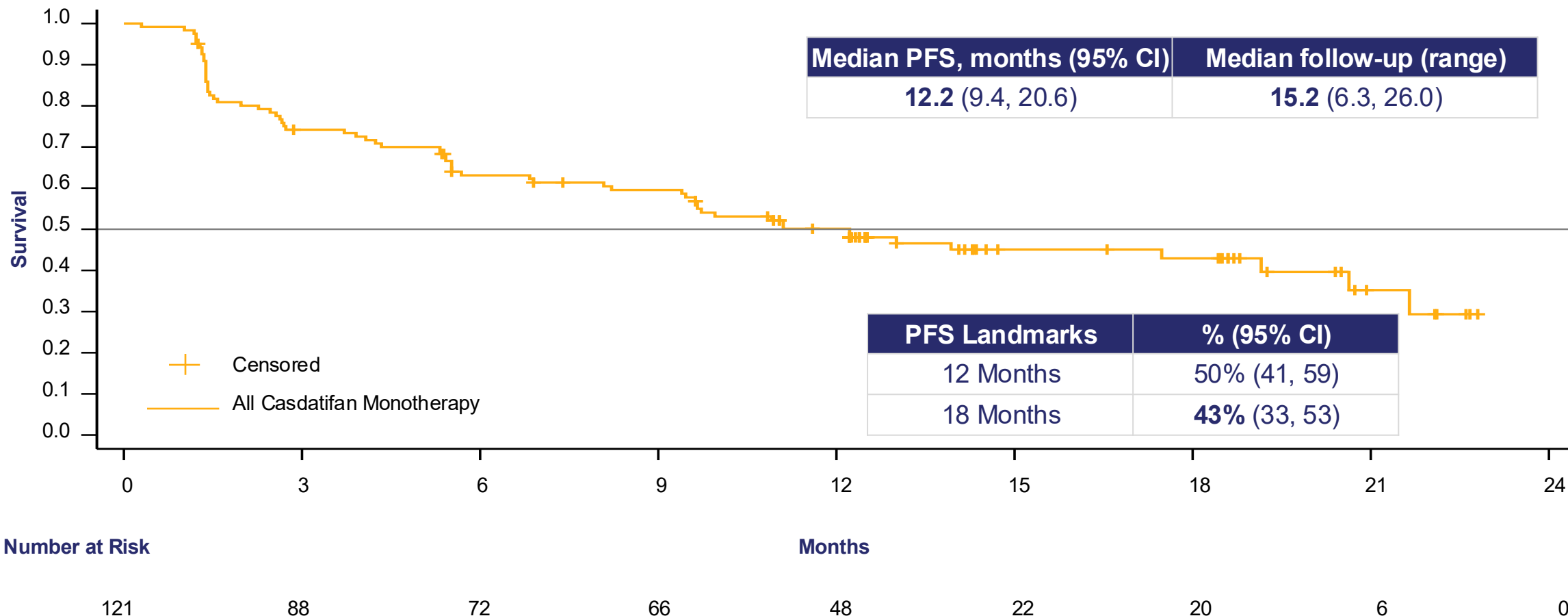
60% Landmark 12-Month PFS compares very favorably to the 34% for belzutifan in LITESPARK-005*

DCO date: August 15, 2025

*Data 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.

CI: confidence interval; DCO: data cut-off; mos: months; NE: not estimable; PFS: progression-free survival; QD: once daily

Median PFS for the Four Monotherapy Cohorts Pooled (n=121) is 2x+ the mPFS for Belz Monotherapy in LS-005



12.2 months mPFS compares to 5.6 mos PFS for belzutifan in LITESPARK-005*

DCO date: August 15, 2025

*Data 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.

belz: belzutifan; CI: confidence interval; DCO: data cut-off; mPFS: median progression-free survival

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IMDC Risk Score Did Not Impact ORRs and Even the Intermediate / Poor Patients Outperformed LS-005 PFS

	100MG QD	ALL POOLED
IMDC Favorable	n=7 (21% of cohort)	n=31 (27% of population)
ORR (95% CI)	29% (4, 71)	32% (17, 51)
Median PFS (months) (95% CI)	NE (0.3; NE)	NE (10.9; NE)
IMDC Intermediate or Poor	n=22	n=87
ORR (95% CI)	41% (21, 64)	31% (22, 42)
Median PFS (months) (95% CI)	NE (5.4; NE)	9.7 (5.5; 17.5)

mPFS in LS-005 for belz in IMDC intermediate / poor patients was 5.3 months¹

DCO date: August 15, 2025

1. Albiges et al, LS-005 Subgroup Analysis, KCRS 2024.

Data 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.

belz: belzutifan; CI: confidence interval; DCO: data cut-off; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; mPFS: median progression-free survival; NE: not estimable; ORR: overall response rate; PFS: progression-free survival; QD: once daily

Casdatifan Was Well Tolerated in All Cohorts, With a Comparable Safety Profile to That of Belzutifan

Safety-Evaluable Population ¹	50mg BID (n=33)	50mg QD (n=31)	100mg QD (n=32)	150mg QD (n=31)	Pooled (n=127)	Belzutifan (LITESPARK-005) ²
Median follow-up, months (range)	22.8 (14.4, 26.0)	19.7 (15.9, 21.3)	12.4 (6.3, 13.5)	14.4 (12.5, 15.5)	15.5 (6.3, 26.0)	
Any TEAEs, n (%)	32 (97)	30 (97)	31 (97)	31 (100)	124 (98)	
Related to casdatifan	31 (94)	29 (94)	29 (91)	31 (100)	120 (95)	
Any Grade ≥3 TEAEs, n (%)	19 (58)	19 (61)	16 (50)	22 (71)	76 (60)	
Related to casdatifan	17 (52)	13 (42)	12 (38)	20 (65)	62 (49)	Serious AEs:
Any Serious TEAEs, n (%)	6 (18)	11 (35)	10 (31)	12 (39)	39 (31)	All-cause: 43%
Related to casdatifan	1 (3)	3 (10)	2 (6)	4 (13)	10 (8)	TRAEs: 13%

Serious TEAEs related to casdatifan have been low for an anti-cancer drug with such meaningful single agent activity

DCO date: August 15, 2025

1. The safety-evaluable population included all dose expansion enrolled patients who received any amount of any study treatment.

2. Belzutifan safety details not reported at IA1. Data from IA2 of LITESPARK-005. Source: Choueiri et al. 2024.

Data 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.

AE: adverse event; BID: twice daily; DCO: data cut-off; QD: once daily; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event

Casdatifan Was Well Tolerated in All Cohorts, With a Comparable Safety Profile to That of Belzutifan

Safety-Evaluable Population ¹	50mg BID (n=33)	50mg QD (n=31)	100mg QD (n=32)	150mg QD (n=31)	Pooled (n=127)	Belzutifan (LITESPARK-005)
Anemia, n (%)						Anemia:
All grades	29 (88)	29 (94)	29 (91)	30 (97)	117 (92)	All grade: 83%
Grade ≥3 related to casdatifan	16 (49)	12 (39)	8 (25)	16 (52)	52 (41)	Grade 3+: 33%
Related to casdatifan leading to interruptions	11 (33)	10 (32)	9 (28)	15 (48)	45 (35)	
Leading to dose reductions	4 (12)	5 (16)	3 (9)	6 (19)	18 (14)	
Leading to discontin.	0	0	0	0	0	
Hypoxia, n (%)						Hypoxia:
All grades	6 (18)	5 (16)	5 (16)	7 (23)	23 (18)	All Grade: 15%
Grade ≥3 related to casdatifan	3 (9)	3 (10)	3 (9)	5 (16)	14 (11)	Grade 3+: 11%
Related to casdatifan leading to interruptions	5 (15)	4 (13)	3 (9)	6 (19)	18 (14)	
Leading to dose reductions	3 (9)	2 (6)	1 (3)	3 (10)	9 (7)	
Leading to discontin.	0	1 (3)	1 (3)	1 (3)	3 (2)	

DCO date: August 15, 2025

Data 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.

BID: twice daily; DCO: data cut-off; QD: once daily

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With Substantial Clinical Benefit and a Well Tolerated Safety Profile, Cas is Positioned to Become the SOC in RCC

In a large cohort of patients (n=121), casdatifan generated robust efficacy data that appears to improve upon "benchmark" data*

- ✓ ~50% higher ORR and the ORR for every cohort was greater than that of LS-005
- ✓ Median PFS was >12 months, ~2x the mPFS seen in LS-005
- ✓ Vast majority of patients experienced tumor reduction and clinical benefit
- ✓ Durable disease control observed for both responders and stable disease patients, with 18-month landmark PFS of 43% as of DCO

100mg QD is considered the optimal dose for Phase 3 studies based on multiple metrics

Similar safety profile to belzutifan, with no new safety signals

- ✓ Hypoxia and anemia rates are in-line with those of belzutifan in LS-005
- ✓ TEAEs easily managed by short dose interruptions or reductions
- ✓ Low rate of discontinuation due to TEAEs

DCO date: August 15, 2025

*Data 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.
cas: casdatifan; DCO: data cut-off; mPFS: median progression-free survival; ORR: overall response rate; PFS: progression-free survival; RCC: renal cell carcinoma; SOC: standard of care; TEAE: treatment-emergent adverse event

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Introducing Dr. Rana McKay



Rana McKay, MD, FASCO

Professor of Medicine and Urology
Associate Director, Clinical Research
Co-Lead of GU Oncology Program
Moore's Cancer Center, UCSD

- Winner of the 2024 Christopher G. Wood Rising Star Award at IKCS Europe
- Winner of the 2023 KCA Trailblazer Award for research on “Dissecting predictors of response to immunotherapy in patients with renal cell carcinoma”
- Winner of the KidneyCan Catalyst Award at 2025 KCRS
- Member of the 2026-29 ASCO nominating committee and current member of the Annual Meeting Education Program Committee’s Genitourinary Cancer – Kidney and Bladder Track

Treatment Paradigm in ccRCC

Dr. Rana McKay

University of California San Diego

Overview of My GU Oncology Practice

RCC



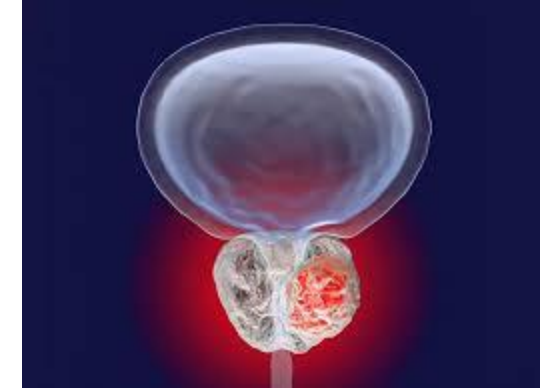
70k U.S. Cases / Year¹

Bladder Cancer



84k U.S. Cases / Year¹

Prostate Cancer



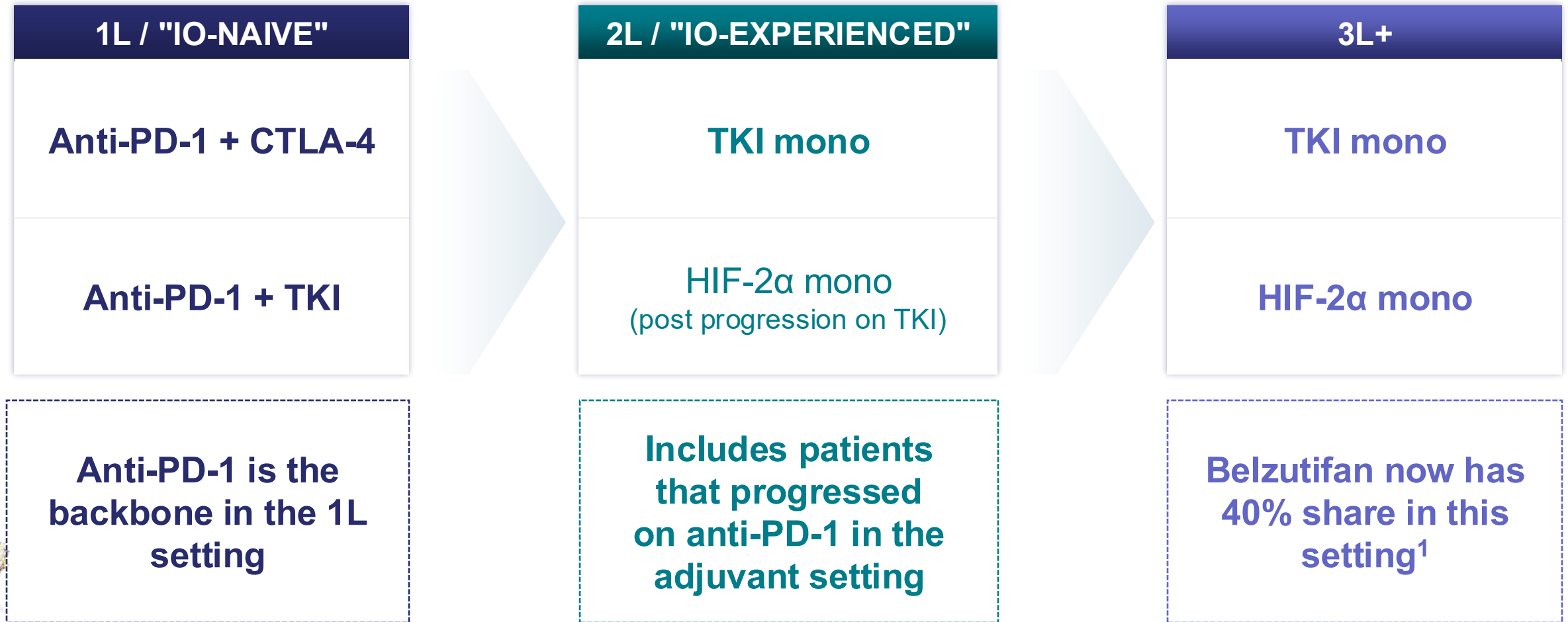
273k U.S. Cases / Year¹

- Types of tumors I treat: ~50% RCC, ~40% Prostate, ~10% Bladder and Other
- Typical ccRCC patient in my clinic is 64-year old male who presents with a large renal mass found incidentally on imaging and then found to have metastatic disease
- I have experience treating patients with belzutifan and casdatifan (the latter in clinical trials)

1. DRG (Clarivate)

ccRCC: clear cell renal cell carcinoma; GU: genitourinary; RCC: renal cell carcinoma

The RCC Patient Journey Today



Listed in order of preference by category.

Source: Adapted from NCCN guidelines.

1. Arcus primary research

1L: first-line; 2L: second-line; CTLA-4: cytotoxic T-lymphocyte associated protein 4; IO: immunotherapy; mono: monotherapy; mTOR: mechanistic target of rapamycin; NCCN: National Comprehensive Cancer Network; PD-1: programmed cell death protein

1; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor

Belzutifan Has Rapidly Established Itself As the Standard of Care in 3L+ ccRCC, Despite Limitations

ORR / Primary Progressive Disease

	Belzutifan (N=374)	Everolimus (N=372)
	IA1	
ORR, % (95% CI)	21.9% (17.8-26.5)	3.5% (1.9-5.9)
Estimated difference in % (95% CI)	18.4 (14.0-23.2); P<.00001*	
CR	2.7%	0
PR	19.3%	3.5%
SD	39.3%	65.9%
PD	33.7%	21.5%
Non-evaluable ^a	1.3%	2.2%
No assessment ^b	3.7%	7.0%

Data cut-off for IA1 of Nov 1, 2022; median follow-up of 18.4 months

*Denotes statistical significance.

Source: Albiges L. et al. Abstract LBA88, ESMO 2023

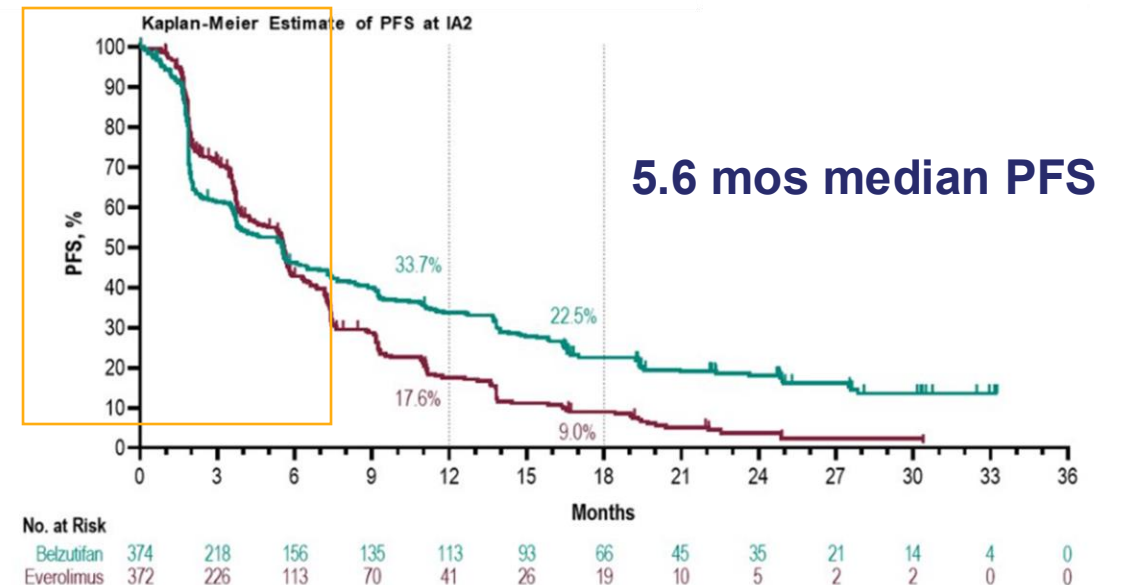
a. Insufficient data for response assessment per RECIST 1.1.

b. No post-baseline assessment available.

3L: third-line; belz: belzutifan; BICR: blinded independent central review; CI: confidence interval; CR: complete response; ccRCC: clear cell renal cell carcinoma; CI: confidence interval; HR: hazard ratio; IA1: first interim analysis; IA2: second interim analysis; mo: month; mos: months; ORR: objective response rate; P: probability; PD: progressive disease; PFS: progression-free survival; PR: partial response; RECIST: Response Evaluation Criteria in Solid Tumors; SD: stable disease; SOC: standard of care

Median PFS / Hazard Ratio

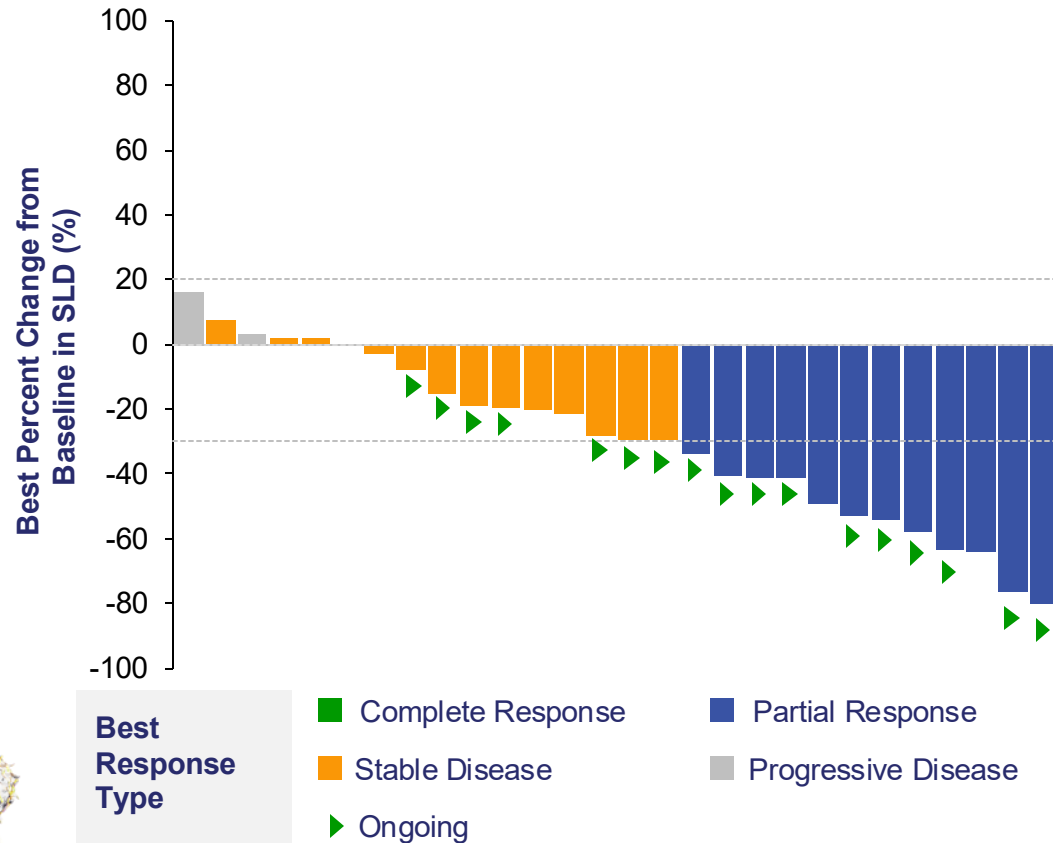
	IA1		IA2	
	Belzutifan	Everolimus	Belzutifan	Everolimus
Events	257 (68.7%)	262 (70.4%)	289 (77.3%)	276 (74.2%)
Median, mo (95% CI)	5.6 (3.9-7.0)	5.6 (4.8-5.8)	5.6 (3.8-6.5)	5.6 (4.8-5.8)
HR (95% CI)	0.75 (0.63-0.90); P <.001*		0.74 (0.63-0.88)	



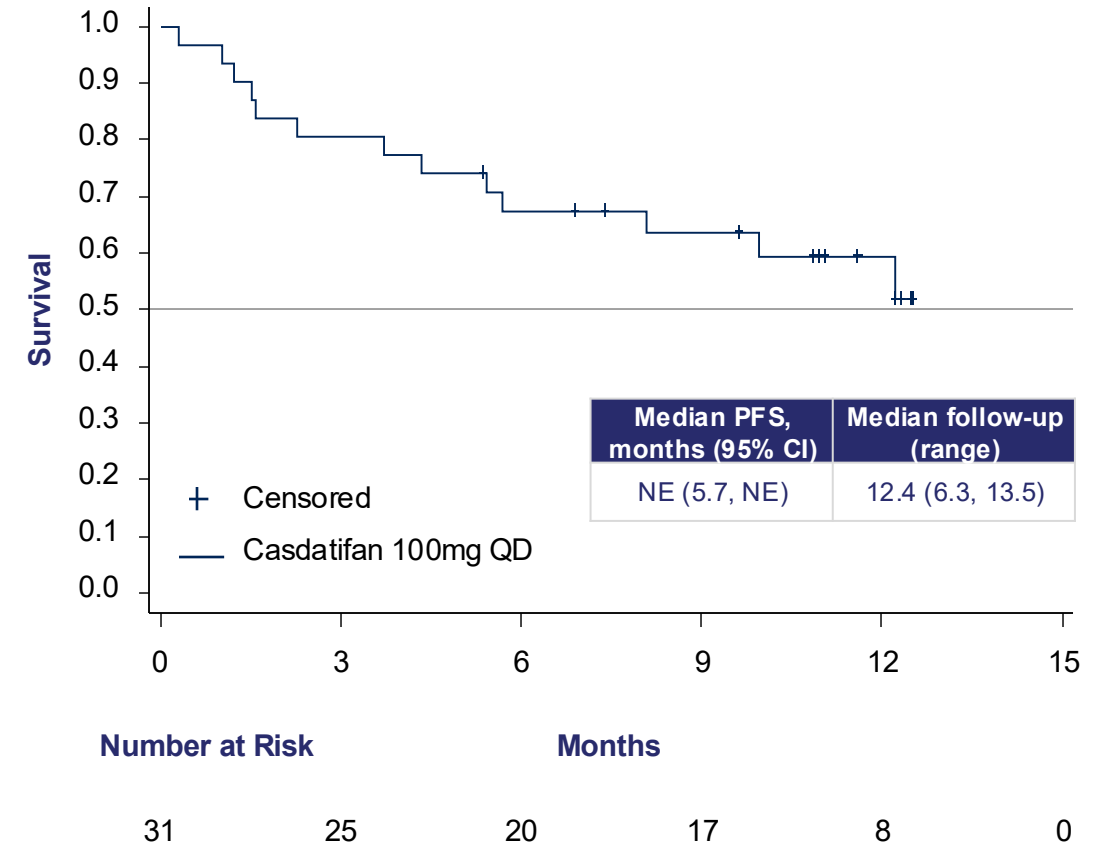
Casdatifan Data Position it to Become an Important Therapeutic Option for Patients

WATERFALL PLOT (100MG QD COHORT)

$n = 31$, cORR: 35% / uORR: 42%*



PFS K-M CURVE (100MG QD COHORT)



Median PFS of >12 months has never been seen before in a late-line refractory population

DCO date: August 15, 2025

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

CI: confidence interval; DCO: data cut-off; K-M: Kaplan-Meier; NE: not estimable; PFS: progression-free survival; QD: once daily; SLD: sum of lesion diameter

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With a 12+ Month PFS, Casdatifan Exceeds All PFS Benchmarks for Monotherapy

Earlier-line patient populations

TRIAL	TRIAL RECRUITMENT COMPLETION YEAR	PATIENT POPULATION	TRIAL DESIGN	cORR	mPFS
ARC-20 (Phase 1b/2)	2025	PDx/TKI Experienced ccRCC (mostly 3L+)	Cas (Pooled) Cas (100mg QD)	31% 35%	12.2m Not reached
TIVO-3 (Phase 3) ¹	2017	3L-4L TKI Experienced ccRCC	Tivozanib vs. sorafenib	18% vs. 8%	5.6m vs. 3.9m
LITESPARK-005 (Phase 3) ²	2022	PDx/TKI Experienced ccRCC (mostly 3L-4L)	Belz vs. everolimus	22% vs. 4%	5.6m vs 5.6m
RECORD-1 (Phase 3) ³	2007	ccRCC with prior sunitinib and/or sorafenib (mostly 3L+)	Everolimus + BSC vs placebo + BSC	2% vs. 0%	4.9m vs. 1.9m
METEOR (Phase 3) ⁴	2014	2L+ TKI Experienced ccRCC (mostly 2L)	Cabo vs everolimus	17% vs. 3%	7.4m vs. 3.9m
Lenva + ev (Phase 2) ⁵	2013	2L TKI Experienced ccRCC	Lenva + everolimus vs. Lenva vs. everolimus	43% vs. 27% vs 6%	14.6m vs. 7.4m vs. 5.5m
AXIS (Phase 3) ⁶	2010	2L ccRCC	Axitinib vs sorafenib	19% vs. 9.9%	6.7m vs. 4.7m
CONTACT-03 (Phase 3) ⁷	2021	PDx Experienced ccRCC (did <u>not</u> require prior TKI)	Atezo + cabo vs. cabo	41% vs. 41%	10.6m vs. 10.8m
CANTATA ⁸	2019	PDx Experienced ccRCC (did <u>not</u> require prior TKI)	Tela + cabo vs. cabo	31% vs 28%	9.2m vs. 9.3m

DCO date for casdatifan: August 15, 2025

1. Rini et al 2020 (TIVO-3); 2. Choueiri et al 2024 (LS-005); 3. Motzer et al 2010 (RECORD-1); 4. Choueiri et al 2016 (METEOR); 5. Motzer et al 2015 (lenva + everolimus); 6. Rini et al 2011 (AXIS); 7. Pal et al 2023 (CONTACT-03); 8. Tannir et al 2022 (CANTATA)

Data 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; 3L: third-line; 4L: fourth-line; atezo: atezolizumab; belz: belzutifan; BSC: Biopharmaceutics Classification System; cabo: cabozantinib; cas: casdatifan; cORR: confirmed overall response rate; ccRCC: clear cell renal cell carcinoma; IDCO: data cut-off; lenva: lenvatinib; m: months; mPFS: median progression-free survival; PFS: progression-free survival; tela: telegenastat; TKI: tyrosine kinase inhibitor

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Avoiding Overlapping Toxicity is Key and Positions Casdatifan as the Optimal Combination Partner

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

Checkmate-9ER (cabo + nivo): increases in hepatitis, diarrhea, endocrinopathies

cabo: cabozantinib; CTLA-4: cytotoxic T-lymphocyte antigen 4; nivo: nivolumab; PD-1: programmed cell death protein 1; PPE: palmar-plantar erythrodysesthesia; TKI: tyrosine kinase inhibitor

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PEAK-1 Is Evaluating Cas On Top of the Most Widely Used TKI, Cabozantinib

Cabo Monotherapy is the Gold Standard in IO-Experienced ccRCC

- ✓ Easy to titrate
(60mg=>40mg=>20mg)¹
- ✓ Significant experience with managing cabo-related toxicities
- ✓ Multiple registrational studies and substantial data support cabo's use in 1L and 2L ccRCC
- ✓ >2x greater usage than lenvatinib in the U.S.², 10x greater usage in certain ex-US countries

Opportunity to Improve Upon Cabo Monotherapy

PHASE 3 TRIAL	STUDY ARMS	N	MEDIAN PFS FOR CABO MONO
CONTACT-03³	atezo + cabo vs. cabo	263 vs. 259	10.8m
METEOR⁴	cabo vs. everolimus	320 vs. 328	7.4m
CANTATA⁵	Telaglena- stat + cabo vs. cabo	221 vs. 223	9.3m

1. Welireg package insert

2. MIDAS, Arcus primary research

3. Pal et al 2023

4. Choueiri et al 2016

5. Tannir et al 2022

1L: first-line; 2L: second-line; AE: adverse events; atezo: atezolizumab; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; lenva: lenvatinib; m: months; mono: monotherapy; mPFS: median progression-free survival; nivo: nivolumab; PD-1: programmed cell death protein 1; PFS: progression-free survival; tivo: tivozanib; TKI: tyrosine kinase inhibitor

Targeting the IO-Experienced ccRCC Patient Population, Including Patients Who Progress after Adjuvant Therapy

PATIENT POPULATION:

- Unresectable, locally advanced or metastatic ccRCC
- Measurable disease per RECIST 1.1
- Have had prior anti-PD-1/PD-L1 (either in adjuvant or 1L metastatic setting)
- Have not received cabozantinib
- HIF-2 α -inhibitor naïve

STRATIFICATION FACTORS:

- IMDC Risk Score
- Prior VEGF
- Region

N~700

R
2:1

100mg CASDATIFAN +
CABOZANTINIB

PLACEBO + CABOZANTINIB

PRIMARY ENDPOINT:

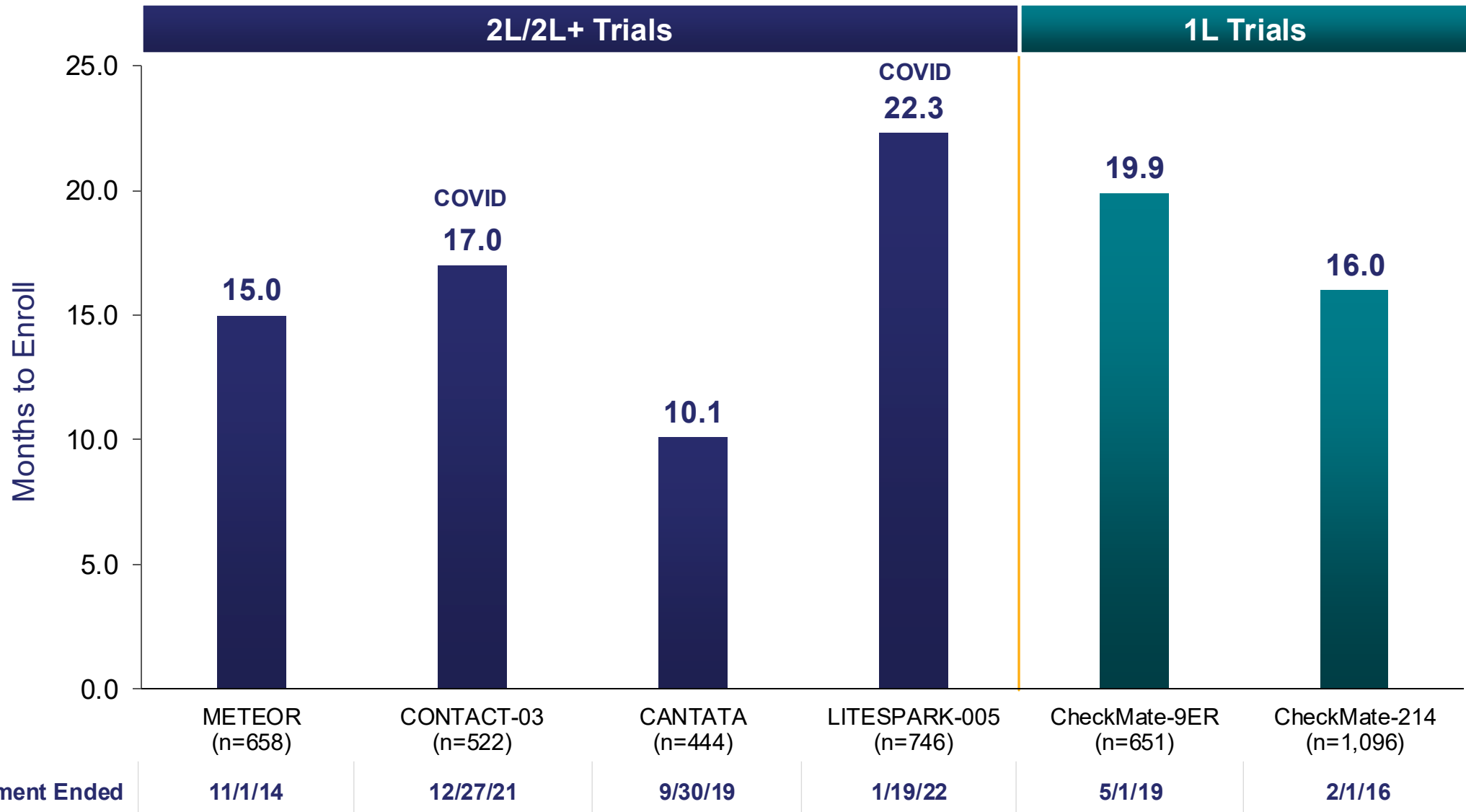
- PFS

KEY SECONDARY ENDPOINTS:

- OS
- ORR, DOR, DCR

PEAK-1 is Currently Enrolling

RCC Studies Have Historically Enrolled Quickly, Which Bodes Well for PEAK-1



Source: Study Publications

1L: first-line; 2L: second-line; EPO: Erythropoietin; RCC: renal cell carcinoma

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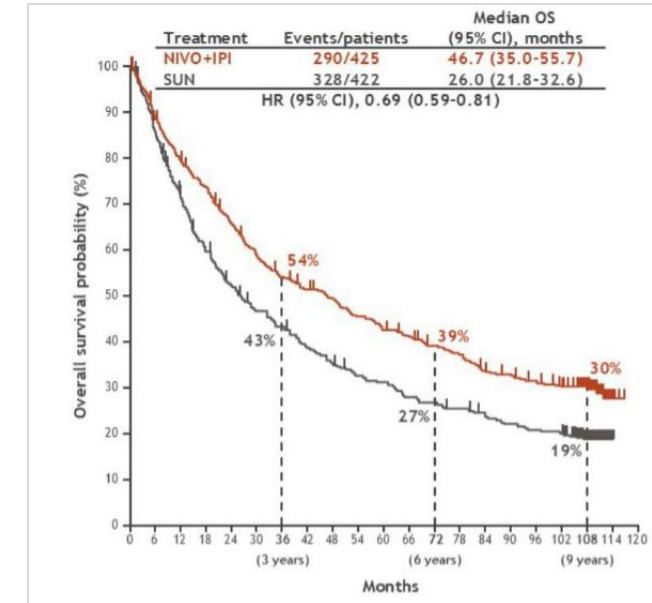
Opportunity for Durable Remission With a TKI-Free Regimen in 1L ccRCC

Opportunity for Cas + Volru

- ✓ Anti-PD-1 / anti-CTLA-4 (ipi + nivo) is the most widely used regimen in 1L ccRCC, particularly in the academic setting
- ✓ Best opportunity for patients to achieve durable remission, and enables patients to avoid TKIs in the 1L
- ✓ Greatest liability of nivo-ipi is its high rate of primary progression and shorter PFS relative to anti-PD-1 + TKI
- ✓ **Cas has the potential to reduce this high rate of PD and improve PFS with minimal added toxicity**

Ipi + Nivo Results in Long OS in Patients that Respond to Treatment

OS in Intermediate/Poor Risk¹



PATIENTS WITH INTERMEDIATE/POOR IMDC RISK	IPI + NIVO (N=422)	SUNITINIB (N=422)
mPFS ¹ , mos.	12.4	8.5
cORR ² , %	42%	27%
Progressive disease ² , %	20%	17%

1. Choueiri, et al. ASCO 2025.

2. Motzer et al, NEJM 2018.

1L: first-line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; cORR: confirmed overall response rate; CTLA-4: cytotoxic T-lymphocyte antigen 4; CI: confidence interval; IMDC: International Metastatic RCC Database Consortium; ipi: ipilimumab; mos: months; mPFS: median progression-free survival; nivo: nivolumab; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PD-1: programmed cell death protein 1; TKI: tyrosine kinase inhibitor; volru: volrustomig

eVOLVE-RCC02: Seamless Phase 1b/3 Design to Evaluate Cas + Volru in 1L Advanced ccRCC

PHASE 1B

PHASE 3

PATIENT POPULATION:

- Advanced ccRCC
- No prior systemic therapy for a/m RCC

R
1:1

ARM 1A
volrustomig + casdatifan

ARM 1B
volrustomig + casdatifan

PRIMARY ENDPOINT:

- Safety

SECONDARY ENDPOINTS:

- ORR, DOR, PFS, DCR

R
1:1:1

ARM 3A
volrustomig + casdatifan

ARM 3B
volrustomig monotherapy

ARM 3C (SOC)
nivolumab + ipilimumab

PRIMARY ENDPOINTS:

- PFS
- OS

KEY SECONDARY ENDPOINTS:

- ORR, DOR

Sponsored by AstraZeneca | Phase 1b Is Currently Enrolling

Cas Is Also Being Evaluated in Other Early-Line Settings

EARLIER STAGE DISEASE

Neadjuvant ccRCC casdatifan + zimberelimab

- Improve outcomes of nephrectomy in patients with high-risk tumors
- Prolong event-free survival

NeoSHIFT IST
(Toni Chouieri)

1L ccRCC casdatifan + zimberelimab

- Displace TKI use in 1L
- Reduce number of agents used in combination to minimize toxicity

ARC-20 Cohort

Favorable-risk 1L ccRCC casdatifan mono

- ~25% of 1L ccRCC
- Alternative to watchful waiting

ARC-20 Cohort

Post-IO / TKI-naïve ccRCC casdatifan mono

- Delay TKI use to later lines of therapy

ARC-20 Cohort

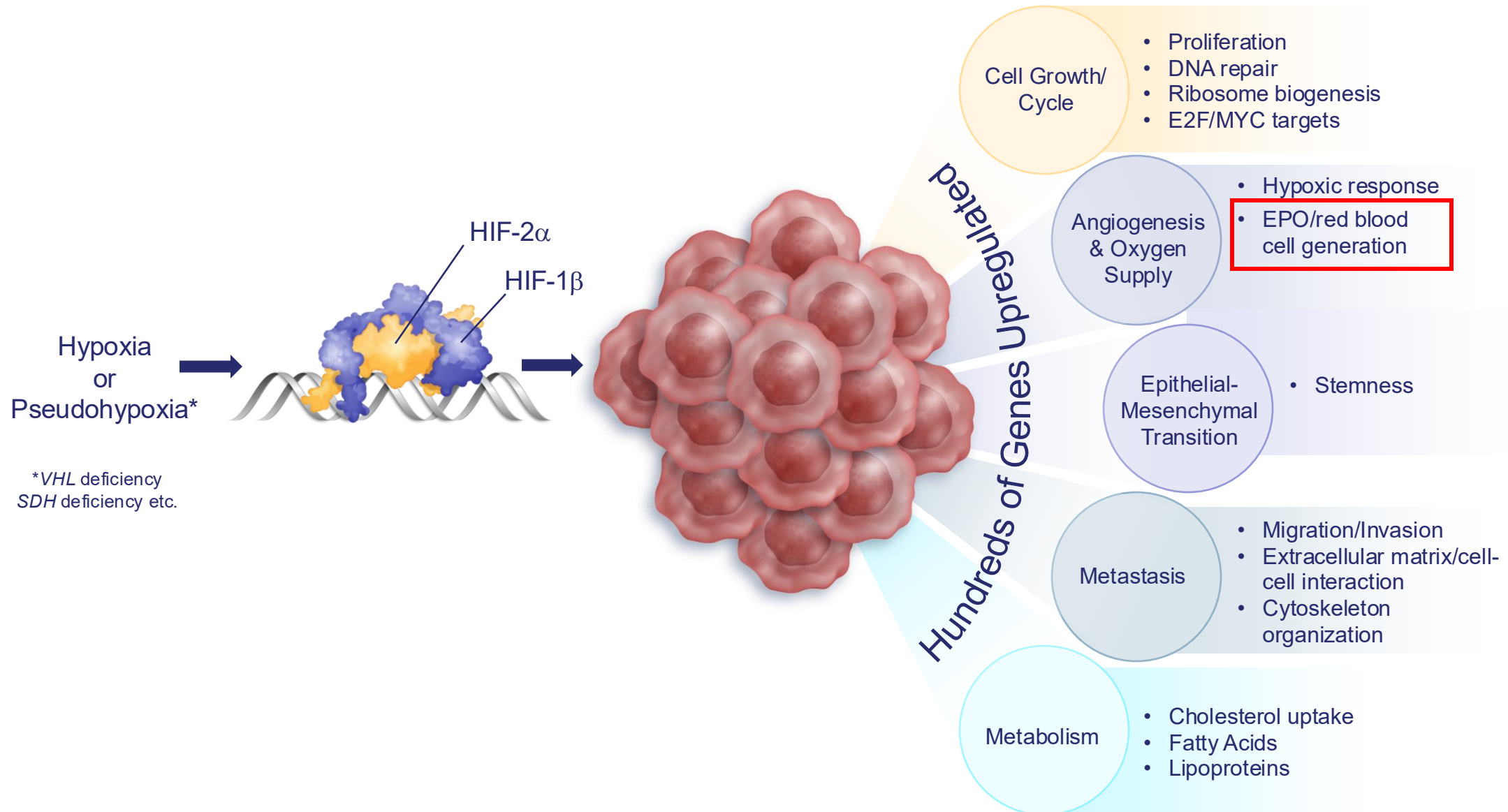
Q&A

Casdatifan Biomarker Data: Relevance of EPO Reduction to Outcomes with Casdatifan

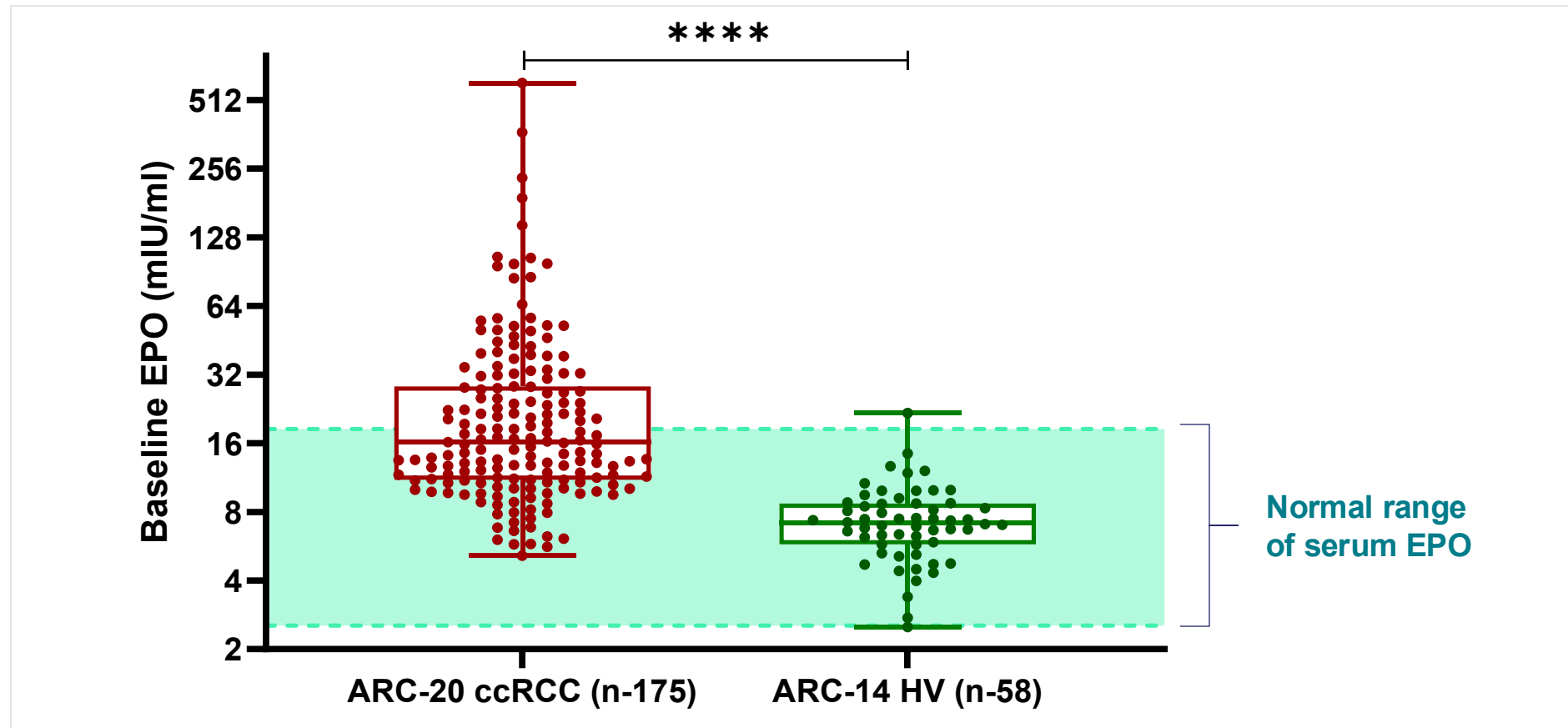
Dr. Juan Jaen

President, Arcus Biosciences

The Abundance of Erythropoietin (EPO) in Blood Makes it a Great PD Marker for Systemic HIF-2 α Activity



ccRCC Patients in ARC-20 Had Higher Baseline Levels of Serum EPO (sEPO) Compared to Healthy Volunteers



Based on available evidence, we believe that tumor lesions may be the source of some of the sEPO detected in ccRCC patients

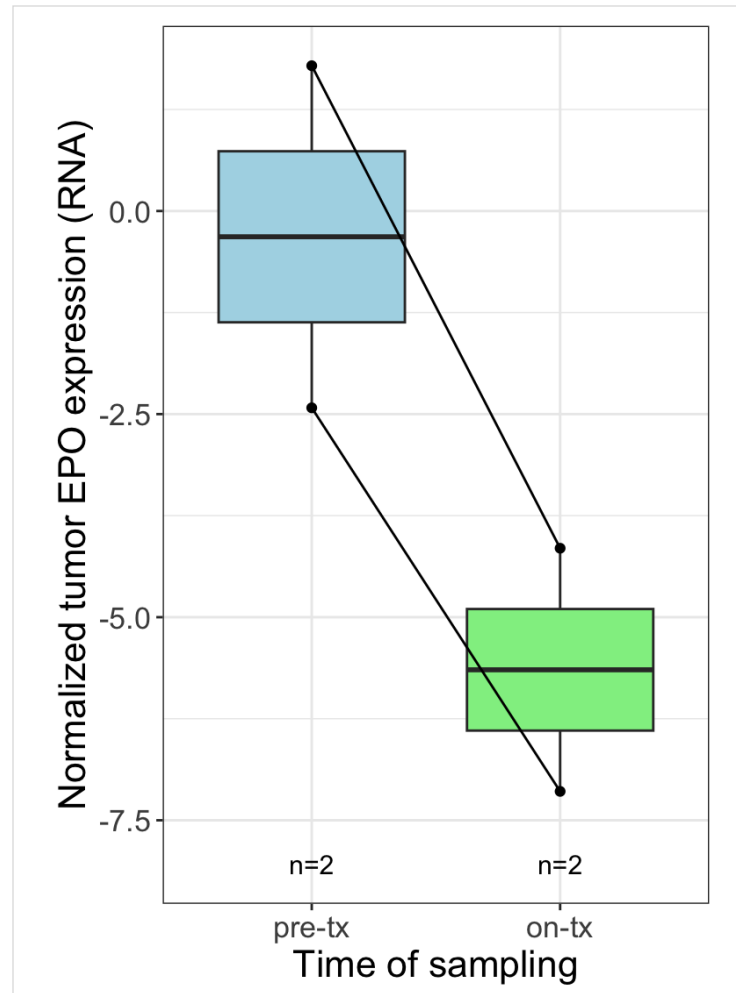
Source: EPO data obtained from ARC-20 ccRCC patients and ARC-14 healthy volunteers. Statistical comparisons between both groups performed using Wilcoxon ranked-sum test, ****p<0.0001.

ccRCC: clear cell renal cell carcinoma; EPO: erythropoietin; HV: healthy volunteer; mIU/ml: milli-international units per milliliter

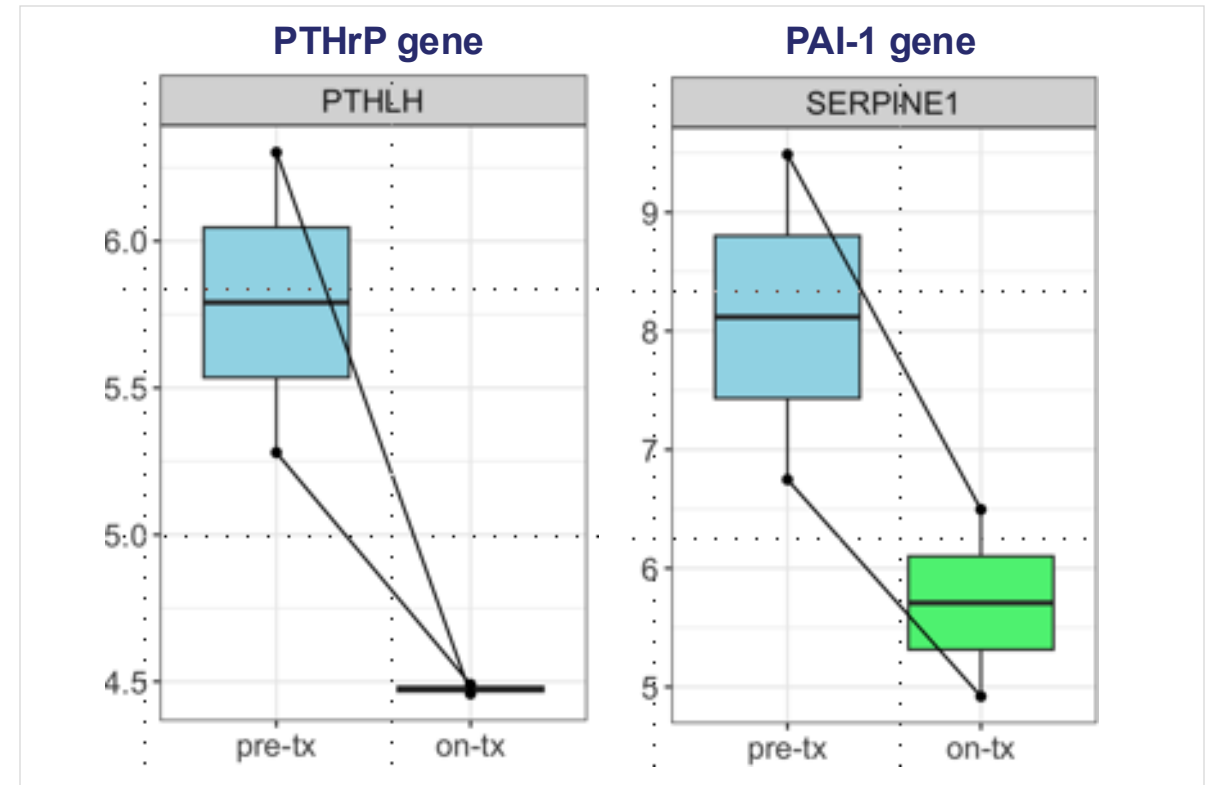
© Arcus Biosciences 2025

Casdatifan Results in Significantly Decreased Expression of *EPO* and Other Known HIF-2 α Dependent Target Genes in the Tumor

Tumor *EPO* expression down >20x On-Tx

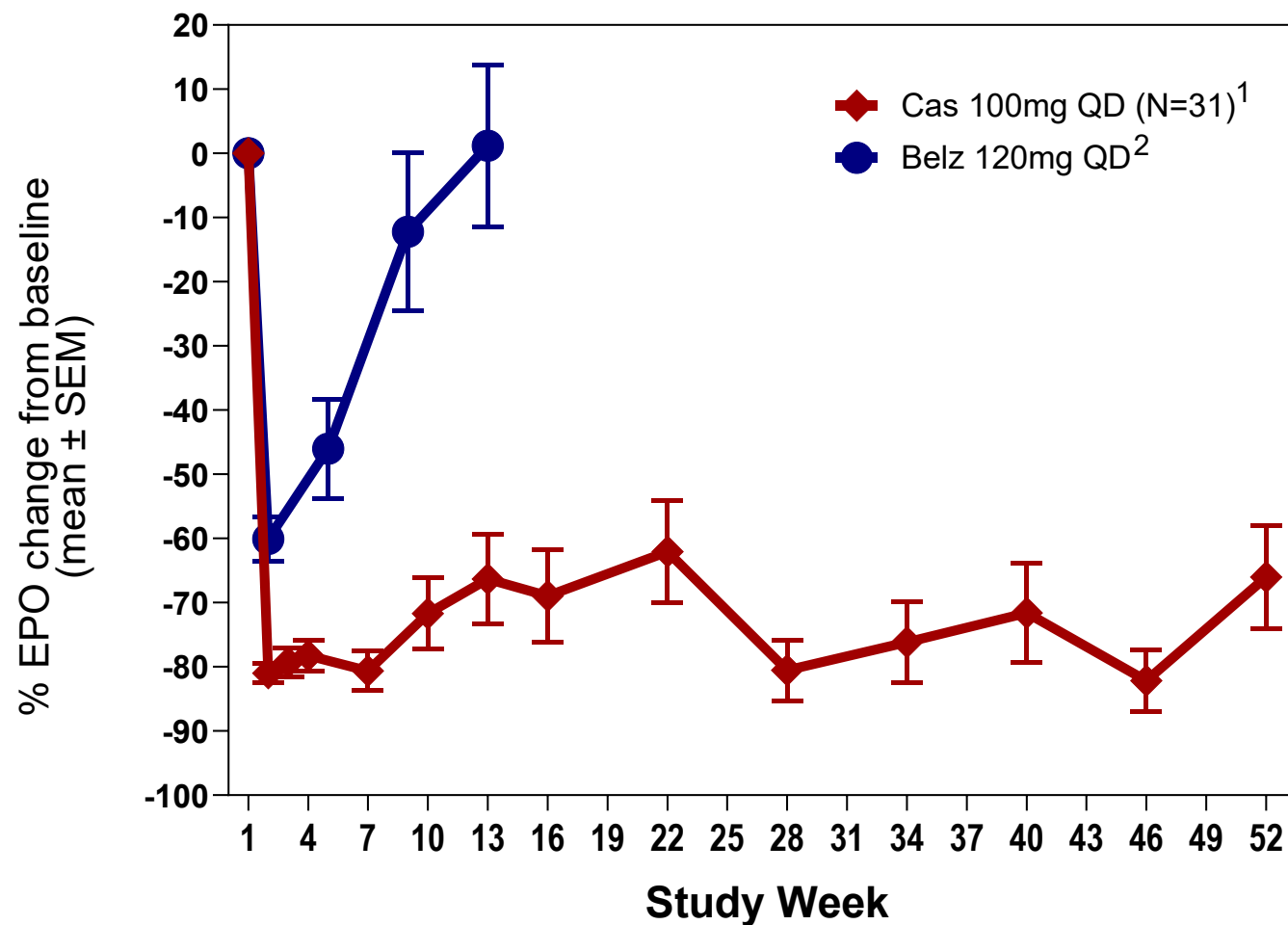


Known HIF-2 α target genes decreased On-Tx



- Archival baseline samples; on-treatment samples 14-20 days after initiation of cas therapy
- 83-85% maximal decrease in sEPO seen in both subjects

Cas Demonstrates Deeper and More Durable sEPO Reduction than Belz



1. EPO data for casdatifan obtained from ARC-20 ccRCC patients on casdatifan monotherapy, as of 8/15/25. Samples taken within 28 days post-ESA use or from subjects that received less than 50% of their assigned casdatifan dose during the previous 4 days were excluded from analysis; Data with incomplete medical records are excluded; Max individuals EPO decrease with casdatifan 100mg QD ranged from 47% to 99%.

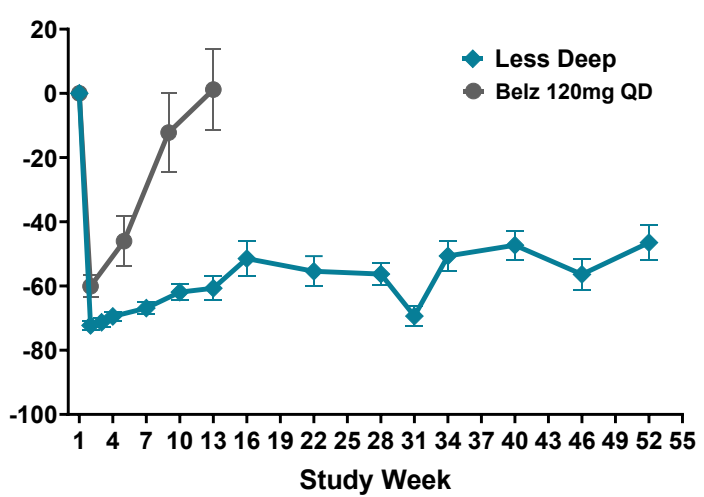
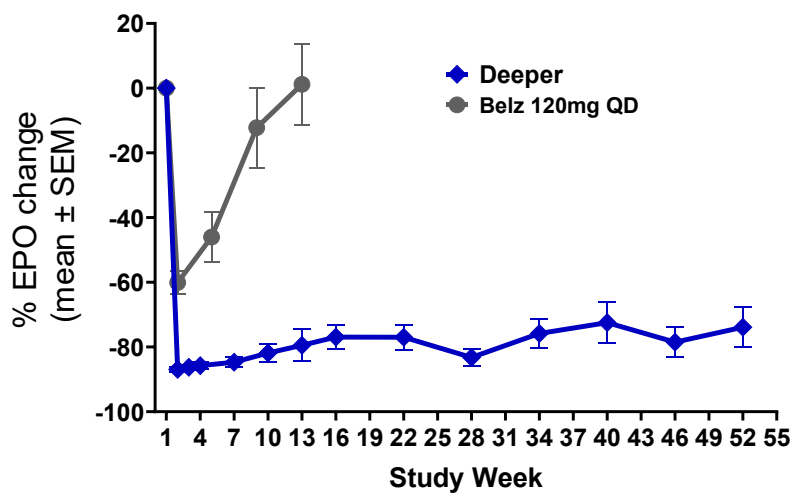
2. Belzutifan data from Marathe DD, J Clin Pharm 2024, Table S3. The error bars for belzutifan represent 90% CI.

belz: belzutifan; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; CI: confidence interval; ESA: erythropoiesis-stimulating agent; EPO: erythropoietin; QD: once daily; SEM: standard error of the mean; sEPO: serum of erythropoietin

The Ability of Casdatifan to Achieve Maximal and Sustained HIF-2α Inhibition (as Reflected by sEPO Changes) Leads to Superior Clinical Efficacy in ARC-20

Patients Segregated into 2 Groups Based on Median best EPO Reduction (-85%) from Baseline

	sEPO Reduction Deeper (n=65)		sEPO Reduction Less Deep (n=64)	
	% (95% CI)	n	% (95% CI)	n
cORR*	44.6% (32.3, 57.5)	29	20.3% (11.3, 32.2)	13
PD	9.2% (3.5, 19.0)	6	26.6% (16.3, 39.1)	17



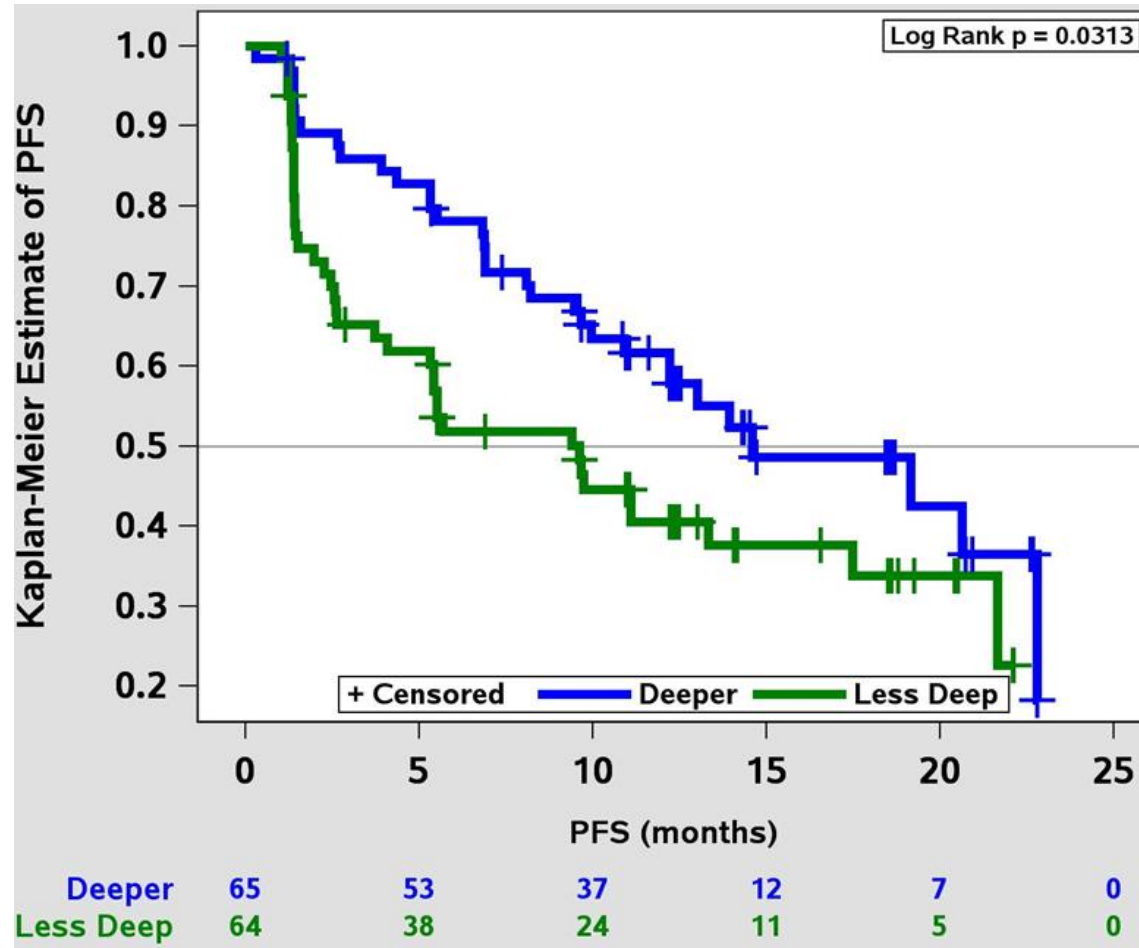
*For the biomarker analysis, there were 42 confirmed responses because the analysis included 8 ccRCC patients from the dose-escalation cohorts of ARC-20 in addition to the 121 patients from the dose-expansion cohorts.

Sources: EPO data for casdatifan obtained from all ARC-20 ccRCC patients on casdatifan monotherapy, as of 8/15/25. Samples taken within 28 days post-ESA use or from subjects that received less than 50% of their assigned casdatifan dose during the previous 4 days were excluded from analysis; Data with incomplete medical records are excluded; Max individual sEPO decrease with casdatifan 100mg QD ranged from 47% to 99%. Belzutifan data from Marathe DD, J Clin Pharm 2024, Table S3. The error bars for belzutifan represent 90% CI.

belz: belzutifan; ccRCC: clear cell renal cell carcinoma CI: confidence interval; CR: confirmed response; EPO: erythropoietin; PD: progressive disease; PR: partial response; QD: once daily; SD: stable disease; SEM: standard error of the mean; EPO: serum of erythropoietin

Extent of sEPO Suppression by Cas Monotherapy is Also Highly Correlated With PFS

Patients Segregated into 2 Groups Based on Median best EPO Reduction (-85%) from Baseline



Best EPO suppression	N	mPFS in months (95% CI)	HR (95% CI) Deeper vs Less Deep
Deeper	65	14.6 (10.9, 22.8)	0.60 (0.37, 0.96)
Less Deep	64	9.6 (4.1, 17.5)	

Sources: EPO data for casdatifan obtained from all ARC-20 ccRCC patients on casdatifan monotherapy, as of 8/15/25. Samples taken within 28 days post-ESA use or from subjects that received less than 50% of their assigned casdatifan dose during the previous 4 days were excluded from analysis; Data with incomplete medical records are excluded; Max individual sEPO decrease with casdatifan 100mg QD ranged from 47% to 99%.

Cas: casdatifan; CI: confidence interval; EPO: erythropoietin; PD: progressive disease; PR: partial response; QD: once daily; SD: stable disease; SEM: standard error of the mean; sEPO: serum of erythropoietin

Key Observations from the EPO Data

- Serum EPO (**sEPO**) is a good marker for HIF-2 α activity in ccRCC tumors
- There is a **strong relationship between sEPO reduction and clinical responses** (rate of primary resistance, ORR, and PFS), **demonstrating the relevance of maximal EPO suppression as a marker of drug impact on tumor HIF-2 α**
- The ability of **casdatifan to hit its target harder** may explain its clinical efficacy profile as **a potential best-in-class HIF-2 α inhibitor**



Panel Conversation

Dr. Bill Kaelin, Dana-Farber Cancer Institute

Dr. Juan Jaen, President, Arcus Biosciences

William Kaelin, MD



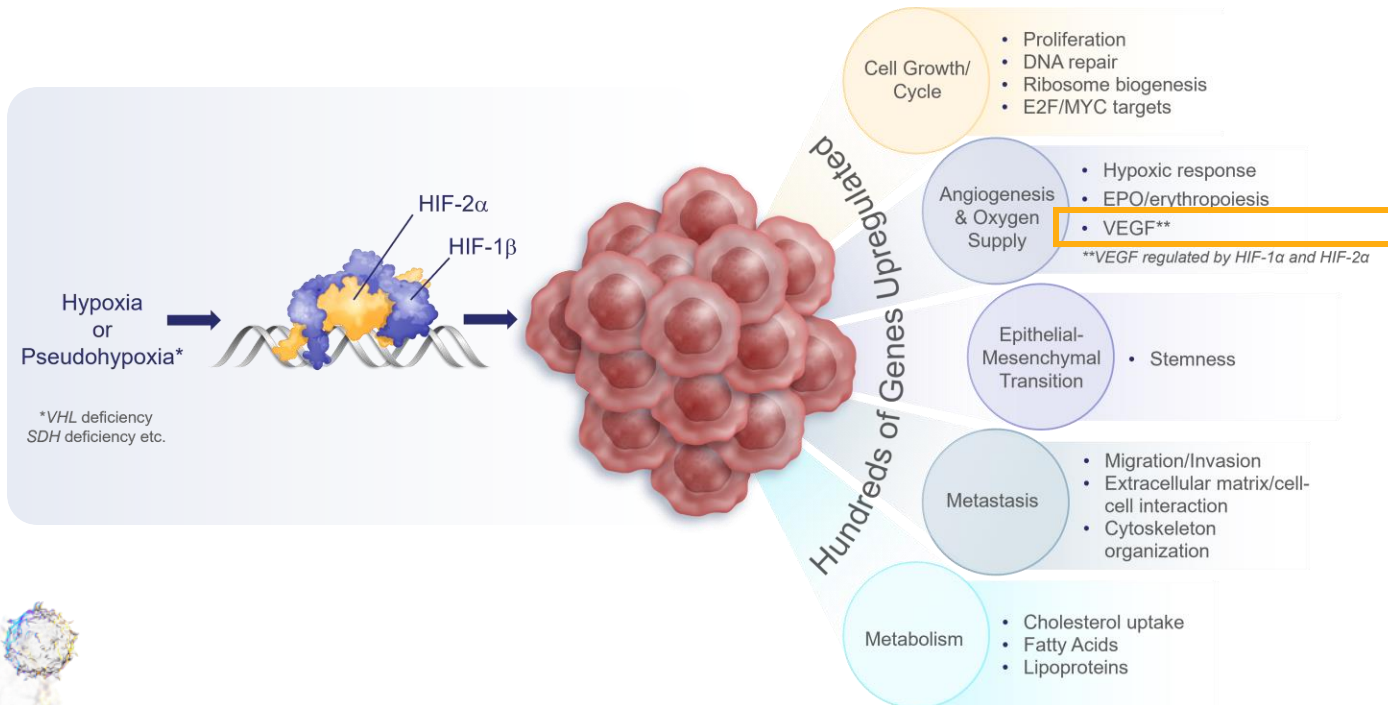
Bill Kaelin

Sidney Farber Professor of Medicine at Dana-Farber Cancer Institute, professor at Harvard Medical School and senior physician scientist at Brigham and Women's Hospital

- 2019 Nobel Laureate in Physiology or Medicine for his discoveries on the molecular role of VHL and HIF in how cells sense and adapt to oxygen availability
- Served on the National Cancer Institute Board of Scientific Advisors, the AACR Board of Trustees, and the IOM National Cancer Policy Board
- Winner of the Paul Marks Prize for cancer research from the Memorial Sloan-Kettering Cancer Center and the Richard and Hinda Rosenthal Prize from the AACR
- Recipient of the prestigious Canada Gairdner International Award
- 2016 winner of the Albert Lasker Basic Medical Research Award
- Elected to National Academy of Sciences

Opportunity for HIF-2 α Inhibition to be Combined With Other Mechanisms

HIF-2 α activates multiple pathways involved in tumorigenesis, in addition to VEGF



Rationale for HIF-2 α -based Regimens in ccRCC

Cas-Based Regimen	Rationale
Cas + VEGFR-TKI	• Largely orthogonal /complementary biologies; • Supportive early data from competitor
Cas + IO	• Early evidence that high HIF-2α signaling correlates with diminished benefit from PDx ($\pm$CTLA-4) therapy
Monotherapy (early and advanced settings)	• Dependence on HIF-2α remains throughout tumor evolution



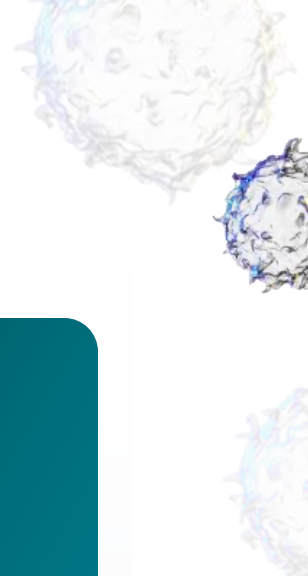
Break

The background is a solid dark blue. Scattered across the slide are several stylized, glowing virus particles. These particles are spherical with a textured, almost crystalline surface. Some particles have a bright yellow or orange core, while others are more translucent. The particles are positioned in the corners and along the edges, creating a sense of depth and scientific focus.

Casdatifan Development Strategy

Dr. Richard Markus
CMO, Arcus Biosciences

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



PATIENT POPULATION:

- Unresectable, locally advanced or metastatic ccRCC
- Measurable disease per RECIST 1.1
- Have had prior anti-PD-1/PD-L1 (either in adjuvant or 1L metastatic setting)
- Have not received cabozantinib
- HIF-2 α -inhibitor naïve

STRATIFICATION FACTORS:

- IMDC Risk Score
- Prior VEGF
- Region

N~700

R
2:1

100mg CASDATIFAN +
CABOZANTINIB

PLACEBO + CABOZANTINIB

PRIMARY ENDPOINT:

- PFS

KEY SECONDARY ENDPOINTS:

- OS
- ORR, DOR, DCR

PEAK-1 is Currently Enrolling

Data Presented at ASCO from the Cas + Cabo Cohort Provide Strong Validation for PEA-1

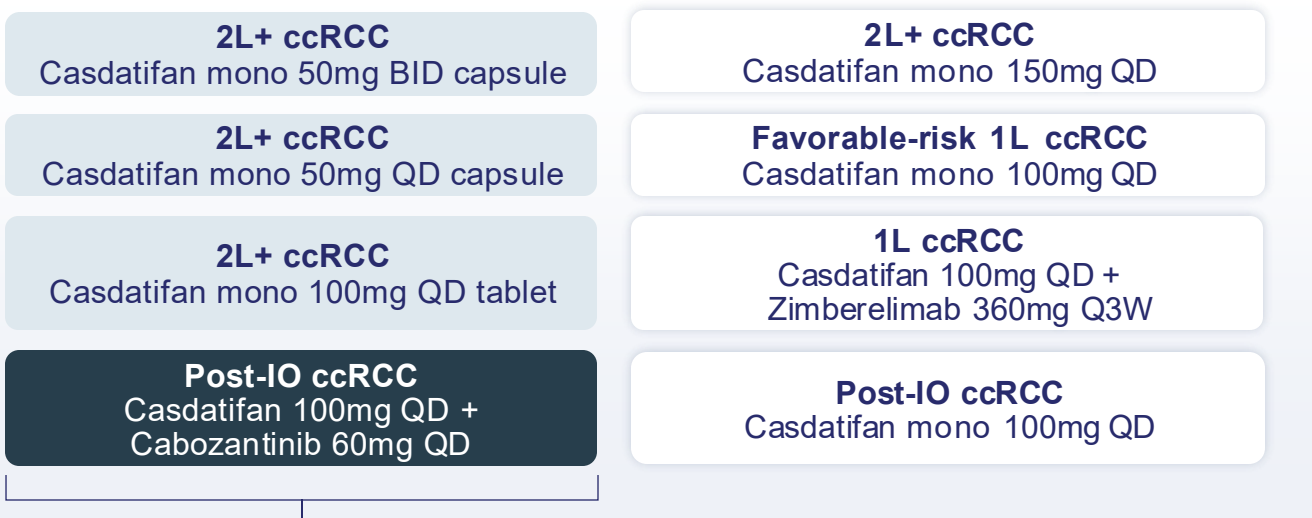
DOSE ESCALATION

Patients with advanced solid tumors
Casdatifan monotherapy



DOSE EXPANSION

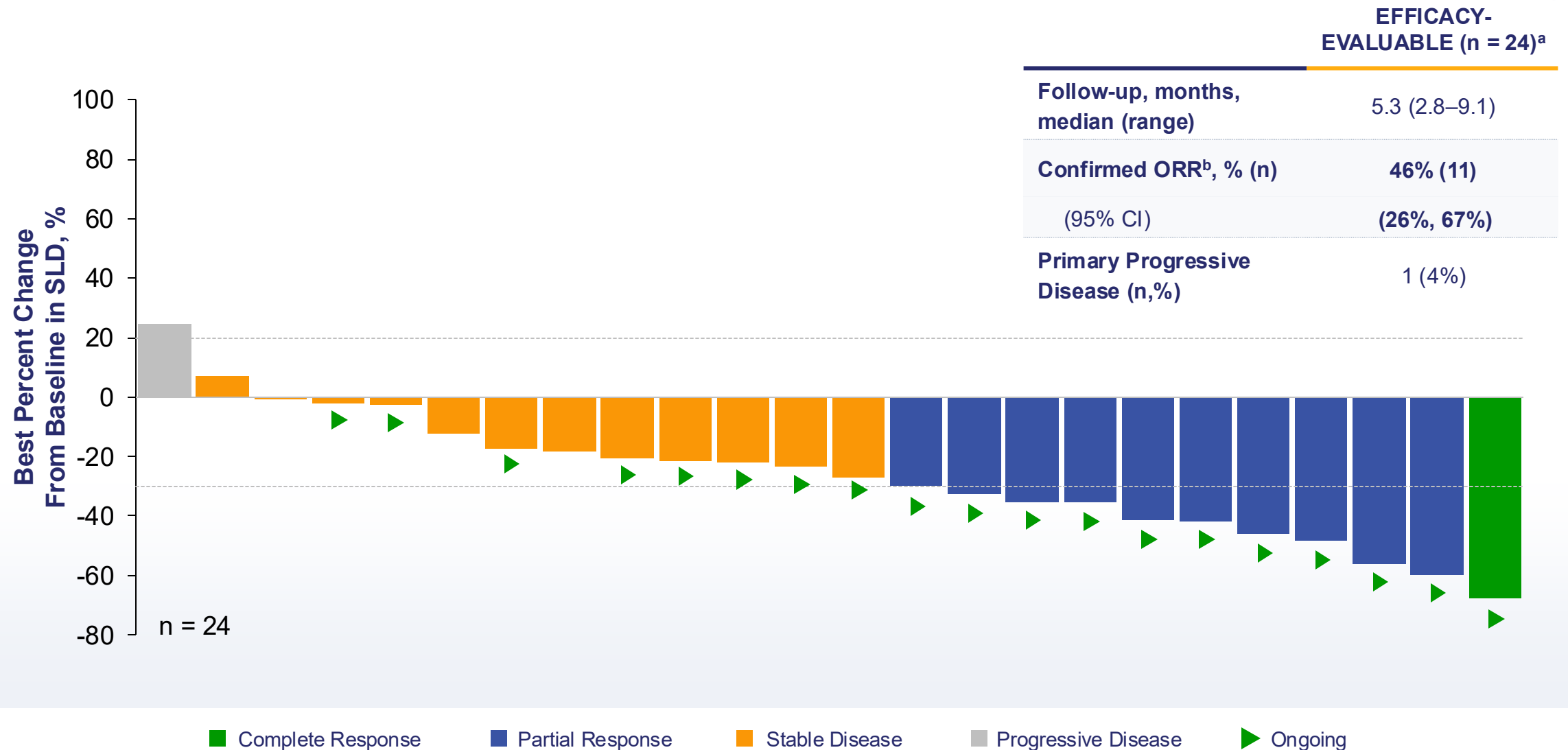
N = ~30 per cohort, except cas + cabo (n=45)



At the March 14 data cut-off:

- **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)

Almost All Cas + Cabo Patients Achieved Tumor Reduction^{a,b}



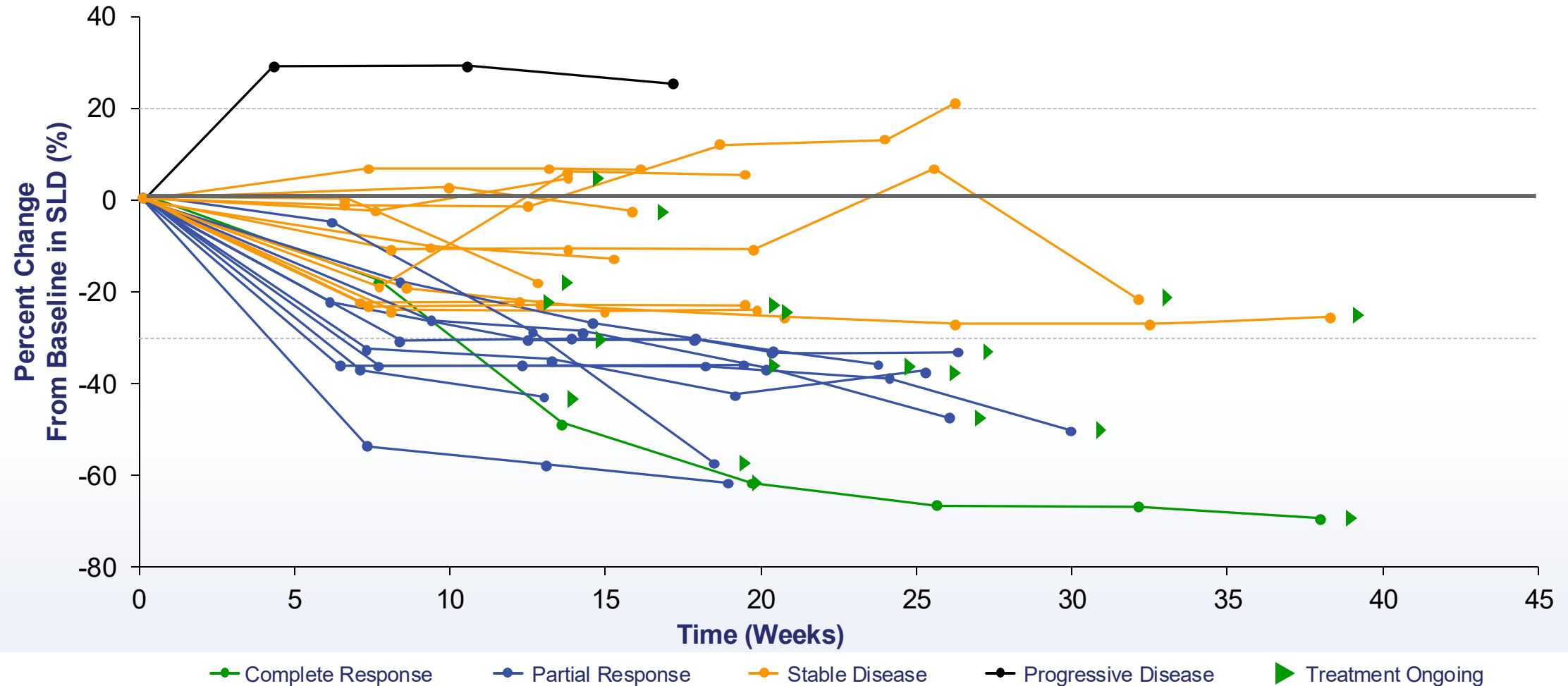
Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cut-off date: March 14, 2025.

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

^bInclusive of one patient who had confirmed PR after March 14, 2025.

Cabo: cabozantinib; cas: casdatifan; SLD: sum of lesion diameter; ORR: overall response rate

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



DCO 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.

DCO: data cut-off; ORR: overall response rate; SLD: sum of lesion diameter

Importantly, AEs Were Well Managed With Dose Reductions, With Very Few Discontinuations

Overlapping toxicities were also minimal which is key when combining two anti-cancer drugs

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

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

^aSafety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cut-off date.

^bTreatment-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.

DCO: data cut-off; TEAE: treatment-emergent adverse event

eVOLVE-RCC02: Seamless Phase 1b/3 Design to Evaluate Cas + Volru in 1L Advanced ccRCC

PHASE 1B

PHASE 3

PATIENT POPULATION:

- Advanced ccRCC
- No prior systemic therapy for a/m RCC

R
1:1

ARM 1A

volrustomig + casdatifan

ARM 1B

volrustomig + casdatifan

PRIMARY ENDPOINT:

- Safety

SECONDARY ENDPOINTS:

- ORR, DOR, PFS, DCR

Initial data from Phase 1b
portion in 2H:26

R
1:1:1

ARM 3A

volrustomig + casdatifan

ARM 3B

volrustomig monotherapy

ARM 3C (SOC)

nivolumab + ipilimumab

PRIMARY ENDPOINTS:

- PFS
- OS

KEY SECONDARY ENDPOINTS:

- ORR, DOR

Sponsored by AstraZeneca | Phase 1b Currently Enrolling

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

EXPANSION COHORTS

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

Data presented at
ASCO GU 2025

Satisfies Project Optimus and confirmed
100mg QD tablet as the "going forward"
dose and formulation

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

1L ccRCC
casdatifan 100mg QD +
zimberelimab 360mg Q3W

Post-IO ccRCC
casdatifan mono 100mg QD

**New cohorts added to ARC-20 and designed to
inform the potential of cas in early-line settings**

Substantially More Data is Coming for Casdatifan

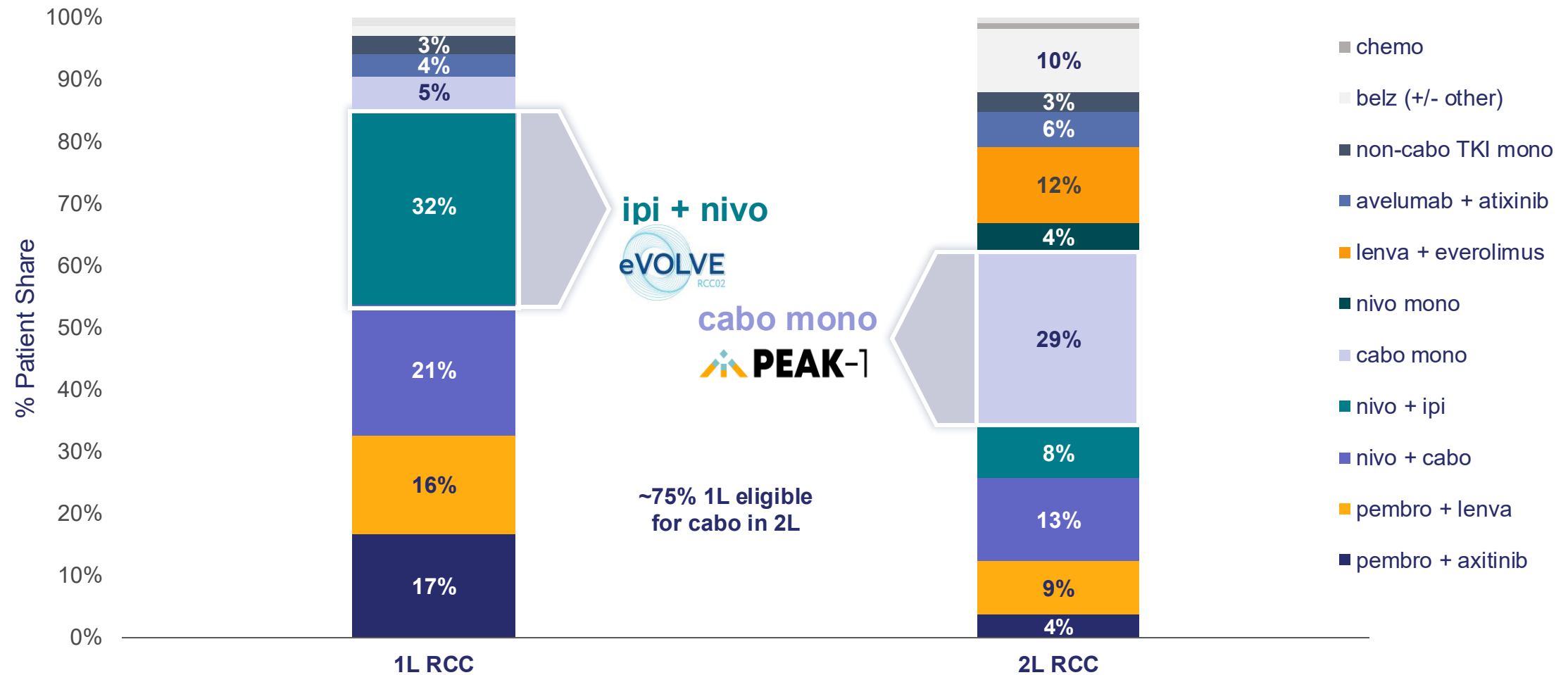
Study	Cohort	Description	Expected Timing
ARC-20	Cas mono in 2L+ ccRCC	Additional analysis	1H:2026
ARC-20	Cas + cabo in IO-experienced ccRCC	ORR, PFS data	Mid-2026
ARC-20	Cas mono in <u>IO-experienced</u> ccRCC	ORR	2H:2026
eVOLVE-RCC-002	1L ccRCC	Safety and Go / No Go Decision on Phase 3	2H:2026

Casdatifan Market Opportunity

Jennifer Jarrett
COO, Arcus Biosciences

Cas CDP Targets the Largest ccRCC Market Segments With Cabo Usage Estimated to be >2x More Than That of Lenva in 2L

2024 ccRCC | US Market Share



Source: Arcus primary research, US May 2024 (n=49)

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

Arcus is Pursuing Differentiated Combos Versus Merck

	Post-IO				
	ADJUVANT	1L (IO NAÏVE)	POST-IO ADJUVANT*	METASTATIC "IO-EXPERIENCED"	2L+
Current market share¹	pembro: 30%	IO+IO: 45% IO+TKI: 50%	N/A	TKI**: 72% HIF-2α: 15%	HIF-2α: 40%
cas combos in Phase 3		cas + volru (HIF-2α + IO + IO)	cas + cabo (HIF-2α + TKI)		
belz combos in Phase 3²	belz + pembro	belz + pembro + lenva (HIF-2α + IO + TKI)	belz + lenva (HIF-2α + TKI)		belz mono (approved)
Other belz combos (Phase 1b/2)²			belz + zanza (HIF-2α + TKI)		

1. Arcus market research, Mar 2025 (n=25, oncology respondents screened for high belzutifan use (>4+ patients in 2L+))

2. Per ct.gov *Received adjuvant pembro **Includes TKI mono, TKI+IO, and TKI+mTOR

1L: first-line; 2L: second-line; 3L: third-line or greater; belz: belzutifan; cas: casdatifan; ccRCC: clear cell renal cell carcinoma IO: immunotherapy; lenva: lenvatinib; mono: monotherapy; pembro: pembrolizumab; TKI: tyrosine kinase inhibitor

Collaboration with AZ Enables Us to Pursue the 1L Setting in a Cost- and Resource-Efficient Manner



- 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 both Phase 1b and Phase 3 portions of the study and study costs to be shared
- **Enables Arcus to target the 1L setting in a cost- and resource-efficient manner**

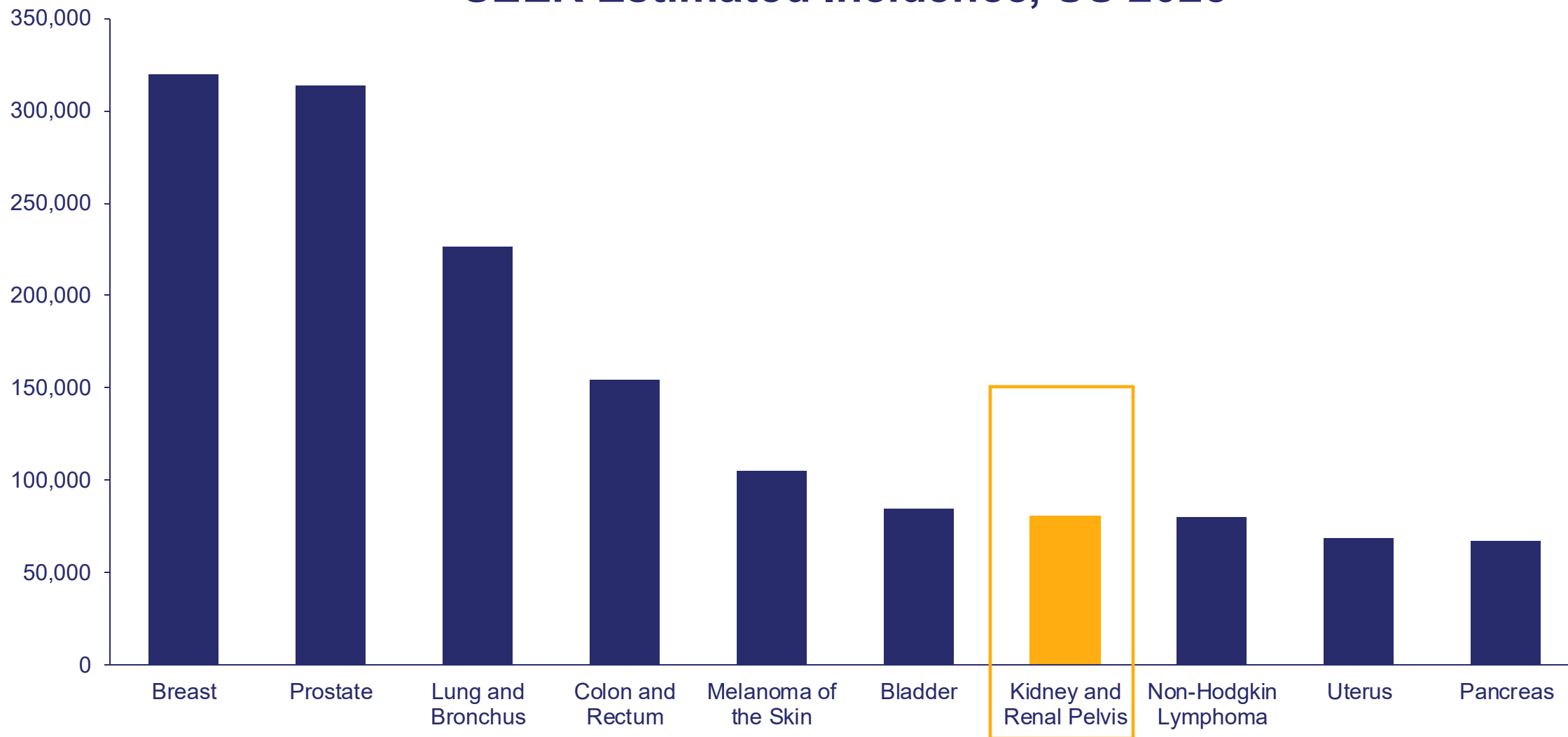


cas + volrustomig
(anti-CTLA-4/anti-PD-1 bispecific)

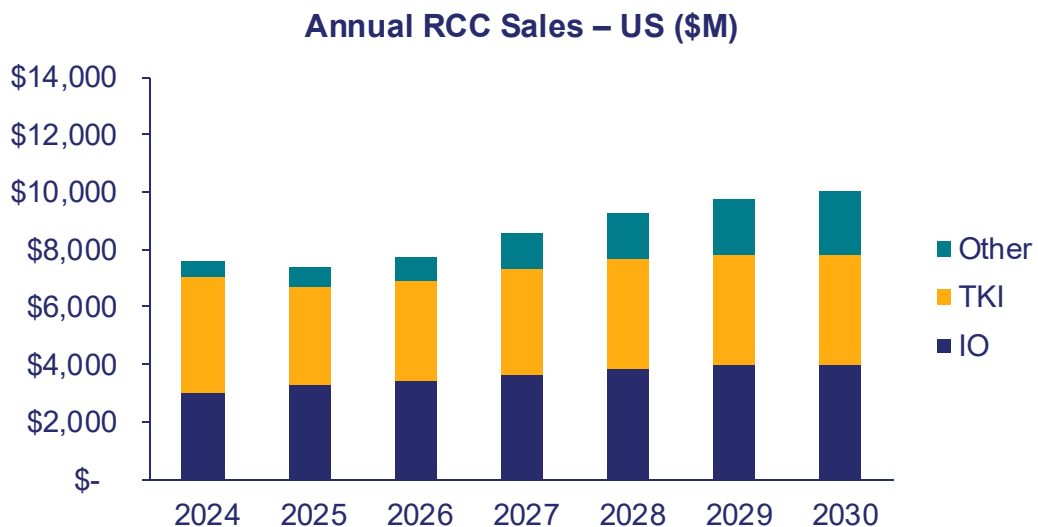
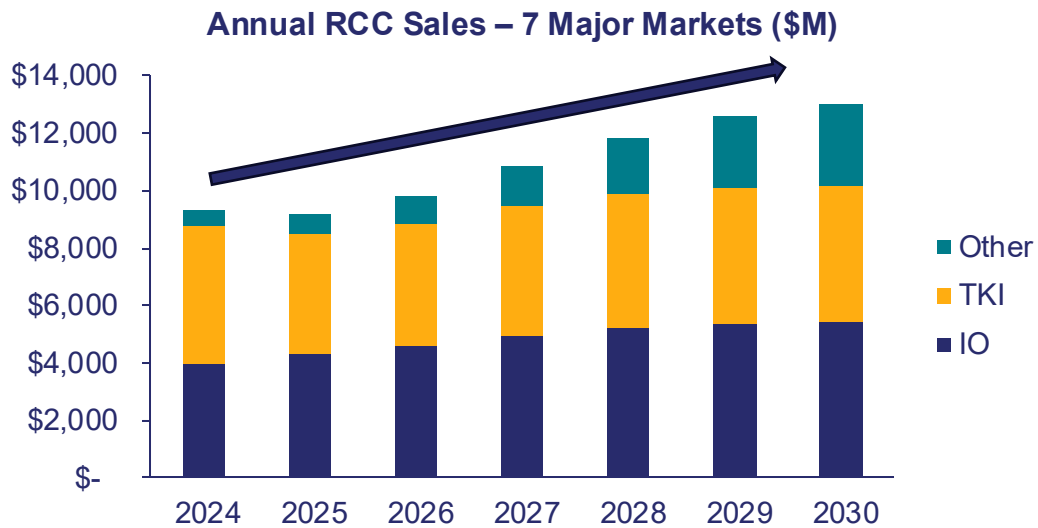
- **Utilizing a seamless Phase 1b/3 design**
- Potential first-in-class, TKI-sparing combination
- As a bi-specific, volru is enabling dual blockade of PD-1 and CTLA-4; *in vitro* data demonstrate that volru results in greater T-cell activation than ipi + nivo
- Volru has demonstrated exciting preliminary data in 1L ccRCC

RCC is One of the Largest Tumor Types

SEER Estimated Incidence, US 2025



And Is a Growing Multi-Billion Dollar Market, Driven by the Introduction of HIF-2 α Inhibition and Long DoT's



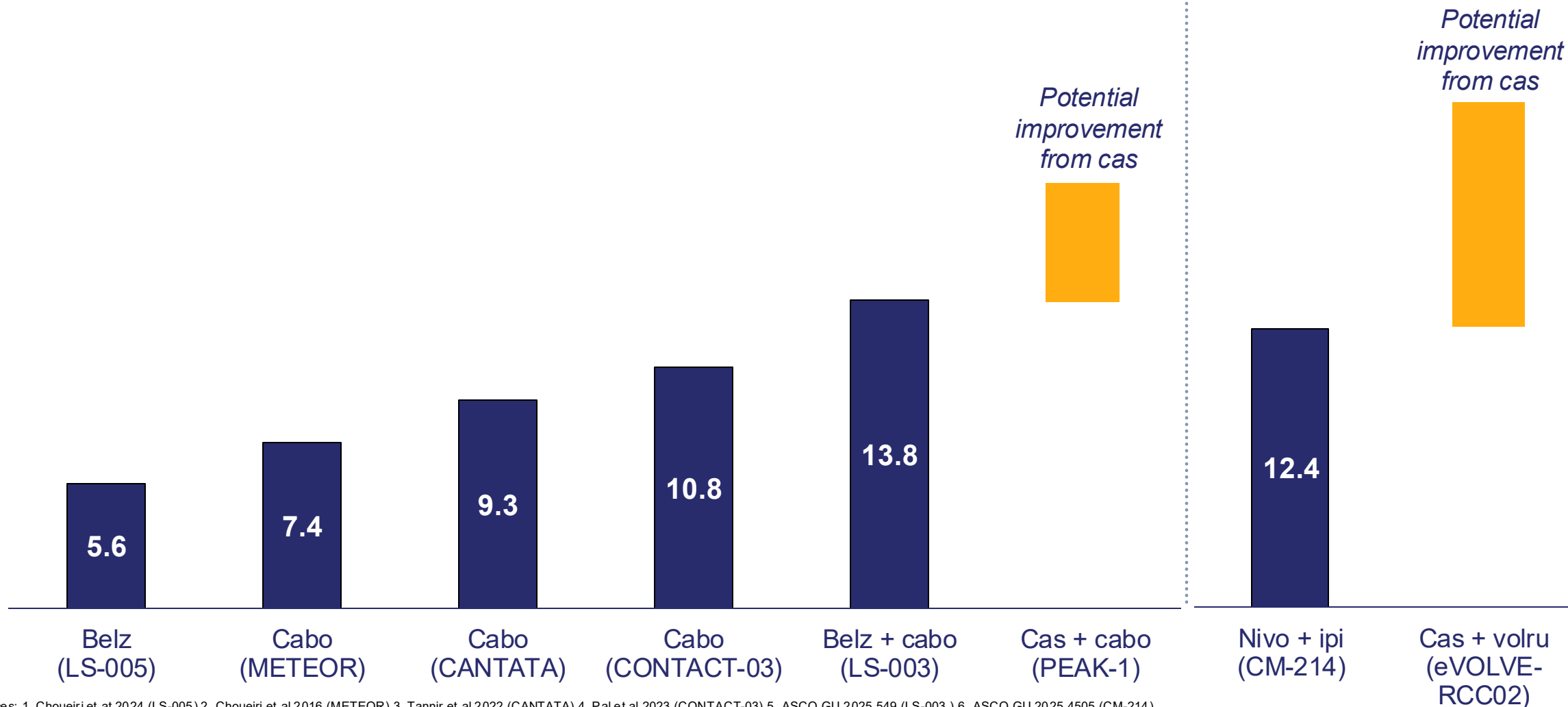
- **RCC is currently a ~\$9B market in Major Markets**
 - This is despite multiple generic TKIs (e.g., axitinib, pazopanib, everolimus, sunitinib)
 - The market is almost entirely dominated by 2 classes of therapy: IO (5 approved agents) and TKI (7+ approved agents)
 - **Each class has approx. \$4B in sales**
- **The RCC market is expected to grow to \$13B by 2030 driven by:**
 - Increasing patient population
 - Introduction of HIF-2 α MOA
 - Increasing DoT and “IO-like” durations of response for HIF-2 α containing regimens
- **There are only 2 agents currently in development in the HIF-2 α class**

Estimating Time on Treatment for Cas + Cabo and Cas + Volru Combinations

2L+ RCC

1L RCC

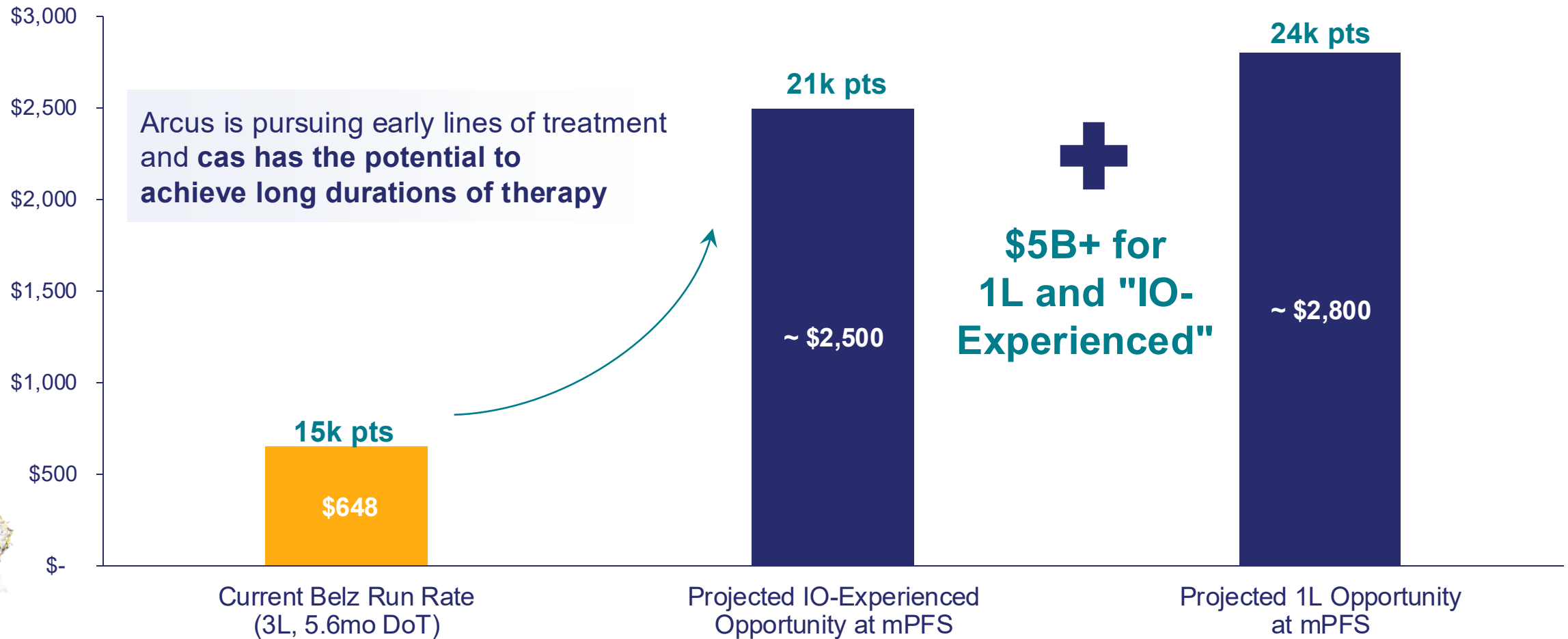
Median PFS (months)



Sources: 1. Choueiri et al 2024 (LS-005) 2. Choueiri et al 2016 (METEOR) 3. Tannir et al 2022 (CANTATA) 4. Pal et al 2023 (CONTACT-03) 5. ASCO GU 2025 549 (LS-003) 6. ASCO GU 2025 4505 (CM-214)
Data 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.
1L: first-line; 2L: second-line; belz: belzutifan; cas: casdatifan; cabo: cabozantinib; ipi: ipilimumab nivo: nivolumab; RCC: renal cell carcinoma; volru: volrustomig

Belzutifan Today is Only "Scratching the Surface" on the RCC Opportunity (G7 countries)

Potential HIF-2α Peak Sales (\$M)



Belz run rate estimated based on Q2'25 sales. 5.6mo DoT assumed based on LS-005 PFS.

Projected potential opportunities based on Arcus analysis across US, EU5 & Japan in 2036. Assumes HIF-2α containing regimens capture 55-75% share of patient population. Epi estimates from DRG (Clarivate)

1L: first-line; 3L: third-line; belz: belzutifan; cas: casdatifan; DoT: duration of treatment; EU5: France, Germany, Italy, Spain, and the United Kingdom; G7 countries: Canada, France, Germany, Italy, Japan, United Kingdom, United States; IO: immunotherapy; mPFS: median progression-free survival; pts: patients; RCC: renal cell carcinoma

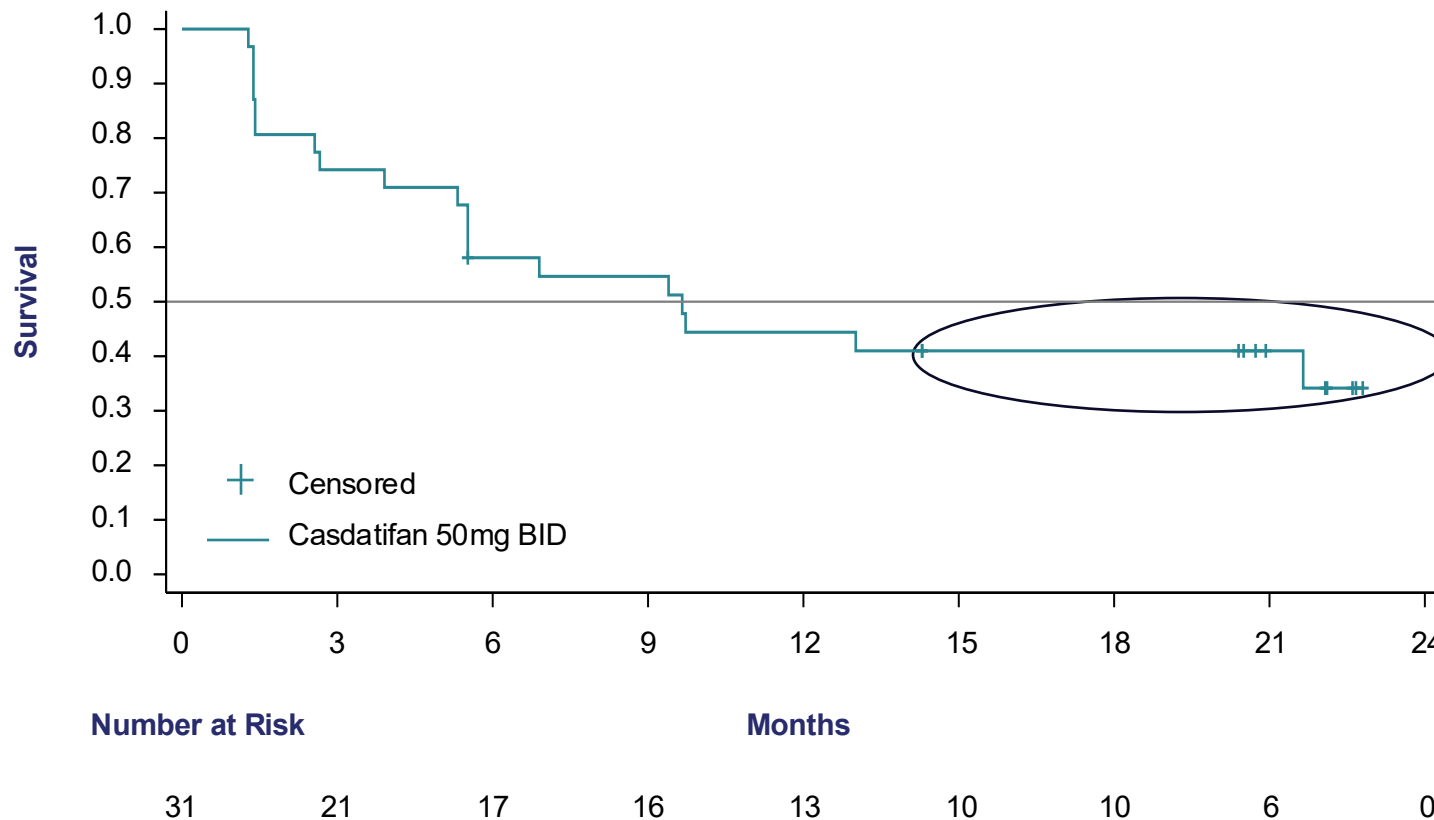
PEAK-1

eVOLVE
RCC02

ARCUS
BIOSCIENCES

Estimating Time on Treatment: "Long Tail" of Cas Treatment Expected to Drive Even Greater Upside Potential

PFS K-M Curve for 50mg BID Cohort (Most Mature Cohort)



- In the most mature cohort of ARC-20 (50mg BID), the landmark 18-month PFS was 41% which demonstrates the "long tail" of HIF-2 α treatment
- The "median" PFS may meaningfully underestimate the "mean" time on treatment
- **Each additional month of time on treatment results in \$150-\$200mm of incremental annual revenue (G7)**

Cas Is Poised to Take Meaningful Share and Grow the Market for ccRCC Therapies

Our Approach to Maximizing the Market Opportunity for Cas in IO-Experienced ccRCC

1

Convert cabo mono users to cas + cabo based on significantly improved efficacy

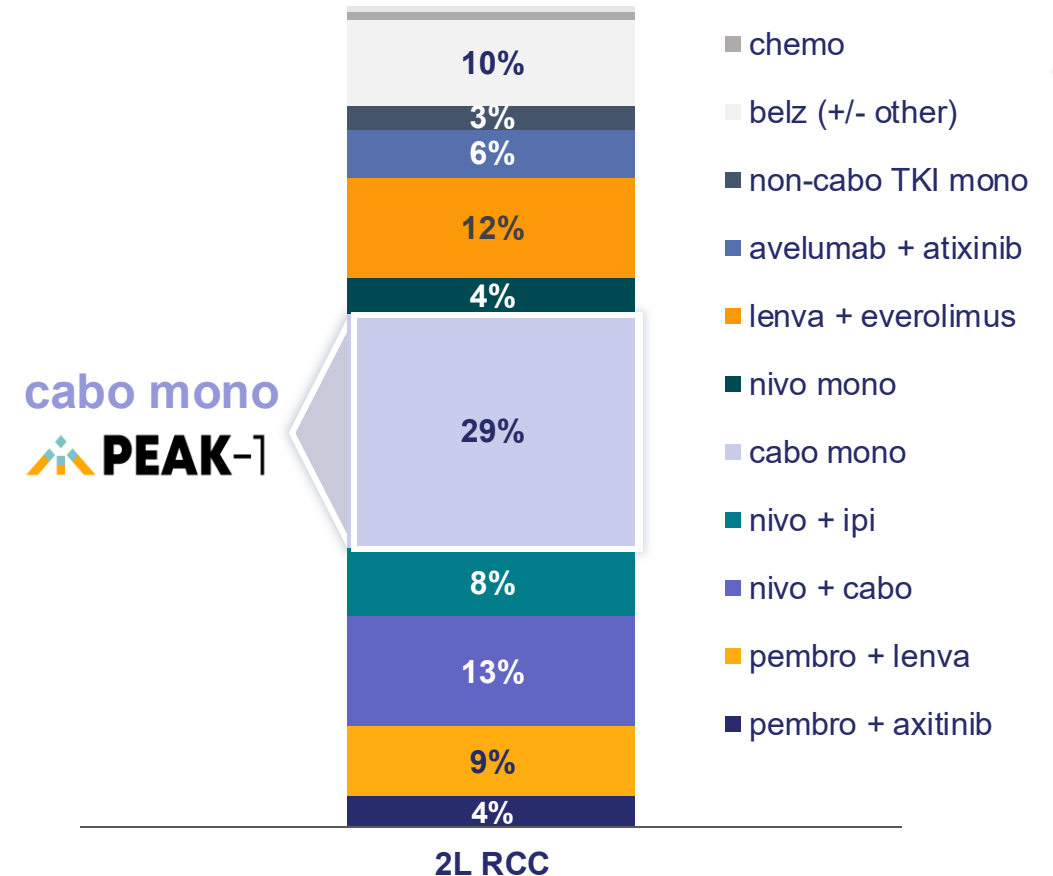
2

Convert other TKI-based regimens (lenva, tivo, axi) to cas + cabo

3

Meaningfully extend duration of treatment while minimizing treatment interruptions

2024 ccRCC | US Market Share



Source: Arcus primary research, US May 2024 (n=49)

axi: axitinib; belz: belzutifan; cabo: cabozantinib; cas:casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; ipi: ipilimumab; lenva: lenvatinib; mono: monotherapy; nivo: nivolumab; pembro: pembrolizumab; tivo: tivozanib; TKI: tyrosine kinase inhibitor

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Longer Term, We Have an Opportunity to Further Expand the Market Opportunity for Cas

Near-Term



Cas + cabo in IO-experienced ccRCC

- Only cabo-containing HIF-2 α regimen

Medium-Term



Cas + volru in 1L ccRCC

- First-to-market TKI-free HIF-2 α regimen in 1L

ARC-20

Cas mono in IO-experienced / TKI-naïve ccRCC

- Enabled by improved / comparable efficacy + better tolerability than TKIs

Cas + anti-PD-1 in 1L ccRCC

- Displace TKIs in the 1L setting

Cas + anti-PD-1 in Neoadjuvant

- New treatment option pre-nephrectomy in a huge patient population

Long-Term

New tumor types, e.g. HCC

- HIF-2 α is involved in multiple pathways that result in tumorigenesis

MORE TO COME



Our Emerging I&I Portfolio

Dr. Juan Jaen
President, Arcus Biosciences

Our I&I Drug Discovery Strategy

IN-HOUSE EXPERTISE IN IMMUNOLOGY has been a core aspect of our discovery group since Arcus founding

MINIMIZE BIOLOGICAL RISK by leveraging validated mechanisms with applications to common diseases with large addressable populations

2-PRONG I&I STRATEGY:

- Small-molecule improvements of cytokine-targeted therapeutics with validated clinical benefit
- Target immune cell types that play key roles in human disease and have been historically “under-studied”
 - Multi-year interest in mast cell biology (e.g., KIT, MRGPRX2), neutrophil biology

Our I&I Drug Discovery Portfolio

TARGET	MODALITY	DISEASE AREA	STATUS
MRGPRX2	SM	CSU, AD	Preclinical
TNF-α (TNFR1)	SM	RA, Psoriasis, IBD	Advanced Discovery
CCR6	SM	Psoriasis	Advanced Discovery
CD89	mAb	RA	Advanced Discovery
CD40 ligand	SM	SLE; MS	Discovery

We expect to select development candidates for at least 3 of these programs within the next 12 months

MRGPRX2 Inhibition for the Treatment of Atopic Skin Diseases

Validated Biology with Multi-Billion \$ Potential

- MRGPX2 is a mast cell-specific G protein-coupled receptor (GPCR) that triggers robust mast cell activation
- Approved biologics are highly successful and effective in treating mast-cell driven diseases
- Dupixent® is approved in AD and CSU, among other indications, and generates >\$15B in LTM sales¹

Opportunity for Improvement

- Anti-IgE (e.g., Xolair®) and anti-IL-4R (e.g., Dupixent®) are not sufficient to address clinical need in CSU and/or AD (non-IgE mast cell pathology)
- KIT mAbs (e.g., barzolvolimab/ Celldex) address mast cell biology but at the cost of some safety/convenience
- MRGPRX2 represents a novel (and potentially safer) way to address mast cell contribution in these conditions
- Need for improved potency/PK relative to early entrants into the clinic

Program Status

- Expect FIH in 2026
- Great opportunity to establish preliminary efficacy in Ph1b study (e.g., CIndU)

1. Sanofi earnings releases

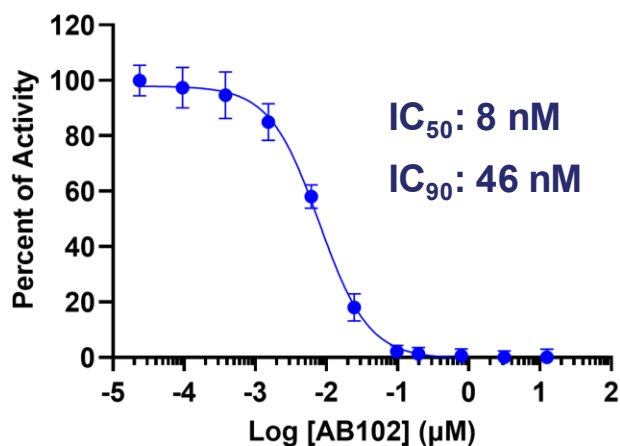
AD: atopic dermatitis; CIndU: chronic inducible urticaria; CSU: chronic spontaneous urticaria; FIH: first-in-human; IgE: immunoglobulin E; KIT: tyrosine kinase receptor for stem cell factor SCF; mAb: monoclonal antibody; MRGPRX2: mas-related G protein-coupled receptor member X2; PK: pharmacokinetics

Key Criteria Expected to Enable an MRGPRX2 Antagonist to be Best-in-Class

Potency

- We perform stringent evaluation of potency in the presence of 100% human serum (reflective of a physiologically relevant setting)
- Several molecules display potencies that can block 90%+ of the effects of MRGPRX2 activators at double-digit nM concentrations (see below for AB102)

Mast cell (LAD2) degranulation (CD107a) in 100% human serum



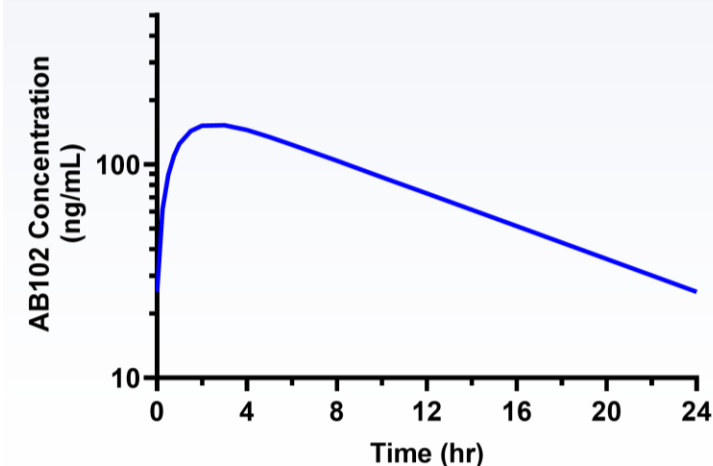
Selectivity / Safety

- Exploratory safety studies completed in 3 species, supportive of desired safety margins
- Competitor molecules have reported preclinical and/or clinical safety signals that might be inconsistent with continued development in dermal indications such as CSU and AD
- Ongoing GLP studies progressing on schedule with AB102; additional molecules continue to be profiled

Human PK

- Based on our predicted human PK for our leading molecule, it could achieve clinically relevant exposures at 1/30 the exposures shown by the leading competitor, with opportunity to push beyond in a meaningful way

Modeled steady-state human PK



Small-molecule Inhibitors of TNF- α with Potentially Improved Efficacy/Safety Relative to anti-TNF- α Biologics

Validated Biology with Multi-Billion \$ Potential

- Anti-TNF antibodies are among the most successful biologic drugs ever developed
- Humira® was the world's top-selling drug for nearly a decade, with peak sales over \$20B^{1,2}
- They are approved in several large autoimmune indications, including rheumatoid arthritis, psoriatic arthritis, Crohn's and ulcerative colitis, among others
- Administered as IV infusion or self-injection

Opportunity for Improvement

- Anti-TNF antibodies block TNF- α signaling at 2 receptors:
 - TNFR1 (pro-inflammatory)
 - TNFR2 (pro-Treg)
- As a result, TNF antibodies can drive a fraction of patients to develop "paradoxical inflammation" (e.g., psoriasis)
- Small-molecule disruptors of TNF- α selectively block only the activation with TNFR1, with potential for efficacy & better safety
- Opportunity for molecules with better potency / human PK, relative to early entrant into the clinic

Program Status

- Final stages of Development Candidate selection
- Potential for FIH in 2026
- Clinical strategy to be disclosed at a later date
 - An orally delivered & safe small molecule could open up many opportunities for combination treatment

Small-molecule CCR6 Antagonists as Potential Therapeutic Alternatives to anti-IL-17 Biologics - Psoriasis

Validated Biology with Multi-Billion \$ Potential

- Anti-IL-17 antibodies have revolutionized the treatment of psoriasis and other skin diseases
 - Cosentyx® has generated \$6.4B in LTM sales¹
- There are currently no orally available options for dealing with the inflammatory effects of IL-17

Opportunity for Improvement

- CCR6 inhibition creates opportunity to interfere with a group of cytokines (beyond IL-17) produced by key inflammatory cells (e.g., $\gamma\delta$ T cells)
- IL-17 is key in fighting certain infections; anti-IL-17 therapy brings with it increased risk of infection
 - Small-molecule CCR6 antagonists may provide greater flexibility for managing safety signals secondary to IL-17 inhibition
- Chemokine field notoriously difficult to drug (requirements for constant target engagement). Leading clinical entrant expected to fall short.
 - Arcus scientists have one of the best records in the industry

Program Status

- Final stages of Development Candidate selection
- Potential for FIH in 2026
- Clinical strategy to be disclosed at a later date
 - An orally delivered & safe small molecule opens up many opportunities for combination treatment

1. Novartis earnings releases
FIH: first-in-human

Q&A

Closing Remarks

Dr. Terry Rosen
CEO, Arcus Biosciences

Cas is Positioned to Become the Standard of Care in RCC

Cohort:	100mg QD (n=31)	All Pooled (n=121)	Belzutifan in LS-005 ¹ (n=374)
Median Follow-up	12.4 mos.	15.5 mos.	18.4 mos.
PD rate	16%	19%	34%
cORR (95% CI)	35% (19, 55)	31% (23, 40)	22% (18-27)
ORR, including responses pending confirmation*	42%*	33%*	
Median PFS (mos.) (95% CI)	Not reached (5.7, NE)	12.2 (9.4, 20.6)	5.6 (5.2, 7.4)
Landmark 12-month PFS	60%	50%	32%

Almost **50%** lower PD

~50% higher ORR
and responses are
very durable

**Meaningfully
longer PFS**

DCO date: August 15, 2025

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

1. Albiges L. et al. Abstract LBA88, ESMO 2023; Choueiri et al. 2024.

Data 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, include and exclusion criteria and many other factors.

Cas: casdatifan; CI: confidence interval; cORR: confirmed overall response rate; DCO: data cut-off; mos: months; NE: not estimable; PFS: progression-free survival; QD: once daily; RCC: renal cell carcinoma; SOC: standard of care

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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-2 α INHIBITOR

ARC-20

Phase 1/1b in
ccRCC

eVOLVE
RCC02

Phase 1b/3 in 1L
ccRCC *Enrolling*

PEAK-1

Phase 3 in 2L
ccRCC *Enrolling*

\$927 MILLION IN CASH*

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

* cash, cash equivalents and marketable securities as of June 30, 2025
** runway estimate based on cash, cash equivalents, marketable securities,
available facilities, and current planned operations

DOMVANALIMAB: THREE PHASE 3 STUDIES

STAR-221

1L Gastric
Ph 3 Data in 2026

STAR-121

1L NSCLC
(PD-L1 all comer)
Ongoing

PACIFIC8

Stage 3 NSCLC
Ongoing

QUEMLICLUSTAT: PHASE 3 FULLY ENROLLED

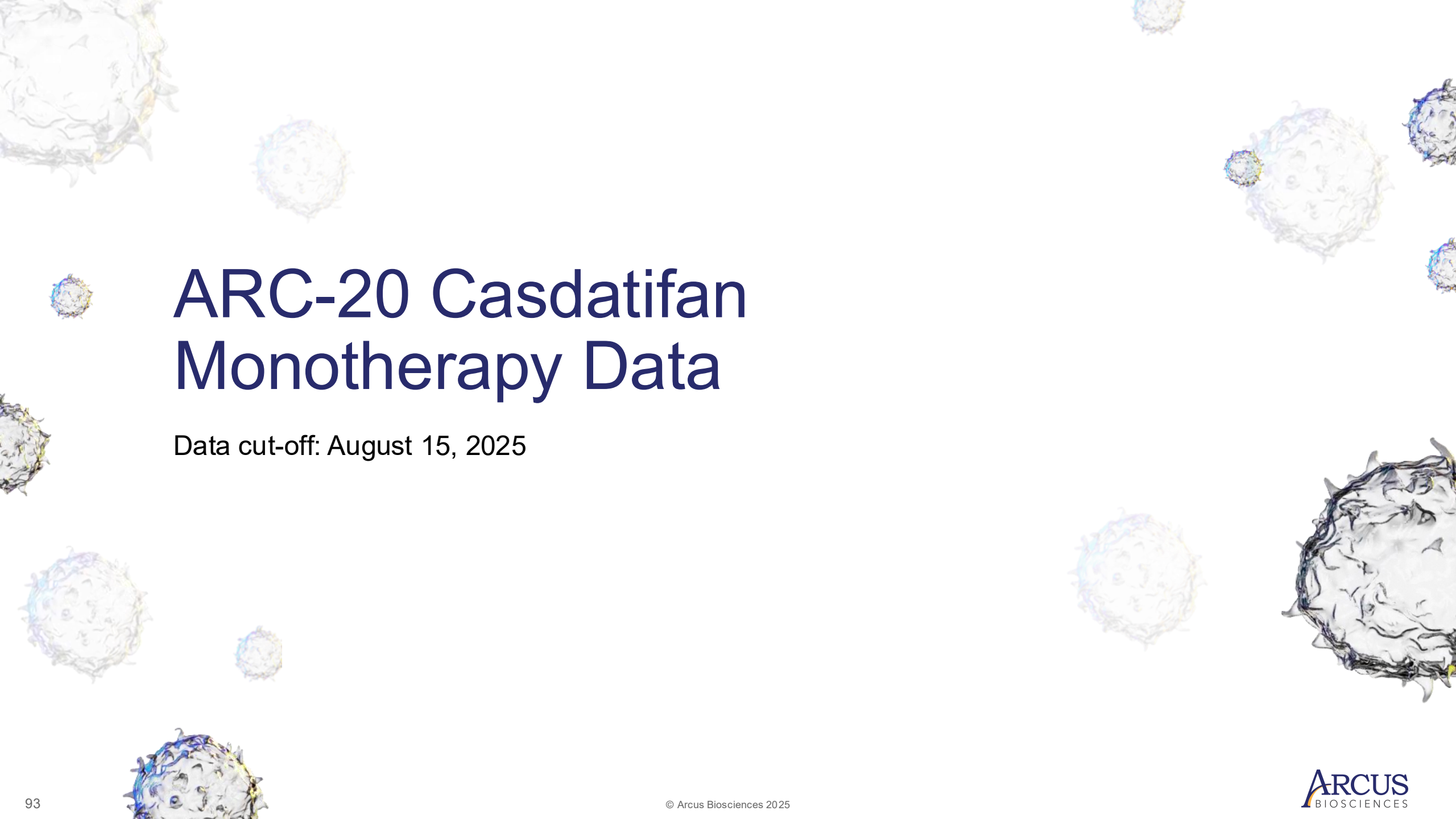
PRISM-1 1L Pancreatic

WORLD-CLASS DRUG DISCOVERY

Small molecules, with focus
on oncology and I&I



Appendix

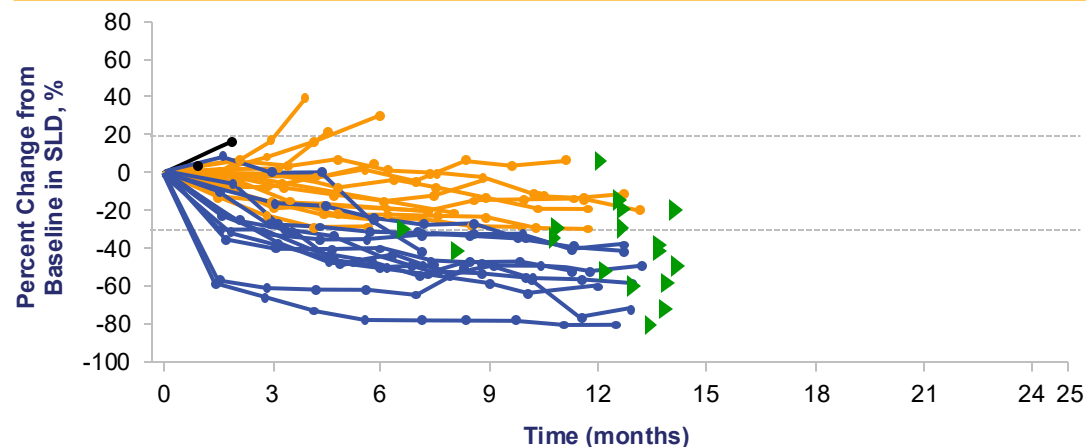


ARC-20 Casdatifan Monotherapy Data

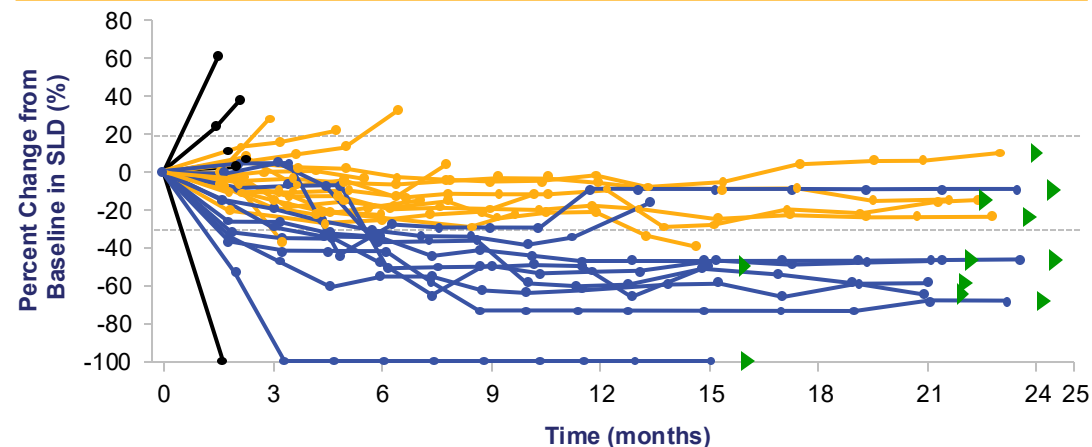
Data cut-off: August 15, 2025

Both Stable Disease Patients and Responders are Benefiting from Treatment

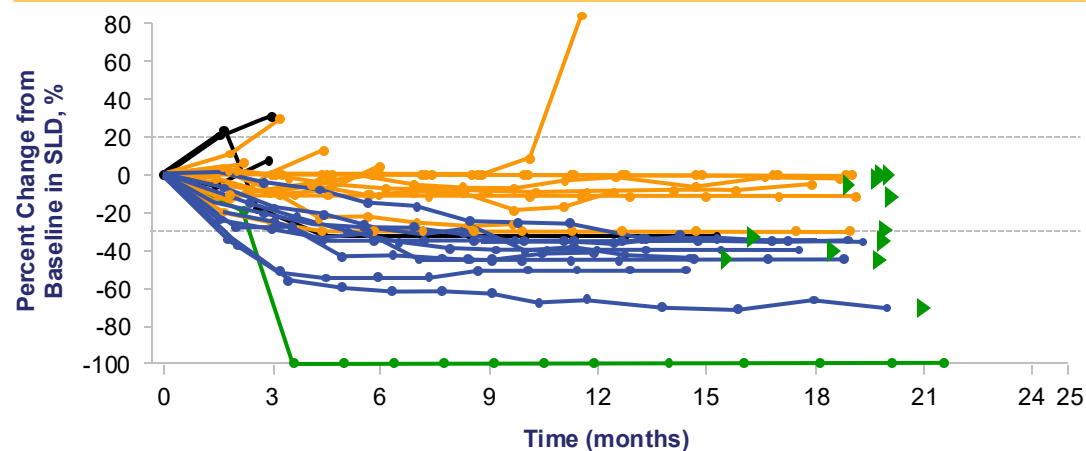
100mg QD Cohort



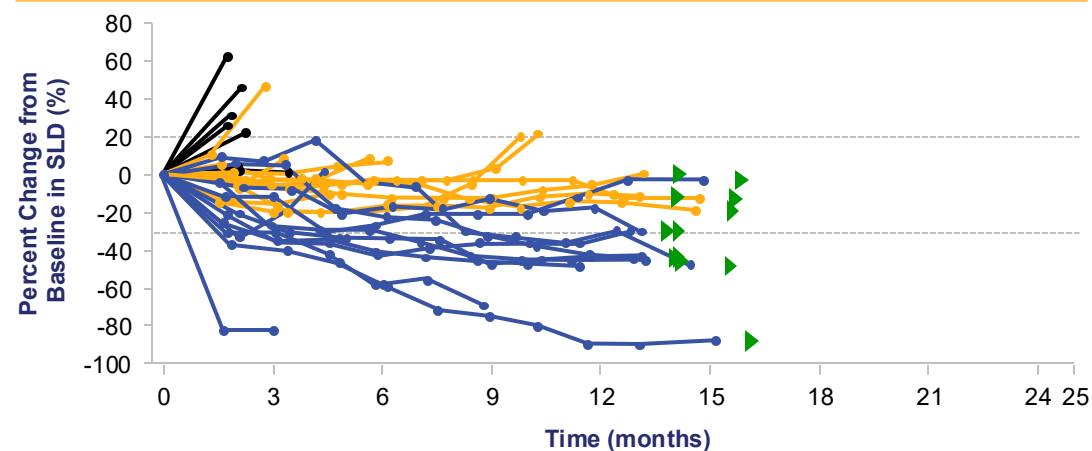
50mg BID Cohort



50mg QD Cohort



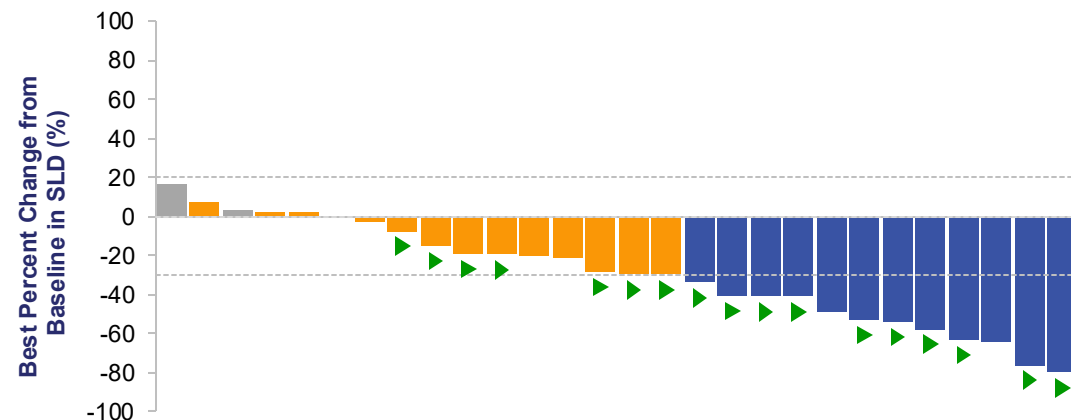
150mg QD Cohort



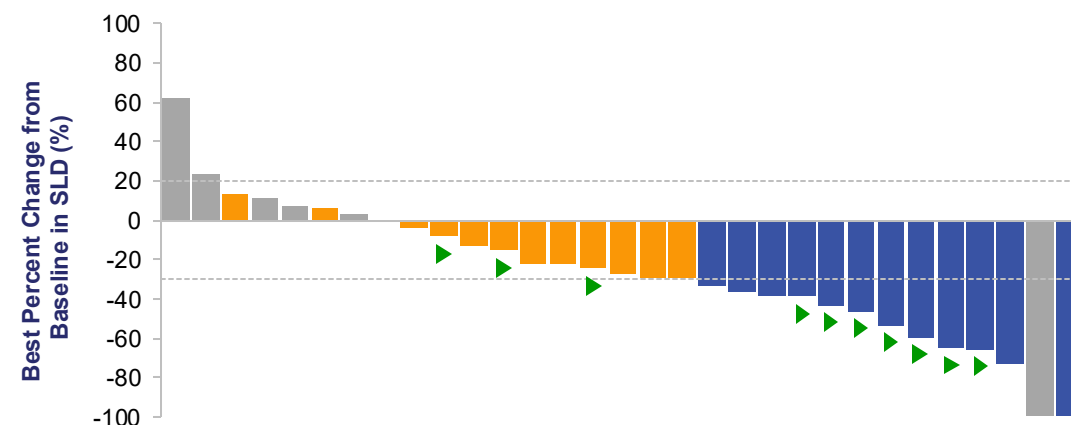
—●— Complete Response (CR) —●— Partial Response (PR) —●— Stable Disease (SD) —●— Progressive Disease (PD) ► Treatment Ongoing

Confirmed Overall Response Rate of 31% Across All Cohorts

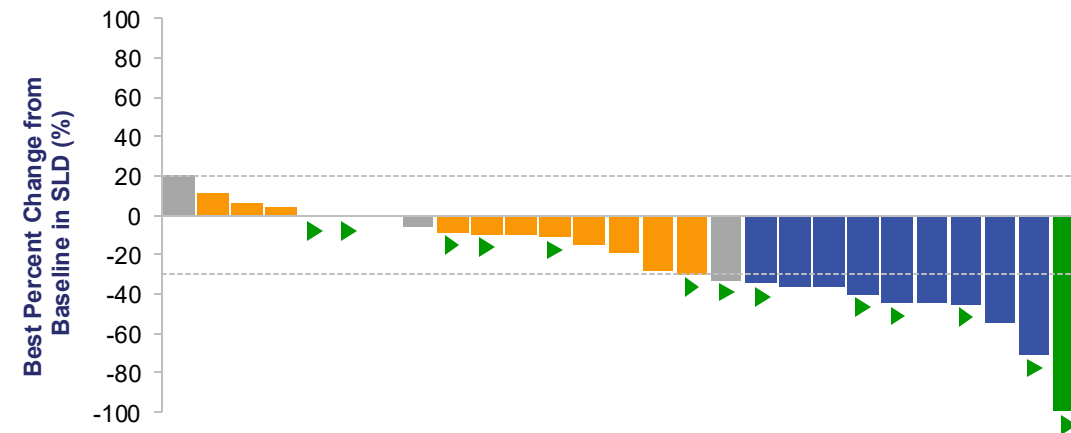
100mg QD Cohort



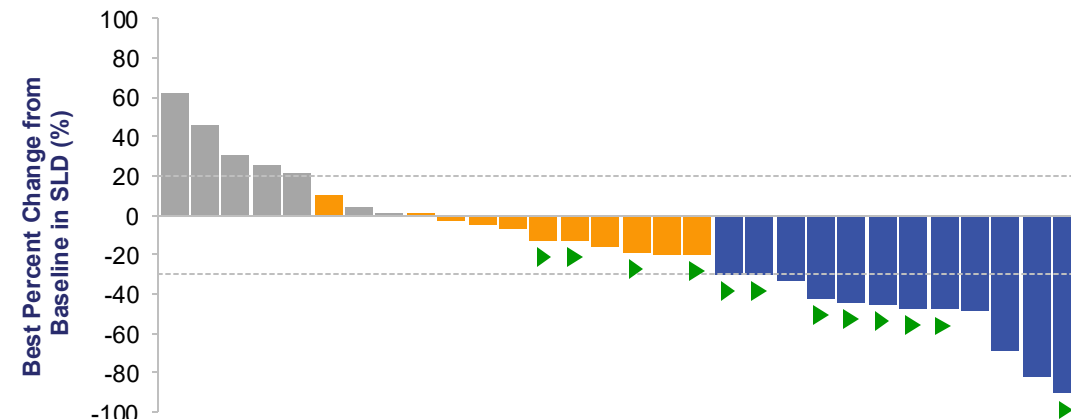
50mg BID Cohort



50mg QD Cohort



150mg QD Cohort



Best Response Type

Complete Response

Stable Disease

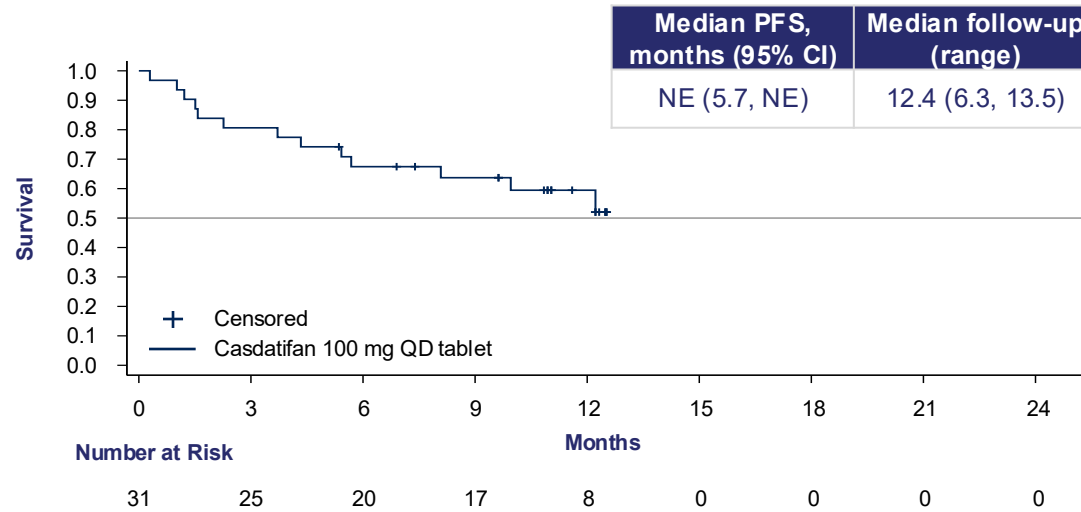
Partial Response

Progressive Disease

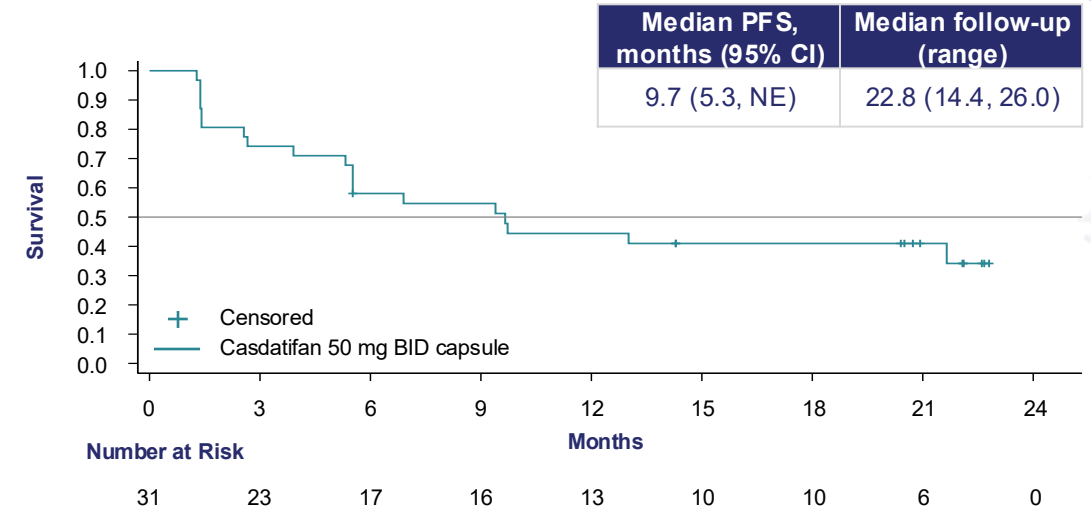
Ongoing

PFS Results are Consistently Better than LS-005, Across All Four Monotherapy Cohorts*

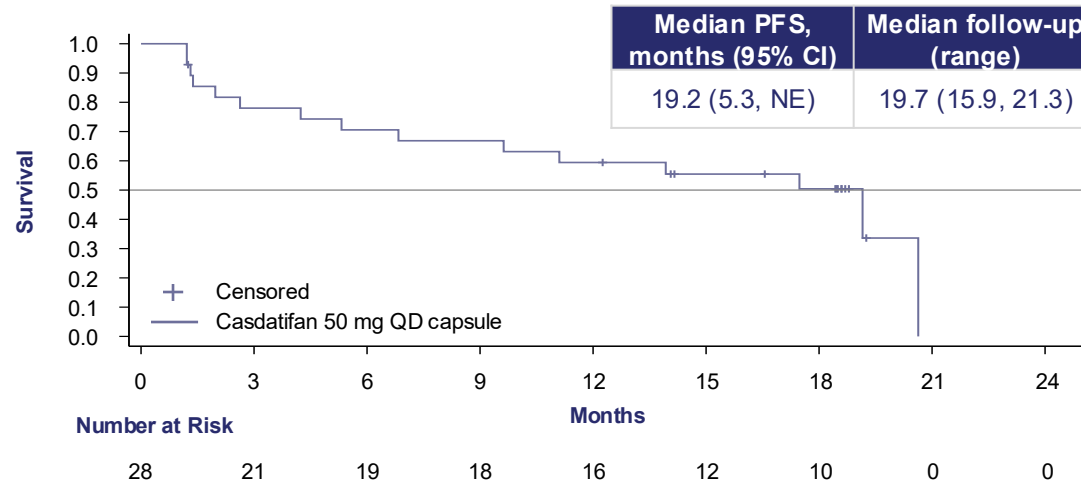
100MG QD COHORT



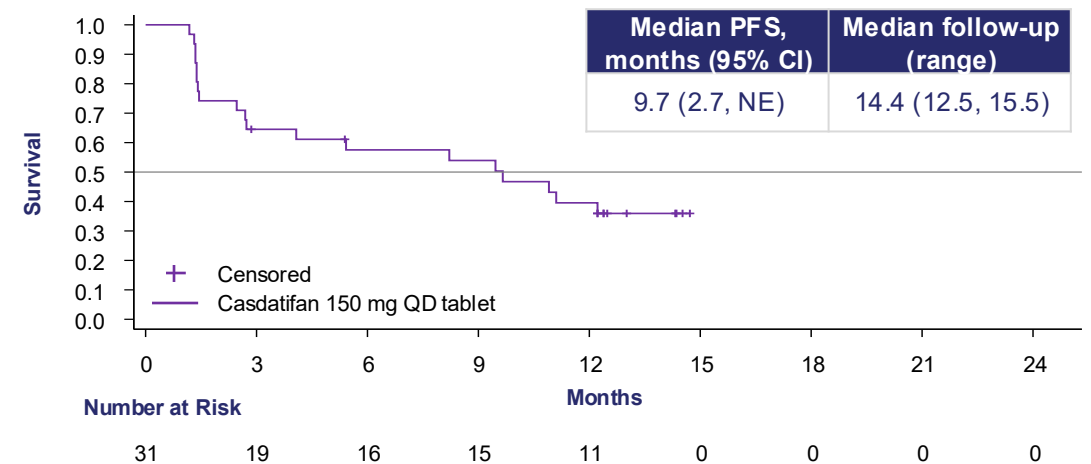
50MG BID COHORT



50MG QD COHORT



150MG QD COHORT



DCO date: August 15, 2025

BID: twice daily; CI: confidence interval; DCO: data cut-off; NE: not estimable; PFS: progression-free survival; QD: once daily

*Data 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, include and exclusion criteria and many other factors.

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