NEWS RELEASE

Arcus Biosciences Presents New Data for its HIF-2a Inhibitor Casdatifan and Discloses First Inflammation Programs at Investor Event

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- Casdatifan data were better on every efficacy measure evaluated, across all four monotherapy cohorts (n=121) of the Phase 1/1b ARC-20 study in late-line metastatic kidney cancer, relative to published data from studies with the only marketed HIF-2a inhibitor
- Median progression-free survival (mPFS) was 12.2 months, and 18-month landmark PFS was 43% in the pooled analysis of all four monotherapy cohorts
- Confirmed overall response rate (ORR) was 35%, with two additional responses pending confirmation, and mPFS had not been reached in the 100mg QD cohort (the Phase 3 PEAK-1 dose and formulation)
- Five new research programs for autoimmune and inflammatory diseases are being announced; first clinical study is expected to be initiated in 2026
- The investor event will be webcast today beginning at 7:00 AM PT / 10:00 AM ET

HAYWARD, Calif.--(BUSINESS WIRE)-- Arcus Biosciences, Inc. (NYSE:RCUS), a clinical-stage, global biopharmaceutical company focused on developing differentiated molecules and combination therapies for people with cancer, today announced new monotherapy data for casdatifan, a HIF-2a inhibitor with best-in-class potential, in late-line metastatic clear cell renal cell carcinoma (ccRCC). At an investor event hosted later today, the Company will share more detail on these data and preview the expansion of its research efforts into autoimmune and inflammatory diseases. Featured presenters will include members of the Arcus management team and key opinion leaders with expertise in HIF-2a biology and treatment of ccRCC.

New Casdatifan Data

“In the 100mg tablet cohort, our Phase 3 dose and formulation, casdatifan showed a 35% confirmed ORR, with two additional responses pending confirmation, and mPFS had not been reached, even with a median follow-up of one year,” said Richard Markus, M.D., Ph.D., chief medical officer at Arcus Biosciences. “Even when we analyzed pooled data for the 121 patients treated with casdatifan monotherapy, casdatifan showed a confirmed ORR of 31% and a median PFS of 12.2 months, which is meaningfully longer than published data from studies with the only marketed HIF-2a inhibitor and for TKIs alone in a similar patient population and setting.”

ARC-20 is a Phase 1/1b dose-escalation and expansion study with four monotherapy cohorts (n=121): 50mg twice daily (BID), 50mg once daily (QD), 100mg QD (tablet) and 150mg QD, all of which evaluated casdatifan in patients with metastatic ccRCC, most of whom had progressed on at least two prior lines of therapy, including both an anti-PD-1 and a VEGFR tyrosine kinase inhibitor (TKI). The patient population was heavily pretreated; in the pooled analysis, more than half (55%) of patients received at least three prior lines of therapy, and more than one quarter (29%) had received at least four prior lines of therapy. Most patients (71%) had an International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk factor of intermediate or poor.

At the time of data cut-off (DCO, August 15, 2025), most patients (81%) had experienced disease control, with either a partial response or stable disease. Seventy-four percent (28 of the 38) of confirmed responders across all four cohorts remained on treatment.

No unexpected safety signals were observed at the time of DCO, and casdatifan had an acceptable and manageable safety profile across all doses. Across all four cohorts, one patient discontinued treatment due to anemia, and four patients (3%) discontinued due to hypoxia. Summaries of the efficacy and safety data are below.

	100mg QD Tablet (Phase 3 dose) (n=31)	Pooled Analysis (50mg BID, 50mg QD, 100mg QD, 150mg QD) (n=121)
Efficacya		
Median Follow-Up	12.4 months	15.2 months
Median PFS [95% CI]	NE [5.7,NE]	12.2 months [9.4,20.6]
18-month PFS [95% CI]	NE	43% [33,53]
12-month PFS [95% CI]	60% [40,75]	50% [41,59]
Confirmed ORR (cORR) [95% CI] Complete Response Partial Response Stable Disease Progressive Disease	35% (11) [19,55] 0 35% (11) 48% (15) 16% (5)b	31% (38) [23,40] 1% (1) 31% (37) 50% (60) 19% (23)
ORR, including responses pending confirmation c	42% (13)	33% (40)
Median Time to Response	2.6 months	2.8 months
Disease Control Rate [95% CI]	84% (26) [66,95]	81% (98) [63,88]

CI: confidence interval; NE: not estimable
a 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 discontinued study treatment due to progressive disease or death.
b Includes three patients with radiological progressive disease and two patients who had clinical progression before the first scan, which have been included but do not meet criteria for progressive disease per RECIST.
c 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%.

	100mg QD Tablet (Phase 3 dose) (n=32)	Pooled Analysis (50mg BID, 50mg QD, 100mg QD, 150mg QD) (n=127)
Safetya		
Any Serious Treatment-Emergent Adverse Events (TEAEs)	31% (10)	31% (39)
Grade ≥3 TEAEs related to casdatifanb		
Anemia	25% (8)	41% (52)
Hypoxia	9% (3)	11% (14)
TEAEs resulting in discontinuation	9% (3)	9% (11)
Anemia c	0	1% (1)
Hypoxia c	3% (1)	3% (4)

a The safety-evaluable population included all dose-expansion enrolled patients who received any amount of any study treatment.
b Grade ≥3 TEAEs related to casdatifan that occurred in more than 5% of patients in the pooled analysis.
c Prespecified events of interest.

Expansion into Immunology and Inflammation (I&I)

“Arcus has an exceptional small-molecule discovery and development team that has demonstrated time and again the ability to create highly effective drug candidates against difficult targets,” said Terry Rosen, Ph.D., chief executive officer of Arcus. “The new data presented today reinforce the best-in-class potential for casdatifan, a small-molecule inhibitor of HIF-2a, a particularly challenging drug discovery target, and we are now applying that same expertise to create and develop drugs that have the potential to address very large markets in inflammation and immunology, including psoriasis and rheumatoid arthritis.”

The advanced discovery and preclinical programs disclosed today provide multiple opportunities to advance into the clinic in 2026. Potential new drug candidates include:

- MRGPRX2 small-molecule inhibitor, a potential treatment for atopic dermatitis and chronic spontaneous urticaria
- TNF-a (TNFR1) small-molecule inhibitor, a potential treatment for rheumatoid arthritis (RA), psoriasis and

inflammatory bowel disease (such as ulcerative colitis)
- CCR6 small-molecule inhibitor, a potential treatment for psoriasis
- CD89 monoclonal antibody, a potential treatment for RA
- CD40L small-molecule inhibitor, a potential treatment for multiple sclerosis and systemic lupus erythematosus

In-house expertise in immunology has been a core aspect of Arcus's discovery group since its founding and has biological synergies with Arcus's cancer immunotherapy programs. The team is leveraging validated mechanisms with applications to common diseases with potentially large addressable populations and has implemented a two-pronged I&I strategy to minimize biological risk: (1) leverage medicinal chemistry capabilities to design and create small-molecule drugs that regulate key cytokines (therapeutically validated by existing biologics); (2) target immune cell types that play key roles in human disease and have been historically "under-studied."

Arcus is hosting an in-person and virtual investor event in New York today, beginning at 7:00 AM PT / 10:00 AM ET, to review the new casdatifan data and I&I programs. Investors may register and log in to the live webcast using the following link: **wsw.com/webcast/cc/rcus4/1445382**. To access a replay of the event and accompanying slide presentation, please visit the "Investors & Media" section of the Arcus Biosciences website at **www.arcusbio.com**.

About Casdatifan (AB521)

Casdatifan is a small-molecule inhibitor of HIF-2a, a master switch that turns on hundreds of genes in response to low oxygen levels; when oxygen levels return to normal, HIF-2a is turned off. In a majority of people with the most common form of kidney cancer (clear cell renal cell carcinoma), this shut-off mechanism is deficient, and HIF-2a remains activated even in the presence of oxygen, causing normal kidney cells to become cancerous.

Casdatifan is designed to provide deeper and more durable inhibition of the HIF-2a pathway. Early clinical studies have shown high response rates and a low primary progression rate relative to clinical benchmarks, warranting further investigation in late-stage studies. Casdatifan, which is administered in pill form once daily, has a safety profile that allows it to be investigated in combination with other treatments.

Arcus is pursuing a broad development program in both the immuno-oncology (IO)-naive and post-IO settings with differentiated combinations to maximize the opportunity for casdatifan in ccRCC. These studies include:

- PEAK-1, an ongoing Phase 3 study evaluating casdatifan plus cabozantinib versus cabozantinib monotherapy as a first- or second-line treatment in patients with metastatic ccRCC who have previously received anti-PD-1/PD-L1 therapy. The primary endpoint is PFS with a key secondary endpoint of overall survival.
- eVOLVE-RCC02, an ongoing Phase 1b/3 study sponsored by AstraZeneca, which is evaluating casdatifan plus

volrustomig, an investigational anti-PD-1/CTLA-4 bispecific antibody, as first-line treatment for participants with ccRCC. The study was designed to support initiation of the Phase 3 portion as efficiently as possible.
- ARC-20, which includes three cohorts evaluating casdatifan in earlier-line settings, including casdatifan plus zimberelimab in first-line ccRCC, casdatifan monotherapy in favorable risk ccRCC and casdatifan monotherapy in immunotherapy-experienced, TKI-naive settings.

Casdatifan is an investigational molecule. Approval from any regulatory authority for its use has not been received, and its safety and efficacy have not been established.

About RCC

According to the American Cancer Society, kidney cancer is among the top 10 most commonly diagnosed forms of cancer among both men and women in the U.S., and an estimated 80,980 Americans will be diagnosed with kidney cancer in 2025. Clear cell RCC is the most common type of kidney cancer in adults. If detected in its early stages, the five-year survival rate for RCC is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 18%. In 2022, approximately 32,200 patients with advanced kidney cancer required systemic therapy in the U.S., with over 20,000 patients receiving first-line treatment.

About the Gilead Collaboration

In May 2020, Arcus established a 10-year collaboration with Gilead to strategically advance our portfolio. Under this collaboration, Gilead obtained time-limited exclusive option rights to all of our clinical programs arising during the collaboration term. Arcus and Gilead are co-developing three investigational products, including zimberelimab (Arcus's anti-PD-1 molecule), domvanalimab (Arcus's anti-TIGIT antibody) and quemliclustat (Arcus's CD73 inhibitor).

The collaboration was expanded in November 2021 and May 2023 to include research directed to two targets for oncology and two targets for inflammatory diseases. Gilead may exercise its option to each inflammatory program at two separate, prespecified time points. If Gilead exercises its option at the earlier time point, Arcus would be eligible to receive up to $420 million in option and milestone payments and tiered royalties for each optioned program. For any other option exercise by Gilead for the two inflammation programs, the parties would have rights to co-develop and share global development costs and to co-promote and share profits in the United States.

Gilead's option rights to casdatifan expired; Arcus Biosciences retains full rights to casdatifan.

About Arcus Biosciences

Arcus Biosciences is a clinical-stage, global biopharmaceutical company developing differentiated molecules and combination therapies for people with cancer. In partnership with industry collaborators, patients and physicians

around the world, Arcus is expediting the development of first- and/or best-in-class medicines against well-characterized biological targets and pathways and studying novel, biology-driven combinations that have the potential to help people with cancer live longer. Founded in 2015, the company has advanced multiple investigational medicines into registrational clinical trials including domvanalimab, an Fc-silent anti-TIGIT antibody being studied in combination with zimberelimab, an anti-PD-1 antibody, for upper gastrointestinal and non-small cell lung cancer, casdatifan, a HIF-2a inhibitor for clear cell renal cell carcinoma, and quemliclustat, a small-molecule CD73 inhibitor for pancreatic cancer. For more information about Arcus Biosciences' clinical and preclinical programs, please visit **www.arcusbio.com**.

Important Information Regarding Data Comparisons

This press release includes comparisons between data from our Phase 1/1b ARC-20 trial and published data from separate trials that are not head-to-head studies. Cross-trial comparisons should be interpreted with caution due to differences in study populations, sample sizes, inclusion and exclusion criteria, trial design, and other factors that may limit direct comparability.

Important Information Regarding Forward Looking Statements

This press release contains forward-looking statements. All statements regarding events or results to occur in the future contained herein are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, the statements in Dr. Markus's and Dr. Rosen's quotes and statements regarding the potential of casdatifan, opportunities and timing of milestones for Arcus's programs in immunology and inflammation, unconfirmed clinical results, and Arcus's expectations regarding initiating one or more clinical studies from its I&I programs. All forward-looking statements involve known and unknown risks and uncertainties and other important factors that may cause Arcus's actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, risks associated with: interim data not being replicated in other studies evaluating casdatifan; the unexpected emergence of adverse events or other undesirable side effects with casdatifan; risks associated with manufacturing or supplying product for clinical trials evaluating casdatifan; adverse data from toxicology studies that affect Arcus's ability to advance development candidates from its immunology and inflammation programs, uncertainties in timelines associated with the conduct of clinical studies and with respect to the regulatory approval process; changes in the competitive landscape for Arcus's programs; and the inherent uncertainty associated with pharmaceutical product development and clinical trials. Risks and uncertainties facing Arcus are described more fully in the "Risk Factors" section of Arcus's most recent periodic report filed with the U.S. Securities and Exchange Commission (SEC) and in other filings that Arcus makes with the

SEC from time to time, which are available at **www.sec.gov**. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Arcus disclaims any obligation or undertaking to update, supplement or revise any forward-looking statements contained in this press release, except to the extent required by law.

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