NEWS RELEASE

Arcus Provides Update on Phase 3 STAR-221 Study and Concentrates Its R&D Investment on Casdatifan and Emerging Inflammation and Immunology Portfolio

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- The Phase 3 STAR-221 study evaluating a domvanalimab-based combination in upper gastrointestinal cancers will be discontinued due to futility
- Arcus is continuing to expand its development program for casdatifan, a potential best-in-class HIF-2a inhibitor with robust single-agent activity, and multiple data readouts are expected in 2026
- Arcus's early development efforts will focus on five programs targeting inflammatory and autoimmune (I&I) diseases; a small molecule targeting MRGPRX2 is expected to enter the clinic in 2026
- With approximately $1B of cash and investmentsi, Arcus expects to be able to fund its planned operations until at least the second half of 2028

HAYWARD, Calif.--(BUSINESS WIRE)-- Arcus Biosciences, Inc. (NYSE:RCUS), a clinical-stage, global biopharmaceutical company focused on developing differentiated molecules and combination therapies for patients with cancer, inflammatory and autoimmune diseases, today announced the discontinuation of the Phase 3 STAR-221 study, being conducted in partnership with Gilead Sciences, Inc., due to futility. The decision is based on the recommendation from the Independent Data Monitoring Committee (IDMC) following its review of data from an event-driven, pre-specified interim analysis of overall survival (OS).

STAR-221 evaluated the anti-TIGIT antibody domvanalimab plus anti-PD-1 antibody zimberelimab and chemotherapy versus nivolumab plus chemotherapy as a first-line treatment for advanced gastric and esophageal cancers. At the interim analysis, the domvanalimab-based combination did not improve OS relative to that of

nivolumab plus chemotherapy. The safety profile for the domvanalimab-based combination was similar to that of nivolumab plus chemotherapy, and there were no new safety findings identified.

“Patients in the domvanalimab-containing arm derived the same benefit as patients treated in the control arm, and there were no new safety concerns,” said Richard Markus, MD, chief medical officer at Arcus. “We are disappointed with this outcome and sincerely thank all those who participated in the study and made this research possible. We remain committed to advancing research for people living with cancer and immune-related diseases.”

The STAR-221 and the Phase 2 EDGE-Gastric studies will be discontinued, and Arcus and Gilead are communicating with investigators to determine appropriate next steps for patients in the study in addition to conducting a detailed analysis to better understand these results.

Future Direction

Arcus’s R&D investment and resources will focus on casdatifan, a potential best-in-class HIF-2a inhibitor, and its emerging small molecule I&I programs.

“The results from STAR-221 are not what we had hoped for, and we have important work ahead to meet the needs of patients on our domvanalimab studies and also accelerate the casdatifan and I&I programs,” said Terry Rosen, chief executive officer of Arcus. “We are fortunate to be well capitalized and plan to focus our resources on casdatifan, including studying new early-line combinations in kidney cancer, broadening its development into new tumor types, and extending our capabilities beyond oncology.”

Casdatifan targets a validated mechanism of action and has shown robust single-agent activity based on data reported from more than 120 patients with late-line clear cell renal cell carcinoma (ccRCC) in the ARC-20 Phase 1/1b clinical study. Those data have shown improvement on every efficacy measure evaluated, including overall response rate and progression-free survival (PFS), relative to reported data for the only marketed HIF-2a inhibitor. Arcus owns all of the rights to casdatifan outside of Japan and certain other Asian territories, which were optioned by Taiho Pharmaceutical Co., Ltd. in October 2025.

Arcus is focused on rapidly developing casdatifan in both immunotherapy (IO)-experienced and first-line metastatic ccRCC, and its clinical investment in 2026 and 2027 will be primarily focused on maximizing the potential of casdatifan. The casdatifan program is expected to have multiple data readouts and cohort and study initiations in 2026 including:

- Early 2026: Additional analyses from the ARC-20 cohorts evaluating casdatifan monotherapy in late-line ccRCC, including updated PFS data for the 100mg once-daily (QD) cohort, which utilizes the selected Phase 3

dose and formulation.

- Mid-2026: More mature data from the ARC-20 cohort evaluating casdatifan plus cabozantinib in the IO-experienced setting. This is the same setting and combination being evaluated in the ongoing Phase 3 PEAK-1 study.
- 2H 2026: Initial data from one or more ARC-20 cohorts evaluating casdatifan in early-line settings, as well as a go-no-go decision on the Phase 3 portion of eVOLVE-RCC02.
- Late 2026: Potential initiation of a Phase 3 registrational study in an early-line or first-line ccRCC setting.

Arcus's oncology portfolio also includes quemliclustat, a small-molecule CD73 inhibitor that completed enrollment of PRISM-1, the Phase 3 study in pancreatic cancer, earlier this year. Results are expected in 2027 for the registrational study, which is evaluating quemliclustat plus gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel in first-line metastatic pancreatic ductal adenocarcinoma.

Arcus's I&I portfolio includes several oral, small molecules being developed in indications currently dominated by injectable drugs. The portfolio includes the following programs: MRGPRX2, TNF, CCR6, CD89 and CD40L. Arcus expects to advance two potentially best-in-class small molecule inhibitors into the clinic in the timeframes noted below:

- 2026: MRGPRX2, a potential treatment for atopic dermatitis and chronic spontaneous urticaria; and
- Late 2026 - early 2027: TNF, a potential treatment for rheumatoid arthritis, psoriasis and inflammatory bowel disease (such as ulcerative colitis).

Domvanalimab, zimberelimab and quemliclustat are investigational molecules, and neither Arcus nor Gilead has received approval from any regulatory authority for any use globally, and their safety and efficacy have not been established. Casdatifan is also an investigational molecule, and Arcus has not received approval from any regulatory authority for any use globally, 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 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. In a majority of people with the most common form of kidney cancer (clear cell renal cell carcinoma), genetic anomalies result in the misregulation of this master switch and transformation of normal kidney cells into cancerous ones. Casdatifan was designed to provide deep and 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.

About Gastric and Esophageal Cancer

According to the World Health Organization, gastric cancer and esophageal cancer are the fifth and seventh leading causes of cancer deaths globally, accounting for more than 1.1 million cancer deaths each year. More than one-third of patients are diagnosed at an advanced stage, when five-year survival rates are only 5-7%.

About the STAR-221 Study

The STAR-221 study is a global, randomized, open-label, Phase 3 trial evaluating domvanalimab plus zimberelimab and chemotherapy versus nivolumab plus chemotherapy as a first-line treatment in locally advanced, unresectable or metastatic HER-2 negative gastric, gastroesophageal junction and esophageal adenocarcinomas. The study enrolled 1,040 patients from nearly 30 countries and participants were randomized 1:1 between two arms:

- 1600mg of domvanalimab intravenously (IV) every four weeks plus 480mg of zimberelimab IV every four weeks plus FOLFOX (oxaliplatin, leucovorin, fluorouracil) every two weeks or 1200mg of domvanalimab plus 360mg of zimberelimab every three weeks plus CAPOX (capecitabine and oxaliplatin) every three weeks.
- 240mg of nivolumab IV every two weeks plus FOLFOX every two weeks or 360mg of nivolumab plus CAPOX every three weeks.

The primary endpoints of the study are overall survival in PD-L1-high tumors (TAP ≥5%), PD-L1-positive tumors (TAP ≥1%) and in the intent-to-treat population (all PD-L1 levels), as assessed by central PD-L1 testing based on Tumor Area Positivity (TAP) score. Key secondary endpoints include progression-free survival (PFS) and patient-reported outcomes (PROs). Secondary endpoints include objective response rate (ORR), duration of response (DOR) and safety.

Taiho Pharmaceutical has development and commercial rights in Japan and other countries in Asia, excluding China, for domvanalimab and zimberelimab, and is conducting the ongoing STAR-221 Phase 3 registrational study in Japan.

More information about STAR-221 is available at **ClinicalTrials.gov**: NCT05568095.

About Domvanalimab

Domvanalimab is the first and most clinically advanced Fc-silent investigational monoclonal antibody that is specifically designed with Fc-silent properties to bind and block to the T-cell immunoreceptor with Ig and ITIM domains (TIGIT), a checkpoint receptor on immune cells that acts as a brake on the anticancer immune response. By binding to TIGIT with Fc-silent properties, domvanalimab is believed to work by freeing up immune-activating pathways and activating immune cells to attack and kill cancer cells without depleting the peripheral regulatory T cells important in avoiding immune-related toxicity. Combined inhibition of both TIGIT and programmed cell death protein-1 (PD-1) is believed to significantly enhance immune cell activation, as these checkpoint receptors play distinct, complementary roles in anti-tumor activity.

About Zimberelimab

Zimberelimab is an anti-programmed cell death protein-1 (PD-1) monoclonal antibody that binds PD-1, with the goal of restoring the antitumor activity of T cells. Zimberelimab has demonstrated high affinity, selectivity and potency in various tumor types. Zimberelimab is being evaluated in the U.S. and globally as a foundational anti-PD-1 treatment option in multiple ongoing clinical studies in combination with other immunotherapies. Guangzhou Gloria Biosciences Co. Ltd., which holds commercialization rights for zimberelimab in greater China, has obtained approval for zimberelimab for the treatment of recurrent or metastatic cervical cancer and for relapsed or refractory classical Hodgkin's lymphoma. Zimberelimab is not approved for any use in the U.S. or other regions outside of China. Gloria conducts its development and commercialization activities independent of Arcus and Gilead.

About Arcus Biosciences

Arcus Biosciences is a clinical-stage, global biopharmaceutical company focused on developing differentiated molecules and combination therapies for patients with cancer, inflammatory and autoimmune diseases. In partnership with industry collaborators, patients and physicians around the world, Arcus is expediting the development of its late-stage portfolio 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 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 for casdatifan 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.

Forward Looking Statement

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, changes in the company's go-forward strategy, operating plans and allocation of resources; the company's anticipated cash runway; the timing of future data readouts and study initiations, including for its MRGPRX2 inhibitor; and the advancement of the company's early discovery portfolio. 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 significantly 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: further changes to the company's strategy and operating plans; risks associated with preliminary and interim data not being guarantees that future data will be similar; the unexpected emergence of adverse events or other undesirable side effects in Arcus's investigational products, including casdatifan; difficulties or delays in initiating or conducting clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials; 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. You are cautioned not to place undue reliance on the 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.

i Based on cash, cash equivalents and marketable securities balance of $841 million as of September 30, 2025 and net proceeds of approximately $270 million from Arcus's November 2025 financing.

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