Q32 Bio Provides Bempikibart Program Update, Including Next Steps for Advancing Alopecia Areata Development Program

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-- SIGNAL-AA demonstrated encouraging clinical activity of bempikibart in patients with alopecia areata (AA), including improvement from baseline on SALT score and meaningful achievement of SALT-20 response --

-- SIGNAL-AD Phase 2a clinical trial in atopic dermatitis demonstrated promising findings in Part A but did not meet primary endpoint in Part B --

-- Across both trials, bempikibart was observed to be safe and well tolerated; demonstrated potent IL-7 and TSLP inhibition via changes in both Th2 biomarkers and T-cells, and desired target engagement --

-- Based on these results, Company plans to advance bempikibart in patients with AA --

WALTHAM, Mass., Dec. 10, 2024 /PRNewswire/ -- Q32 Bio Inc. (Nasdaq: QTTB) ("Q32 Bio"), a clinical stage biotechnology company focused on developing biologic therapeutics to restore immune homeostasis, today announced topline results from the SIGNAL-AA Phase 2a signal finding clinical trial evaluating bempikibart (ADX-914), which identified encouraging clinical activity in patients with alopecia areata (AA). The Company plans to expand the SIGNAL-AA Phase 2a clinical trial and enroll additional patients evaluating bempikibart in AA.

"We are pleased with the emerging signals observed in the SIGNAL-AA Phase 2a clinical trial and based upon these, the positive biomarker data and well tolerated safety profile observed across both trials, we plan to enroll additional patients into the SIGNAL-AA clinical trial to further explore the clinical effects of bempikibart in this patient population. We believe bempikibart has the potential to be an important new treatment option in a disease needing new and safer alternatives to currently approved agents," said Jodie Morrison, Chief Executive Officer of Q32 Bio. "We are disappointed that the SIGNAL-AD trial did not achieve its primary endpoint. Based upon the findings, including the high placebo rate, we plan to conduct a review to better understand the results."

"Results from our analysis of SIGNAL-AA showed clinically meaningful activity and a safety profile that we believe is differentiated from the currently approved therapies for AA. We are encouraged by our findings from this clinical trial, and we look forward to advancing bempikibart as a potential treatment for AA," said Jason Campagna, M.D., Ph.D., Chief Medical Officer of Q32 Bio. "On behalf of Q32 Bio, I want to express my gratitude to the patients, their caregivers, and clinical trial sites that participated across both our bempikibart Phase 2a trials."

The Company is also providing an update on the SIGNAL-AD clinical trial in patients with atopic dermatitis (AD). Although the Company is reporting promising findings in Part A, the trial did not meet its primary endpoint in Part B. Q32 Bio plans to conduct a review of the results.

Topline Results from SIGNAL-AA Phase 2a Clinical Trial:

SIGNAL-AA is a Phase 2a, randomized, double-blind, placebo-controlled, multi-center clinical trial evaluating bempikibart in adult patients with severe and very severe AA (baseline Severity of Alopecia Tool (SALT) scores of 50-100) treated over 24 weeks, with follow-up through 36 weeks. The study is being conducted to evaluate the efficacy and safety of bempikibart 200 mg administered subcutaneously (SC), every-other-week (Q2W) compared to placebo. A total of 44 patients were enrolled in the trial with a primary endpoint of the mean relative percent change in SALT score at 24 weeks compared with baseline.

Following database lock, one site was excluded from the efficacy analysis based on marked protocol violations of entry criteria. This resulted in the removal of three placebo patients, rendering the planned statistical analyses for the primary endpoint inappropriate due to the reduced sample size. On a post-hoc analysis of the remaining per-protocol population of patients with AA (n=27), bempikibart demonstrated an improvement in hair re-growth compared to placebo:

- At week 24: patients treated with bempikibart showed a mean reduction in SALT score of 16% in the bempikibart group vs a reduction of 2% in the placebo group. A Wilcoxon Rank Sum test yielded a p-value of 0.045.
- At week 24: 9% of bempikibart patients in the trial achieved a SALT-20 (SALT score less than or equal to 20) compared to 0% in placebo.
- At week 26: 13% of bempikibart patients achieved SALT-20 compared 0% in placebo.

Bempikibart was observed to be safe and well tolerated in the SIGNAL-AA trial. There were no serious adverse events (SAE) or Grade 3 or higher adverse events related to treatment.

"Advancing bempikibart in AA is supported by preclinical data demonstrating the potential of IL-7Rα inhibition in this disease, and now the resulting data from SIGNAL-AA demonstrated the clinical potential of an IL-7Rα inhibitor in AA. I am encouraged by the biomarker data that provide evidence of biological activity, the safety profile of bempikibart, and the clinical signal of hair regrowth in patients," said Brett King, M.D., Ph.D., of Dermatology Physicians of Connecticut, and former Associate Professor of Dermatology, Yale University School of Medicine. "I believe these clinical results are promising and warrant further advancement to expand upon these findings."

Q32 Bio plans to enroll approximately 20 additional patients in a Part B expansion of the SIGNAL-AA Phase 2a clinical trial to further evaluate bempikibart in AA, including a loading regimen. The Company will defer enrollment into the planned Phase 2 clinical trial of ADX-097 in ANCA-Associated Vasculitis (AAV), previously expected to begin in 2025, to focus efforts on continued enrollment in the ongoing bempikibart AA and ADX-097 renal basket Phase 2 clinical trials.

Topline Results from SIGNAL-AD Phase 2a Clinical Trial:

SIGNAL-AD is a two-part Phase 2a, randomized, double-blind, placebo-controlled, multi-center clinical trial evaluating bempikibart in adult patients with persistent, moderate-to-severe AD. Part A (n=15) was conducted to evaluate safety, pharmacokinetics (PK), and to enable dose selection for Part B of the clinical trial. Part A was randomized 2:1 between bempikibart and placebo in each of two dose cohorts of 2mg/kg or 3mg/kg Q2W SC for 12 weeks.

In Part A, at week 14, improvement in average EASI score from baseline was 58% in patients treated with 2mg/kg Q2W SC and 84% in patients

treated at 3mg/kg Q2W SC, and 72% on a pooled basis, compared to 38% in patients treated with placebo.

In Part B, which evaluated both efficacy and safety of bempikibart compared to placebo, patients were enrolled 1:1 in the bempikibart 200 mg Q2W SC (n=52) and placebo (n=54) arms for 12 weeks of treatment. The primary endpoint is the mean percent change from baseline to week 14 in the Eczema Area and Severity Index (EASI) score. At week 14, data from Part B demonstrated that patients treated with bempikibart showed a 74% improvement in average EASI from baseline, compared to 76% for the placebo group (p= not statistically significant). Results of the primary endpoint were generally consistent when stratified for pre-specified baseline entry criteria. Bempikibart was observed to be safe and well tolerated in the SIGNAL-AD trial. There were no serious adverse events (SAE) or Grade 3 or higher adverse events related to treatment. Q32 Bio plans to conduct a review of the SIGNAL-AD results.

Biomarker Results in SIGNAL-AD and SIGNAL-AA:

Across SIGNAL-AD and SIGNAL-AA, bempikibart at 200mg Q2W SC demonstrated favorable PK and target engagement as demonstrated by substantial reductions in biomarkers of Th2 and Th1. These results include:

- A reduction in Th2 biomarkers, including TARC, IgE and eosinophils, which was consistent with the type of biomarker impact previously observed with other agents that have demonstrated utility in atopic dermatitis, such as IL-4Rα, IL-13 and OX40 ligand-targeted agents.
- An expected modulation of T-cells, with a 20-30% reduction, consistent with target engagement and IL-7Rα blockade.

Q32 Bio believes these results demonstrate that bempikibart is a potent inhibitor of both TSLP and IL-7 signaling as evidenced by robust changes in both Th2 biomarkers and T-cells. The Company believes the mechanism of action of bempikibart has the potential to be active in other Th2 and Th1 driven diseases, including asthma, COPD, ulcerative colitis (UC), rheumatoid arthritis (RA), celiac disease, multiple sclerosis (MS) and others.

"These impressive biomarker data represent a meaningful advancement in the clinical understanding of how inhibition of IL-7Rα can be leveraged to treat autoimmune and inflammatory diseases," said Shelia Violette, Ph.D., Co-Founder and Chief Scientific Officer of Q32 Bio. "Based upon its observed mechanism of action, bempikibart continues to show strong potential as an IL-7Rα inhibitor to treat AA and other diseases."

The Company has published an updated investor presentation with additional details regarding the bempikibart update for review by interested parties. The updated presentation can be found on the company website at www.Q32Bio.com under Investors & Media.

About Q32 Bio

Q32 Bio is a clinical stage biotechnology company developing biologic therapeutics targeting potent regulators of the innate and adaptive immune systems to re-balance immunity in autoimmune and inflammatory diseases. Q32 Bio's lead programs, focused on the IL-7 / TSLP receptor pathways and complement system, address immune dysregulation to help patients take back control of their lives.

Q32 Bio's program for adaptive immunity, bempikibart (ADX-914), is a fully human anti-IL-7Rα antibody that re-regulates adaptive immune function for the treatment of autoimmune diseases being evaluated in a Phase 2 program. The IL-7 and TSLP pathways have been genetically and biologically implicated in driving several T cell-mediated pathological processes in numerous autoimmune diseases. Q32 Bio's program for innate immunity, ADX-097, being evaluated in a Phase 2 program, is based on a novel platform enabling tissue-targeted regulation of the complement system without long-term systemic blockade – a key differentiator versus current complement therapeutics.

For more information, visit www.Q32Bio.com.

Availability of Other Information About Q32 Bio

Investors and others should note that we communicate with our investors and the public using our company website www.Q32Bio.com, including, but not limited to, company disclosures, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference call transcripts and webcast transcripts, as well as on X (formerly Twitter) and LinkedIn. The information that we post on our website or on X or LinkedIn could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

Forward-Looking Statements

This communication contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, and other federal securities laws. Any statements contained herein which do not describe historical facts, including, among others, our beliefs, observations, expectations and assumptions regarding the topline data from the SIGNAL-AA Phase 2a and the safety, tolerability, clinical activity including biomarker data, potential efficacy and potential benefits of bempikibart; plans and expectations for Part B of the SIGNAL-AA Phase 2a clinical trial are forward-looking statements, which involve risks and uncertainties that could cause actual results to differ materially from those discussed in such forward-looking statements.

Forward-looking statements are based on management's current beliefs and assumptions, which are subject to risks and uncertainties and are not guarantees of future performance. Such risks and uncertainties include, among others, the risk that additional data, or the results of ongoing data analyses, may not support our current beliefs and expectations for bempikibart, future clinical studies, including the Part B of the SIGNAL-AA Phase 2a clinical trial, may not be completed in a timely manner or at all, might be more costly than expected or might not yield anticipated results, the Company may need additional funding to complete its clinical studies, which may not be available on favorable terms or at all, and such other risks and uncertainties identified in the Company's periodic, current and other filings with the U.S. Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 and any subsequent filings with the Commission, which are available at the SEC's website at www.sec.gov. Any such risks and uncertainties could materially and adversely affect the Company's results of operations and its cash flows, which would, in turn, have a significant and adverse impact on the Company's stock price. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. The Company disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Contacts:
Investors: Brendan Burns
Media: Sarah Sutton
Argot Partners
212.600.1902
Q32Bio@argotpartners.com

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