X4 Pharmaceuticals Announces Presentation of Positive Data from Ongoing Phase 1b Clinical Trial of Mavorixafor in Waldenström's Macroglobulinemia at EHA 2021

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Robust decreases in serum IgM at low- and mid-doses suggest best-in-class potential for mavorixafor plus ibrutinib therapy in double-mutation Waldenström's patients; meaningful increases in hemoglobin levels suggest reduction in cancer burden in bone marrow

At 6 months, patients achieved median IgM level reductions of 60%-75%, with one patient achieving normal IgM, and two of four patients (50%) had >50% reduction in IgM from baseline

e-Poster now available online; pre-recorded presentation by lead author Dr. Steven Treon available to EHA conference attendees

Conference call and webcast today at 7:00 am ET with X4 management and poster co-author Dr. Christian Buske

BOSTON, June 11, 2021 (GLOBE NEWSWIRE) -- **X4 Pharmaceuticals, Inc.** (Nasdaq: XFOR), a leader in the discovery and development of novel therapies targeting diseases resulting from dysfunction of the CXCR4 pathway, today announced positive preliminary efficacy and safety data from its ongoing Phase 1b clinical trial of its lead candidate mavorixafor, in combination with ibrutinib, in Waldenström's macroglobulinemia patients with both MYD88 and CXCR4 mutations. These data are included in a poster published today at this year's European Hematology Association (EHA) Annual Congress.

"We are very pleased to present this exciting first look at the data from our ongoing Phase 1b trial in double-mutation Waldenström's patients," said Diego Cadavid, M.D., Chief Medical Officer of X4 Pharmaceuticals. "Despite still being in the low- and mid-dose ranges of mavorixafor, we are already seeing robust decreases in IgM levels – an important signal of clinical response – showing the potential benefit for mavorixafor in combination with ibrutinib. The combination therapy is demonstrating good tolerability and promising results across additional pharmacodynamic parameters, including increases in total hemoglobin and mobilization of white blood cells. We look forward to presenting longer-term data and an expanded data set from this trial later in the year."

"While ibrutinib has significantly advanced the treatment of Waldenström's macroglobulinemia, we have observed that there remains a clinical unmet need for patients with concurrent CXCR4 and MYD88 mutations," said Steven Treon, M.D., Ph.D., FACP, FRCP, Director of the Bing Center for Waldenström's Macroglobulinemia at Dana-Farber Cancer Institute, Professor of Medicine at Harvard Medical School, and the poster's lead author. "I am encouraged by the preliminary safety and efficacy data from the ongoing combination trial of ibrutinib and mavorixafor in this difficult-to-treat patient population and look forward to continuing this important research."

Key Highlights of the Preliminary Low- and Mid-Dose Phase 1b Results

- As of April 15, 2021, 8 patients had been enrolled in the Phase 1b clinical trial with a median duration of treatment of 156 days; data presented are primarily from patients in Cohort A who received low- and mid-range doses of mavorixafor plus ibrutinib; 4 patients were treated for more than six 28-day cycles.
- Mavorixafor exposures tracked with sustained and dose-dependent increases in white blood cell counts, confirming target engagement and mavorixafor mechanism of action.
- All patients (100%) experienced reductions in serum IgM and no patients' disease progressed while on treatment.
- At 6 months, mavorixafor plus ibrutinib showed signs of meaningful reductions in IgM versus comparable, previously published data of ibrutinib monotherapy in double-mutation patients:
    - Patients achieved median reductions of 60%-75% in serum IgM levels normalized to baseline; this compares to published ibrutinib monotherapy reductions of 38%-45% in double-mutation patients.
    - 2 out of 4 patients (50%) had >50% reduction in serum IgM from baseline; comparable reductions have been reported in only 28%-38% of double-mutation patients on ibrutinib monotherapy.
    - One patient achieved IgM levels within normal range, a key criterion for a complete response.
- All patients with hemoglobin levels below normal at baseline had increases during treatment, with a median change in hemoglobin of >20 g/L, approaching normal levels and suggesting reduction in cancer burden in the bone marrow.
- Mavorixafor and ibrutinib exposures were consistent with previous single-agent studies, suggesting no drug-drug interactions.

- Data suggest that mavorixafor plus ibrutinib is well tolerated with no serious adverse events reported.
- Patient enrollment and dose escalation to the highest mavorixafor dose (600 mg) continues.

The e-poster (EP784) entitled: *"Preliminary Clinical Data From a Phase 1b Study of Mavorixafor and Ibrutinib in Patients With Waldenström's Macroglobulinemia With MYD88 and CXCR4 Mutations"* is now available on the X4 corporate website. Conference attendees can access an accompanying audio presentation by Dr. Treon on the **Congress website.**

X4 will host a conference call and webcast at 7:00 am ET today that will include presentations by X4 senior executives and a "Fireside Chat" and Q&A with poster co-author Christian Buske, M.D., Director of the Institute of Experimental Cancer Research and Attending Physician, Senior Consultant at the University Hospital of Ulm, and Founder and Coordinator of the European Consortium for Waldenström's Macroglobulinemia.

The conference call can be accessed by dialing (866) 721-7655 (domestic) or (409) 216-0009 (international), followed by the conference ID: 4492859. The live webcast will be accessible on the Events & Presentations page of the company's website at **investors.x4pharma.com**. The conference call slide deck will be made available upon completion of the event and the webcast replay will be available approximately two hours after the completion of the event on X4's website.

This Phase 1b clinical trial is being conducted with the support of AbbVie Inc. and The Leukemia & Lymphoma Society's Therapy Acceleration Program® (LLS TAP).

About Waldenström's Macroglobulinemia and Associated CXCR4 Mutations
Waldenström's macroglobulinemia is a rare B-cell lymphoproliferative disorder characterized by increased immunoglobulin M (IgM). Greater than 90% of patients with Waldenström's have acquired mutations in the MYD88 gene, with a subset (30%–40%) also having mutations in chemokine receptor CXCR4. The presence of the CXCR4 mutation is associated with greater cancer burden, higher serum IgM levels, and increased risk of developing a serious emergent condition called symptomatic hyperviscosity syndrome. Importantly, the presence of CXCR4 mutations has been shown to negatively impact patients' response to ibrutinib (a BTK inhibitor), as manifested by delayed response, inferior depth of response, and/or shorter progression-free survival.

About Mavorixafor and the Phase1b Clinical Trial in Waldenström's Macroglobulinemia
Mavorixafor is an oral small-molecule antagonist of the CXCR4 receptor with a demonstrated ability to inhibit binding of its ligand, CXCL12; this inhibition of CXCR4 has been shown to sensitize Waldenström's cells with both MYD88 and CXCR4 mutations to BTK antagonists, such as ibrutinib. The ongoing Phase 1b, open-label, multicenter, single-arm study (NCT04274738) examines intra-patient dose escalation, safety, pharmacokinetics, and pharmacodynamics of mavorixafor in combination with ibrutinib in patients with a diagnosis of Waldenström's macroglobulinemia and confirmed MYD88 and CXCR4 genetic mutations. In the study, patients are initiated on oral, once-daily doses of ibrutinib 420 mg and mavorixafor 200 mg (low dose); in Cohort A, patients are escalated to 400 mg mavorixafor (mid-dose) after 28 days if fewer than two dose-limiting toxicities are observed at the low dose; in Cohort B, patients are escalated from 200 mg to 400 mg and finally to 600 mg (high dose) after each dose level is deemed tolerable. Patients are followed for adverse events and change from baseline in serum IgM and hemoglobin, pharmacokinetics, and pharmacodynamic markers, including peripheral white blood cell counts (WBCs).

About X4 Pharmaceuticals
X4 Pharmaceuticals is a late-stage clinical biopharmaceutical company and a leader in the discovery and development of novel therapies for the treatment of diseases resulting from dysfunction of the CXCR4 pathway, with a focus on rare diseases and those with limited treatment options. The company's lead candidate, mavorixafor, is a first-in-class, small molecule antagonist of chemokine receptor CXCR4 being developed as a once-daily oral therapy. X4 believes that inhibition of the CXCR4 receptor creates the potential for mavorixafor to provide therapeutic benefit across a wide variety of diseases, including primary immunodeficiencies and certain types of cancer. The efficacy and safety of mavorixafor, dosed once daily, is currently being evaluated in a global Phase 3 clinical trial in patients with WHIM syndrome, and in two Phase 1b clinical trials – in combination with ibrutinib in patients with Waldenström's macroglobulinemia, and as monotherapy in patients with severe congenital neutropenia (SCN). X4 is continuing to leverage its insights into CXCR4 biology at its corporate headquarters in Boston, Massachusetts and at its research facility in Vienna, Austria, and is discovering and developing additional product candidates. For more information, please visit www.x4pharma.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These statements may be identified by the words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target," or other similar terms or expressions that concern X4's expectations, strategy, plans, or intentions. Forward-looking statements include, without limitation, statements regarding the clinical development of mavorixafor for the treatment of Waldenström's macroglobulinemia and primary immunodeficiencies, the potential benefits of mavorixafor in the treatment of Waldenström's macroglobulinemia or any other indication, and the availability and timing of future data from X4's ongoing clinical trial of mavorixafor for the treatment of Waldenström's macroglobulinemia. Any forward-looking statements in this press release are based on management's current expectations and beliefs. Actual events or results may differ materially from those expressed or implied by any forward-looking statements contained herein, including, without limitation, the risk that trials and studies may be delayed and may not have satisfactory outcomes, the risk that initial or interim results from a clinical trial may not be predictive of the final results of the trial or the results of future trials, the potential adverse effects arising from the testing or use of mavorixafor or other product candidates, and other risks and uncertainties, including those described in the section entitled "Risk Factors" in X4's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 6, 2021, and in other filings X4 makes with the SEC from time to time. X4 undertakes no obligation to update the information contained in this press release to reflect new events or circumstances, except as required by law.

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