NEWS RELEASE

Citius Pharmaceuticals, Inc. and Citius Oncology, Inc. Announce Promising Preliminary Results of an Investigator-Initiated Phase I Clinical Trial of Pembrolizumab (KEYTRUDA®) and LYMPHIR™ in Cancer Patients with Recurrent Solid Tumors

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Study, in patients with solid tumors focusing on gynecological malignant tumors such as ovarian, endometrial, and cervical, nearing completion with three remaining subjects to be enrolled

27% Objective Response Rate (ORR)

33% Clinical Benefit Rate (CBR) with a median Progression Free Survival (PFS) of 57 weeks

Chemotherapy-free immunomodulatory regimen well-tolerated with no documented serious immune-related adverse events

CRANFORD, N.J., Nov. 11, 2024 /PRNewswire/ -- Citius Pharmaceuticals, Inc. ("Citius Pharma" or the "Company") (Nasdaq: CTXR) and Citius Oncology, Inc. ("Citius Oncology") (Nasdaq: CTOR), today announced promising preliminary results from an ongoing investigator-initiated Phase I clinical trial evaluating the safety and efficacy of a combined regimen of pembrolizumab and LYMPHIR™ (denileukin diftitox-cxdl or E7777) in patients with recurrent solid tumors. The data was summarized in a poster presentation titled "T-regulatory Cell Depletion with E7777 (denileukin diftitox-xcdl) Combined with Pembrolizumab in patients with recurrent solid tumors: Phase I trial" presented at the Society for Immunotherapy of Cancer (SITC) 2024 Annual Meeting held November 8-10, 2024

(Abstract 614).

The trial is being conducted by Haider Mahdi, M.D., Assistant Professor, Department of Obstetrics, Gynecology & Reproductive Sciences, at the University of Pittsburgh. The study aims to identify an optimal dose for future trials and explore the impact of a treatment regimen combining pembrolizumab and LYMPHIR on the tumor immune microenvironment.

"We have seen promising results in patients with heavily pre-treated recurrent or metastatic gynecologic tumors and will enroll three additional patients before completing the Phase I portion of this study," said Mahdi. "We will further investigate in patients with gynecologic tumors and those with other solid tumor histologies. We want to explore the impact of this therapy on Tregs, host immune-effector cells and the tumor microenvironment."

"The preliminary results from this Phase I trial of patients with recurrent gynecological cancers are highly encouraging. This novel chemo-free immunomodulatory combination regimen has been well tolerated, including at the highest dosage. This efficacy data strongly suggests that LYMPHIR may have the ability to improve and prolong the anti-tumor activity of immune checkpoint inhibitors. To date, this unique regimen has not been associated with significant immune-related adverse events. Moreover, of the 15 evaluable patients, one third experienced a clinical benefit with a median of more than 12 months of progression free survival," stated Dr. Myron Czuczman, Chief Medical Officer of Citius Pharmaceuticals and Citius Oncology.

"There is reason to be optimistic about the potential of LYMPHIR to boost a patient's response to pembrolizumab by temporarily depleting Tregs that modulate the tumor microenvironment, without triggering an autoimmune response from the patient's body. We believe the positive signals from this data support expanding the research in a Phase II study to further evaluate the combination's benefits across a broader range of solid tumor types," he added.

PD-1 inhibitors such as pembrolizumab are a type of immune checkpoint inhibitor that works by blocking the PD-1 protein on T cells, enabling the immune system to recognize and attack cancer cells. Pembrolizumab, developed by Merck and sold under the brand name KEYTRUDA®, is the leading PD-1 inhibitor and world's most prescribed drug, generating $25 billion in sales in 2023.

Preliminary Results

The results of this chemotherapy-free regimen combining two immuno-modulator agents, pembrolizumab (anti-PD-1) and LYMPHIR (transient Treg depletion) demonstrated:

- An overall response rate (ORR) of 27% (4/15) and a clinical benefit rate of 33% (5/15) among evaluable

patients; and,

- Median progression-free survival (PFS) for patients achieving clinical benefit of 57 weeks, with a range of 30 to 96 weeks.
- Notably, two of the four patients who achieved partial remission had received prior checkpoint inhibitors (i.e. anti-PD-1 therapy). This highlights the therapeutic potential of LYMPHIR plus immune checkpoint inhibitors to be effective in patients who fail prior anti-PD-1/L1 therapy.

The trial enrolled 21 patients with recurrent or metastatic solid tumors. Among the evaluable participants, four patients achieved a partial response, and one patient demonstrated durable stable disease lasting over six months. The combination regimen was generally well tolerated, with most adverse events related to the patients' underlying disease. Importantly, no significant immune-related adverse events were observed, and only one case of dose-limiting toxicity (capillary leak syndrome) was reported at the highest dose level (12 mcg/kg).

Table 1: Efficacy Data

	Value
Patients Enrolled	21
Patients Evaluable for Response	15
Partial Responses (PR)	4 (27 %)
Stable Disease (≥ 6 months)	1
Clinical Benefit Rate (CBR)	33% (PR + SD ≥ 6 months)
Median Progression-Free Survival (PFS)	57 weeks (range: 30-96 weeks)

Table 2: Safety Data

	Value
Dose-Limiting Toxicities (DLTs)	1 (Capillary Leak Syndrome at 12 mcg/kg)
Immune-Related Adverse Events (irAEs)	None documented (≥ Grade 3)
Adverse Events (Grade ≥ 3)	Most related to underlying disease

Trial Design

The Phase I trial is an open-label study designed to evaluate the safety and preliminary efficacy of pembrolizumab, an anti PD-1 inhibitor, in combination with LYMPHIR in patients with recurrent or metastatic solid tumors. The trial employs a dose-escalation approach, with LYMPHIR administered in four dose levels (3, 6, 9, and 12 mcg/kg) in

combination with pembrolizumab (200 mg) on a 21-day cycle for eight cycles. Following the combination regimen, patients receive pembrolizumab monotherapy as maintenance therapy. The study utilizes the Time-to-Event Continual Reassessment Method (TITE-CRM) to assess dose-limiting toxicities (DLTs) and determine the recommended Phase II dose (RP2D).

Key inclusion criteria include measurable disease, ECOG performance status of 0-1, and adequate organ function. Patients with recurrent or metastatic solid tumors who have received at least one prior line of therapy were eligible for enrollment.

The trial enrolled patients with a variety of recurrent or metastatic solid tumors, including ovarian, endometrial, and cervical cancers.

- Ovarian Cancer: Ovarian cancer is the eighth most common cancer in women worldwide, with an estimated 324,000 new cases diagnosed annually. In the United States, approximately 240,000 women are currently living with ovarian cancer.

- Endometrial Cancer: Worldwide, approximately 420,000 new cases are diagnosed each year. Endometrial cancer is the most common gynecologic cancer in the United States, with approximately 66,000 new cases diagnosed each year. It is estimated that over 600,000 women in the U.S. are living with endometrial cancer.

- Cervical Cancer: Cervical cancer remains a major health concern globally, with around 660,000 new cases annually. It is the fourth most common cancer among women. In the United States, approximately 11,500 women are diagnosed each year.

About LYMPHIR™ (denileukin diftitox-cxdl)

LYMPHIR is a targeted immune therapy for relapsed or refractory cutaneous T-cell lymphoma (CTCL) indicated for use in Stage I-III disease after at least one prior systemic therapy. It is a recombinant fusion protein that combines the IL-2 receptor binding domain with diphtheria toxin fragments. The agent specifically binds to IL-2 receptors on the cell surface, causing diphtheria toxin fragments that have entered cells to inhibit protein synthesis. After uptake into the cell, the DT fragment is cleaved and the free DT fragments inhibit protein synthesis, resulting in cell death. Denileukin diftitox-cxdl demonstrated the ability to deplete immunosuppressive regulatory T lymphocytes (Tregs) and antitumor activity through a direct cytocidal action on IL-2R-expressing tumors.

In 2021, denileukin diftitox received regulatory approval in Japan for the treatment of CTCL and PTCL. Subsequently, in 2021, Citius acquired an exclusive license with rights to develop and commercialize LYMPHIR in all markets except for Japan and certain parts of Asia. LYMPHIR was approved by the FDA in August 2024.

INDICATION

LYMPHIR is an IL2-receptor-directed cytotoxin indicated for the treatment of adult patients with r/r Stage I-III cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: CAPILLARY LEAK SYNDROME

Capillary leak syndrome (CLS), including life-threatening or fatal reactions, can occur in patients receiving LYMPHIR. Monitor patients for signs and symptoms of CLS during treatment. Withhold LYMPHIR until CLS resolves, or permanently discontinue based on severity.

WARNINGS AND PRECAUTIONS

Capillary Leak Syndrome

LYMPHIR can cause capillary leak syndrome (CLS), including life-threatening or fatal reactions. CLS was defined in the clinical trials as the occurrence of at least 2 of the following symptoms at any time during LYMPHIR therapy: hypotension, edema, and serum albumin <3 g/dL. These symptoms were not required to occur simultaneously to be characterized as capillary leak syndrome.

As defined, CLS occurred in 27% of patients in the pooled population across 3 clinical trials, including 8% with Grade 3. There was one (0.8%) fatal occurrence of CLS. Of the patients with CLS, 22% had recurrence. The majority of CLS events (81%) occurred within the first 2 cycles of treatment. The median time to onset from Cycle 1, Day 1 was 6.5 days (range: 1 to 77), the median duration of CLS was 14 days (range: 2 to 40), and 75% of patients had resolution. The most common symptoms included edema, hypoalbuminemia, and hypotension. Pleural effusion, pericardial effusion, and dehydration also occurred.

Regularly assess patients for weight gain, new onset or worsening of edema, dyspnea, and hypotension (including orthostatic changes). Monitor serum albumin levels prior to the initiation of each cycle of therapy and more often as clinically indicated.

Withhold, reduce dose, or permanently discontinue based on severity. If LYMPHIR is withheld, resume LYMPHIR following resolution of CLS and when serum albumin is greater than or equal to 3 g/dL.

Visual Impairment

LYMPHIR can cause serious visual impairment, including changes in visual acuity and color vision. In the pooled population across 3 clinical trials, visual impairment occurred in 9%, with Grade 1 in 8% and Grade 2 in 1%. The most commonly reported symptom was blurred vision. Of the patients with visual impairment, 67% had resolution of their visual impairment.

Perform baseline ophthalmic examination and monitor as clinically indicated. If patients experience symptoms of visual impairment, such as changes in visual acuity, changes in color vision, or blurred vision, refer for ophthalmologic evaluation.

Withhold LYMPHIR until visual impairment resolves or permanently discontinue based on severity.

Infusion-Related Reactions

LYMPHIR can cause serious infusion-related reactions. Infusion-related reactions were reported in 69% of patients in the pooled population across 3 clinical trials of patients who received LYMPHIR, with Grade 3 infusion-related reactions in 3.4% [see Adverse Reactions (6.1)]. Eighty-three percent of infusion-related reactions occurred in Cycles 1 and 2. The most common symptoms included nausea, fatigue, chills, musculoskeletal pain, vomiting, fever, and arthralgia.

Premedicate patients for the first three cycles prior to starting a LYMPHIR infusion [see Dosage and Administration (2.3)]. Monitor patients frequently during infusion. For Grade 2 or higher infusion reactions, premedicate at least 30 minutes prior to each subsequent infusion with a systemic steroid for at least 3 cycles.

Interrupt or discontinue LYMPHIR based on severity [see Dosage and Administration (2.4)]. Institute appropriate medical management.

Hepatotoxicity

LYMPHIR can cause hepatotoxicity. In the pooled safety population, elevated ALT occurred in 70% of patients, with Grade 3 ALT occurring in 22%; elevated AST occurred in 64% of patients, with Grade 3 AST elevation occurring in 9%. For Grade 3 events, median time to onset was 8 days (range: 1 to 15 days); median time to resolution was 15 days (range: 7 to 50 days); all cases of Grade 3 ALT or AST elevations resolved [see Adverse Reactions (6.1)]. Elevated total bilirubin occurred in 5% of patients, with Grade 3 occurring in 0.9%.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold, reduce dose,

or permanently discontinue LYMPHIR based on severity.

Embryo-Fetal Toxicity

Based on its mechanism of action, LYMPHIR can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to the initiation of LYMPHIR. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment and for 7 days following the last dose of LYMPHIR.

ADVERSE REACTIONS

The most common adverse reactions (≥20%), including laboratory abnormalities, are increased transaminases, albumin decreased, nausea, edema, hemoglobin decreased, fatigue, musculoskeletal pain, rash, chills, constipation, pyrexia, and capillary leak syndrome

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on its mechanism of action, LYMPHIR can cause fetal harm when administered to a pregnant woman. There are no available data on the use of LYMPHIR in pregnant women to evaluate for a drug-associated risk. No animal reproductive and developmental toxicity studies have been conducted with denileukin diftitox.

Denileukin diftitox-cxdl causes depletion of regulatory T lymphocytes (Treg), immune activation, and capillary leak syndrome, compromising pregnancy maintenance. Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.

Lactation

Risk Summary

No data are available regarding the presence of denileukin diftitox-cxdl in human milk, the effects on the breastfed child, or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with LYMPHIR and for 7 days after the last dose.

Females and Males of Reproductive Potential

Based on its mechanism of action, LYMPHIR can cause fetal harm when administered to a pregnant woman.

Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating LYMPHIR.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with LYMPHIR and for 7 days after the last dose.

Infertility

Males

Based on findings in rats, male fertility may be compromised by treatment with. The reversibility of the effect on fertility is unknown.

Pediatric Use

Safety and effectiveness of LYMPHIR in pediatric patients have not been established.

Geriatric Use

Of the 69 patients with Stage I-III r/r CTCL who received LYMPHIR, 34 patients (49%) were 65 years of age and older and 10 patients (14%) were 75 years of age and older. Clinical studies of LYMPHIR did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

You may report side effects to the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**. You may also report side effects to Citius Pharmaceuticals at 1-844-459-6744.

Please read Important Safety Information and **full Prescribing Information**, including Boxed WARNING, for LYMPHIR™.

Please see **Prescribing Information** for KEYTRUDA® (pembrolizumab) and **Medication Guide** for KEYTRUDA.

About Citius Oncology, Inc.

Citius Oncology, Inc. (Nasdaq: CTOR) is a platform to develop and commercialize novel targeted oncology therapies. In August 2024, its primary asset, LYMPHIR, was approved by the FDA for the treatment of adults with relapsed or refractory CTCL who had had at least one prior systemic therapy. Management estimates the initial market for LYMPHIR currently exceeds $400 million, is growing, and is underserved by existing therapies. Robust intellectual property protections that span orphan drug designation, complex technology, trade secrets and pending patents for immuno-oncology use as a combination therapy with checkpoint inhibitors would further support Citius Oncology's competitive positioning. For more information, please visit **www.citiusonc.com**.

About Citius Pharmaceuticals, Inc.

Citius Pharmaceuticals, Inc. (Nasdaq: CTXR) is a biopharmaceutical company dedicated to the development and commercialization of first-in-class critical care products. In August 2024, the FDA approved LYMPHIR, a targeted immunotherapy for an initial indication in the treatment of cutaneous T-cell lymphoma. Citius Pharma's late-stage pipeline also includes Mino-Lok®, an antibiotic lock solution to salvage catheters in patients with catheter-related bloodstream infections, and CITI-002 (Halo-Lido), a topical formulation for the relief of hemorrhoids. A Pivotal Phase 3 Trial for Mino-Lok and a Phase 2b trial for Halo-Lido were completed in 2023. Mino-Lok met primary and secondary endpoints of its Phase 3 Trial. Citius is actively engaged with the FDA to outline next steps for both programs. Citius Pharmaceuticals owns 92% of Citius Oncology. For more information, please visit **www.citiuspharma.com**.

Forward-Looking Statements

This press release may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Such statements are made based on our expectations and beliefs concerning future events impacting Citius. You can identify these statements by the fact that they use words such as "will," "anticipate," "estimate," "expect," "plan," "should," and "may" and other words and terms of similar meaning or use of future dates. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock price. Factors that could cause actual results to differ materially from those currently anticipated, and, unless noted otherwise, that apply to Citius Pharma and Citius Oncology, are: risks relating to the results of research and development activities, including those from our existing and any new pipeline assets; risks related to research using our assets but conducted by third parties; our need for substantial additional funds; Citius Pharma's ability to meet Nasdaq's continued listing standards; our ability to commercialize LYMPHIR and any of our other product candidates that may be approved by the FDA; the estimated markets for our

product candidates and the acceptance thereof by any market; the ability of our product candidates to impact the quality of life of our target patient populations; our dependence on third-party suppliers; our ability to procure cGMP commercial-scale supply; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; uncertainties relating to preclinical and clinical testing; the early stage of products under development; market and other conditions; risks related to our growth strategy; patent and intellectual property matters; our ability to identify, acquire, close and integrate product candidates and companies successfully and on a timely basis; government regulation; competition; as well as other risks described in our SEC filings. These risks have been and may be further impacted by any future public health risks. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings which are available on the SEC's website at **www.sec.gov**, including in Citius Pharma's Annual Report on Form 10-K for the year ended September 30, 2023, filed with the SEC on December 29, 2023, Citius Oncology's Current Report on Form 8-K, filed with the Commission on August 16, 2024 (as amended by Amendment No. 1 to Form 8-K, filed on August 26, 2024), both as updated by our subsequent filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof, and we expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law.

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