CytomX Therapeutics, Inc. Logo

CytomX Therapeutics Provides Business Update and Outlines 2023 Company Priorities

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- CX-2029 (CD71 conditionally activated ADC) continued to demonstrate encouraging anti-cancer activity in squamous tumors in the now completed Phase 2 Cohort Expansion Study. AbbVie and CytomX to determine next steps for program in 2023 -

- CytomX and Moderna announce today, separately, a strategic collaboration to research and develop messenger RNA-based conditionally activated therapeutics -

- Broad pipeline progress anticipated in 2023 including continued advancement of clinical stage partnered programs, filing of two INDs for next generation wholly owned programs and broadening of R&D activities in field of T-Cell Bispecifics (TCBs) -

- CytomX to host conference call today at 5 p.m. EST / 2 p.m. PST -

SOUTH SAN FRANCISCO, Calif., Jan. 05, 2023 (GLOBE NEWSWIRE) -- CytomX Therapeutics, Inc. (Nasdaq: CTMX), a leader in the field of conditionally activated, localized biologics, today announced its 2023 company priorities and provided a pipeline update which included anticipated milestones for 2023, recent progress and achievements in its wholly owned and collaboration pipeline, and a data update for the Phase 2, CX-2029 cohort expansion study. The company will host a call with investors today to review the CX-2029 cohort expansion study data and potential key pipeline events for 2023.

"We are delighted to enter 2023 with strong momentum across all areas of our business. CytomX's scientific depth and leadership in pioneering the field of conditionally activated, localized biologics has enabled us to build a robust therapeutic pipeline and continue to attract elite partners with a shared vision of pursuing bold science to positively impact the lives of people with cancer," said Sean McCarthy, D.Phil., chief executive officer and chairman of CytomX Therapeutics. "For CX-2029 specifically, we have pushed the boundaries of biologics localization with our Probody® technology to create a therapeutic window for the previously undruggable target, CD71. The full CX-2029 Phase 2 cohort expansion data continues to demonstrate encouraging clinical activity in unselected, heavily pre-treated patients with tumors of squamous histology and we look forward to working with our partner AbbVie to determine the next steps for this program," continued Dr. McCarthy.

"We also start 2023 with an exciting new collaboration with Moderna that combines the power of our respective technologies to break new ground in oncology and other areas of unmet medical need. This latest alliance comes just weeks after our announcement of a major new collaboration with Regeneron. These collaborations underscore CytomX's innovation and leadership and further strengthen our organizational foundation as we build for the future. Looking further out into 2023, we expect to make meaningful progress with AbbVie and BMS, to continue Phase 1 investigation of our first T-cell engaging therapy (CX-904) and to file INDs for two new wholly owned programs," continued Dr. McCarthy.

CX-2029 PHASE 2 COHORT EXPANSION DATA UPDATE

Study Highlights and Next Steps:

- The updated study results reflect an August 5, 2022, full data cut and an October 4, 2022, data snapshot for efficacy.
- The data demonstrate encouraging clinical activity in unselected, heavily pre-treated patients with tumors of squamous histology including a 21% objective response rate (ORR) in squamous esophageal cancer and a 10% ORR in squamous non-small cell lung cancer (sqNSCLC).
- The adverse event (AE) profile was consistent with Phase 1 observations with anemia (82.6%) being the most common treatment related adverse event (TRAE). Anemia was managed with transfusions, dose delays, and reductions.
- Treatment discontinuation rate due to AEs was 3.3% as a result of anemia.
- CytomX and AbbVie will determine potential next steps for CX-2029 in 2023.

Study Background:

- The enrolled study cohorts included advanced esophageal/gastro-esophageal junction cancer (E/GEJ), squamous non-small cell lung cancer (sqNSCLC), and head and neck squamous cell carcinoma (HNSCC). The efficacy-evaluable study population included 29 patients with E/GEJ, 30 patients with sqNSCLC, and 28 patients with HNSCC. These patients had received at least one dose of CX-2029 at 3 mg/kg and had at least one post baseline assessment, including, per protocol, 5 patients (2 sqNSCLC and 3 HNSCC) enrolled in the previously reported dose escalation phase. Patients were not selected for CD71 expression.

Data Highlights:

- In the 29 efficacy evaluable patients with E/GEJ, 14 patients had squamous esophageal cancer.
    - In the 14 patients with squamous esophageal cancer, the ORR was 21.4% (3 patients) and 35.7% (5 patients) had a best response of stable disease (SD). As of the Oct 4th data snapshot, 5 patients remained on study (3 confirmed partial responses (cPRs) and 2 SD), 3 of whom had already been on study for 24 weeks, suggesting promising durability of response.

- There were no confirmed responses in E/GEJ patients with non-squamous tumors. 4 patients had a best response of stable disease with two on study greater than 6 months.
- In the 30 efficacy evaluable patients with sqNSCLC, objective response rate (ORR) by local investigator was 10.0%. 56.7% (17 sqNSCLC patients) of patients had a best response of stable disease.
- In 28 patients with HNSCC, the confirmed ORR was 4% (1 patient with duration of response of approximately 12 months) and 46.4% (13 patients) had a best response of SD, including one with duration of response of approximately 10 months, and one unconfirmed PR.

Summary table of the efficacy results: (For Discussion on Conference Call)

Efficacy Evaluable Population [a]	Esophageal Squamous n=14**	Esophageal Adeno/GEJ /Other n=15	SqNSCLC n=30	HNSCC n=28**
Complete Response (CR)	0	0	0	0
Partial Response (PR)	3 (21.4)	0 (0.0)	3 (10.0)	2 (7.1)
Confirmed PR (%)	3 (21.4)	0 (0.0)	3 (10.0)	1 (3.6)
Unconfirmed PR (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)
Stable Disease	5 (35.7)	4 (26.7)	17 (56.7)	13 (46.4)
Disease Control Rate*	8 (57.1)	4 (26.7)	20 (66.7)	15 (53.6)
Progressive Disease	5 (50.0)	11 (73.3)	10 (33.3)	12 (42.9)

[a]Includes patients who received at least one post-baseline assessment and includes 5 patients from Part B dosed at 3 mg/kg Q3W
* A best response of CR, PR, or SD at the first post-baseline assessment
**1 patient not evaluable

Safety:

Safety analysis was conducted on all patients who received at least one dose of CX-2029 at 3 mg/kg (N=92). The median number of prior therapies in the metastatic setting was three (range, 1-12) for sqNSCLC, four (range, 1-9) for HNSCC, and three (range, 1-6) for Esophageal. All patients with sqNSCLC had received prior platinum and prior checkpoint inhibition; in HNSCC, all but one patient received prior platinum and all but two, prior checkpoint inhibition; in G/EJ, 100% of patients received prior platinum; in squamous esophageal, 60% of patients received prior checkpoint inhibition, and in non-squamous esophageal 20% of patients received prior checkpoint inhibition therapy.

- The safety profile was consistent with previous observations, with no new safety signals identified. The most common treatment-related adverse events (TRAEs) in 10% or more of patients (All Grade, Grade 3+) were anemia (82.6%, 76.1%), infusion related reactions (70.7%, 3.3%), neutropenia (23.9%, 17.4%), fatigue (17.4%, 1.1%), nausea (13.0%, 1.1%), and diarrhea (10.9%, 0%). There was 1 febrile neutropenia event (Grade 3) reported.
- The most common reason for treatment discontinuation was disease progression (77.1%), three patients (3.3%) discontinued due to treatment-related anemia.
- Five squamous esophageal patients were still on treatment as of the October 4th, 2022, data snapshot.

EXPANDING R&D ACTIVITIES IN FIELD OF T-CELL ENGAGING BISPECIFICS (TCBS)

The localization of the potent activity of T-cell engagers in solid tumors is a major opportunity in cancer research and development and the Probody® platform may be ideally suited to unlock this important modality. In addition to CX-904, CytomX has developed significant expertise and capabilities in TCB discovery and clinical candidate optimization through its biologic masking strategies which has resulted in meaningful pre-clinically pipeline opportunities in both its wholly owned and collaboration pipeline.

CX-904 (EGFRxCD3 bispecific) Phase 1 Clinical Study Ongoing

The first patient in the CX-904-101 Phase 1 study was dosed in May 2022. The trial continues to enroll patients with advanced solid tumors and has successfully advanced through the single-patient cohort phase of dose escalation. The trial has now entered the “3+3” stage of dose escalation and continues to enroll patients. The continued progression of CX-904 is a key priority for the company in 2023 with the primary goal of assessing safety and determining a recommended dose, or doses, for subsequent expansions in select tumor types. This program is partnered with Amgen in a global co-development alliance.

Progress in Astellas TCB Collaboration

Under the agreement with Astellas, the companies are collaborating on conditionally activated TCB programs with CytomX eligible to receive future preclinical, clinical and commercial milestones. CytomX retains a cost share and co-commercialization option on a select number of targets. The progress in the collaboration demonstrates Astellas’ and CytomX’s commitment to leveraging T-cell engaging bispecifics for cancer immunotherapy.

Regeneron Bispecific Collaboration Initiated

In November 2022, CytomX announced its collaboration with Regeneron to enable the development of investigational next-generation bispecific immunotherapies using CytomX’s Probody ® and Regeneron's Veloci-Bi® platforms. The Probody® platform has the potential to widen the therapeutic window and help minimize off-target effects for these next-generation T-cell engaging therapies, potentially addressing tumor types that have historically been unresponsive to immunotherapy. CytomX received a $30 million upfront payment in December 2022 and is eligible for up to

approximately $2 billion in research, development, regulatory and sales-based milestones.

EMERGING NEXT-GENERATION WHOLLY OWNED PIPELINE: TWO INDS TARGETED FOR 2023

CytomX's continued investment in cutting-edge science and leadership in the field of biologics localization has resulted in a depth of understanding in protease biology and the tumor microenvironment that enables the company to pursue a broad range of pipeline opportunities and continuously raise the bar for investigational medicines that enter the clinic. For CytomX's next generation molecules, the company has selected the previously validated anti-cancer targets, EpCAM and IFNa2b, respectively, that have been limited in their potential due to systemic toxicities. In the molecular design of CX-2051 and CX-801, we have incorporated our platform expertise and clinical learnings to optimize predicted therapeutic index in order to potentially broaden the clinical utility of these promising targets through tumor localized conditional activation.

CX-801, Interferon-alpha 2b (IFNa2b)

Interferon-alpha 2 beta is an approved immunotherapeutic that has demonstrated clinical activity in multiple cancer types, including in combination with checkpoint inhibitors. IFNa2b provides a potentially superior approach to activating anti-tumor immune responses than other cytokines. CX-801 is a dually masked, conditionally activated version of IFNa2b that has the potential to become a unique centerpiece of combination therapy for a wide range of tumor types. The company plans to rapidly advance this potentially best-in-class program towards clinical evaluation with an IND filing targeted for the second half of 2023.

CX-2051, Antibody Drug Conjugate (ADC) targeting EpCAM

EpCAM is a high potential oncology target that has been clinically validated with locally administered, approved cancer therapies. However, efforts to generate systemic anti-EpCAM therapeutics have, to date, not been successful due to toxicities in epithelial tissues. CX-2051, a conditionally activated ADC, is tailored to optimize the therapeutic index for EpCAM-expressing epithelial cancers. CX-2051's payload is camptothecin, a topoisomerase-1 inhibitor, that has a well characterized profile base on the strong clinical activity observed with other topoisomerase-1 inhibiting ADCs. CX-2051 has demonstrated a wide predicted therapeutic index and strong preclinical activity and tolerability in multiple preclinical models, including colorectal cancer. The company anticipates filing an IND for this novel ADC in the second half of 2023.

BMS ANTI-CTLA-4 PROBODY® PROGRAMS

Bristol Myers Squibb (BMS) continues to make important progress in its next-generation CTLA-4 programs, including with BMS-986249, the Probody version of ipilimumab and BMS-986288, a non-fucosylated CTLA-4 targeting Probody.

CytomX anticipates continued progress from Bristol Myers Squibb on these programs in 2023.

BMS-986249 (Masked version of ipilimumab)

BMS is evaluating BMS-986249 in a randomized Phase 2 study in combination with nivolumab, versus ipilimumab plus nivolumab, in patients with advanced melanoma. The combination is also being studied in advanced hepatocellular carcinoma, castration-resistant prostate cancer, and triple-negative breast cancer. At ESMO 2022, BMS presented promising updated Phase 1 data for BMS-986249 from an ongoing Phase 1/2 study in patients with advanced cancers. These data demonstrated that as a monotherapy and in combination with nivolumab, BMS-986249 may be tolerated at higher doses than standard ipilimumab clinical dosing. Clinical activity was also demonstrated in multiple tumor types, including melanoma and a particularly encouraging case study of a response in microsatellite-stable colorectal cancer.

BMS-986288 (Non-fucosylated CTLA-4 targeting Probody)

BMS also continues to study the non-fucosylated CTLA-4-targeting Probody, BMS-986288, in a Phase 1 / 2 study, both as monotherapy and also in combination with nivolumab, in patients with advanced solid tumors. This strategy is aimed at enhancing the clinical benefit of ipilimumab by superior antigen presenting cell (APC)-mediated T cell priming.

MODERNA ALLIANCE

The new collaboration, announced today, will combine CytomX's Probody® Platform with Moderna's mRNA technologies to generate and develop therapeutics for oncology and non-oncology conditions. CytomX will receive a $35 million upfront payment with the potential for up to approximately $1.2 billion in research, development, regulatory and sales-based milestones. The research collaboration will leverage core scientific advances at Moderna and CytomX. Moderna's mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases, and autoimmune diseases. CytomX's Probody technology enables proteins to be activated locally in diseased tissue, while remaining masked in systemic circulation. These advances open up the strategy of encoding potent, masked biologics with mRNA, for the potential treatment of a wide range of diseases.

2023 KEY MILESTONES AND OUTLOOK

CytomX enters 2023 in a strong strategic position and with significant momentum in its pipeline. In 2023, the company expects to see the continued realization of our vision for conditionally activated, localized therapies through key pipeline milestones including:

- **CX-904 (EGFRxCD3):** Continue patient enrollment and dose escalation in ongoing Phase 1 study
- **File 2 New INDs:** CX-801 (IFNa2b) and CX-2051 (EpCAM) projected in 2H 2023
- **CX-2029 (CD71):** Determine next steps with AbbVie
- **BMS CTLA-4:** Continued clinical progress on BMS-986249 and BMS-986288
- **Collaborations:** Initiation of R&D activities with our newest collaborators, Regeneron and Moderna

The company also remains in a strong financial position with cash into 2025 and a capital allocation, financing and business development strategy focused on both managing variable financial market conditions and delivering meaningful long-term value for patients and stakeholders.

Conference Call & Webcast

CytomX management will host a conference call and a simultaneous webcast today, January 5th 2023 at 5 p.m. ET (2 p.m. PT). A live webcast of the call can be accessed via the Events and Presentations page of CytomX's website at https://ir.cytomx.com/events-and-presentations. A replay of the webcast will also be available for 30 days following the call.

About CytomX Therapeutics

CytomX is a clinical-stage, oncology-focused biopharmaceutical company dedicated to destroying cancer differently. By pioneering a novel class of conditionally activated biologics, powered by its Probody® technology platform, CytomX's goal is to transcend the limits of current cancer treatments. CytomX's robust and differentiated pipeline comprises seven therapeutic candidates across multiple treatment modalities including antibody-drug conjugates ("ADCs"), T-cell engaging bispecific antibodies ("TCBs"), and immune modulators such as cytokines and checkpoint inhibitors ("CPIs"). CX-2029 is an investigational conditionally activated antibody-drug conjugate (ADC) directed toward CD71, which has demonstrated encouraging antitumor activity in patients with squamous non-small cell lung cancer and is being developed in collaboration with AbbVie. CytomX's clinical pipeline also includes cancer immunotherapeutic candidates against validated targets such as the CTLA-4-targeting Probody therapeutics, BMS-986249 and BMS-986288, partnered with Bristol Myers Squibb, as well as CX-904, a conditionally activated T-cell-engaging bispecific antibody targeting the epidermal growth factor receptor (EGFR) on tumor cells and the CD3 receptor on T cells, which is partnered with Amgen. In addition, CytomX has a diverse preclinical portfolio of wholly-owned assets including CX-801, an interferon alpha-2b Probody cytokine that has broad potential applicability in traditionally immuno-oncology sensitive as well as insensitive (cold) tumors and CX-2051, a conditionally activated ADC directed toward EpCAM, with potential applicability across multiple EpCAM-expressing epithelial cancers. CytomX has also established strategic collaborations with multiple leaders in oncology, including AbbVie, Amgen, Astellas, Bristol Myers Squibb, Regeneron and Moderna. For more information about CytomX and how it is working to make conditionally activated treatments the new standard-of-care in the fight against cancer, visit www.cytomx.com and follow us on LinkedIn and Twitter.

CytomX Therapeutics Forward-Looking Statements

This press release includes forward-looking statements. Such forward-looking statements involve known and unknown risks, uncertainties and other important factors that are difficult to predict, may be beyond our control, and may cause the actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied in such statements, including those related to the future potential of partnerships or collaboration agreements. Accordingly, you should not rely on any of these forward-looking statements, including those relating to the potential benefits, safety and efficacy or progress of CytomX's or any of its collaborative partners' product candidates, including CX-2029, BMS-986249, BMS-986288, pacmilimab, CX-904, CX-801, and CX-2051, the potential benefits or applications of CytomX's Probody platform technology, CytomX's ability to develop and advance product candidates into and successfully complete clinical trials, including the ongoing and planned clinical trials of CX-2029, BMS-986249, BMS-986288, pacmilimab, and CX-904, and the timing of the commencement of clinical trials, initial and ongoing data availability, investigational new drug applications and other development milestones. Risks and uncertainties that contribute to the uncertain nature of the forward-looking statements include: the unproven nature of CytomX's novel Probody Platform technology; CytomX's clinical trial product candidates are in the initial stages of clinical development and its other product candidates are currently in preclinical development, and the process by which preclinical and clinical development could potentially lead to an approved product is long and subject to significant risks and uncertainties, including the risk that the COVID-19 worldwide pandemic may continue to negatively impact the business, research and clinical operations of CytomX or its partners, including the development of preclinical drug candidates due to delays in and disruption of research activities and the development of clinical drug candidates due to delays in or disruption of clinical trials, including impacts on the enrollment of patients in clinical trials or other clinical trial disruptions; the possibility that the results of preclinical research and early clinical trials may not be predictive of future results; the possibility that CytomX's clinical trials will not be successful; the possibility that current preclinical research may not result in additional product candidates; CytomX's dependence on the success of CX-2029, BMS-986249, BMS-986288, pacmilimab, CX-904, CX-801, and CX-2051; CytomX's reliance on third parties for the manufacture of the Company's product candidates; and possible regulatory developments in the United States and foreign countries. Additional applicable risks and uncertainties include those relating to our preclinical research and development, clinical development, and other risks identified under the heading "Risk Factors" included in CytomX's Quarterly Report on Form 10-Q filed with the SEC on November 8, 2022. The forward-looking statements contained in this press release are based on information currently available to CytomX and speak only as of the date on which they are made. CytomX does not undertake and specifically disclaims any obligation to update any forward-looking statements, whether as a result of any new information, future events, changed circumstances or otherwise.

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