Delcath Systems, Inc. Announces FDA Approval of HEPZATO KIT™ for the Treatment of Adult Patients with Unresectable Hepatic-Dominant Metastatic Uveal Melanoma

August 14, 2023

HEPZATO KIT is the only FDA approved liver-directed therapy to treat metastatic uveal melanoma

Approval includes treatment naïve and previously treated patients and is not limited by HLA genotype

Delcath to hold Business Update Call on August 15, 2023 at 8:00 a.m. Eastern Time

NEW YORK, Aug. 14, 2023 /PRNewswire/ -- Delcath Systems, Inc. (Nasdaq: DCTH), an interventional oncology company focused on the treatment of primary and metastatic cancers of the liver, announced that today the US Food and Drug Administration (FDA) approved HEPZATO KIT (melphalan/Hepatic Delivery System) as a liver-directed treatment for adult patients with metastatic uveal melanoma (mUM) with unresectable hepatic metastases affecting less than 50% of the liver and no extrahepatic disease, or extrahepatic disease limited to the bone, lymph nodes, subcutaneous tissues, or lung that is amenable to resection or radiation.

mUM is a rare and aggressive form of metastatic cancer with a US incidence of approximately 1,000 cases per year. Ninety percent of mUM involves the liver, and liver failure is often the cause of death. National Comprehensive Cancer Network (NCCN) guidelines recommend liver-directed therapies for mUM patients with liver metastases. HEPZATO KIT is the only liver-directed therapy approved by the FDA for the treatment of mUM and percutaneous hepatic perfusion (PHP), the procedure enabled by HEPZATO KIT, is already included in the NCCN guidelines.

"FDA approval of HEPZATO KIT marks the beginning of a new chapter for Delcath and the culmination of the Company's commitment to bring this treatment option to patients suffering from metastatic uveal melanoma," said Gerard Michel, Delcath's Chief Executive Officer. "We look forward to partnering with cancer centers across the country to build a network of treatment sites trained in the use of this novel therapy."

The Company plans to have commercial product available in the fourth quarter, and patients will continue to be enrolled and treated at Expanded Access Program (EAP) sites.

The approval of HEPZATO KIT was based primarily on the results of the FOCUS Study (NCT02678572), a Phase 3, single arm, multicenter, open label study, which administered HEPZATO (melphalan) via the hepatic delivery system (HDS) during a PHP procedure. Ninety-one (91) patients received treatment every 6 to 8 weeks, for up to 6 treatments. The main efficacy endpoints were objective response rate (ORR) and duration of response (DoR) as assessed by an independent review committee using RECIST v1.1. ORR was 36.3% (95% CI: 26.4, 47.0) and median DoR was 14 months (95% CI: 8.3, 17.7). The Disease Control Rate (DCR) observed in treated patients was 73.6% (95% CI: 63.3, 82.3) with 7 complete responses (7.7%), and 26 (28.6%) partial responses.

The patient population enrolled in the FOCUS Study included patients with hepatic and extra-hepatic lesions subject to a treatment plan, as well as both treatment naïve (56.0%) and previously treated (44.0%) patients, irrespective of HLA genotype.

The HEPZATO KIT prescribing information has a boxed warning, which includes three sections: toxicity related to the procedure, myelosuppression and a Risk Evaluation and Mitigation Strategy program, commonly known as REMS, to manage and mitigate

these risks. Serious adverse events associated with the PHP procedure with the HEPZATO KIT, such as hemorrhage, hepatocellular injury, and thromboembolic events, occurred in less than 5% of treated patients. Myelosuppressive adverse events including thrombocytopenia, anemia, and neutropenia, are well-known and predictable side effects of melphalan and are routinely managed with standard supportive care measures.

The HEPZATO KIT REMS is designed to ensure consistent conduct of the PHP procedure and that only treatment teams who have received appropriate training perform the PHP procedure.

"HEPZATO KIT is the only liver-directed therapy that can treat the whole liver," said Vojislav Vukovic, Delcath's Chief Medical Officer. "Scientific literature supports that HEPZATO KIT may have broad applicability in other tumor types, and we intend to expand our development efforts beyond uveal melanoma given the high incidence of unresectable hepatic dominant tumors."

The approval effectively triggers the second tranche of financing tied to the previously announced March 29, 2023 Private Investment in Public Equity (PIPE) financing. Participants in the PIPE have 21 days to exercise their Tranche A warrants, translating to up to approximately $34.9 million of additional funding to Delcath. In addition, upon the Company's announcement of recording at least $10.0 million in quarterly U.S. revenue from the commercialization of HEPZATO KIT, participants in the PIPE will have 21 days to exercise their Tranche B warrants, resulting in up to an additional $24.9 million in funding to Delcath.

About HEPZATO KIT

HEPZATO KIT is a combination product that administers HEPZATO (melphalan), a well-known and long-approved chemotherapeutic agent, directly to the liver through Delcath's novel device delivery system, the Hepatic Delivery System (HDS), which permits higher drug exposure in target tissues while limiting systemic toxicity. The use of the HDS allows a healthcare provider team to surgically isolate the liver while the hepatic venous blood is filtered during melphalan infusion and subsequent washout during a Percutaneous Hepatic Perfusion (PHP) procedure. PHP, which can only be performed with Delcath's HDS, results in loco-regional delivery of a relatively high melphalan dose.

About Hepatic-Dominant Metastatic Uveal Melanoma

Uveal melanoma is a very rare form of cancer that affects melanocytes in the eye with approximately 5% of all melanomas being uveal. The US incidence of primary uveal melanoma is approximately 2,000 cases per year. While surgical or radiation therapy of the primary tumor is generally successful, approximately half of all patients with uveal melanoma will develop metastatic disease, primarily due to this inability to treat early micro-metastases of the primary tumor. The metastases occur predominantly in the liver (~90% of patients), and less commonly in the lungs and bones.

Prior to the approval of HEPZATO KIT, there was no approved liver-directed therapy for patients with metastatic uveal melanoma. There is one systemic therapy, KIMMTRAK® (tebentafusp-tebn), approved for a subset of mUM patients with HLA-A*02:01-positive unresectable or metastatic uveal melanoma. Because most patients, regardless of HLA-A*02:01 status, eventually progress, there is a need for both first line treatment of HLA-A*02:01- negative patients and second line treatment for HLA-A*02:01-positive patients.

The treatment of liver metastases is critical since liver failure is most often the cause of death for patients with metastatic uveal melanoma. Because of this, National Comprehensive Cancer Network guidelines recommends liver-directed therapies for patients with metastases to the liver, including embolization (i.e., transarterial chemoembolization, radioembolization or immunoembolization), ablative procedures (i.e., thermal ablation, cryotherapy) as well as PHP which can only be performed with the HEPZATO KIT. It is noteworthy that PHP was already on guidelines prior to FDA approval.

Metastatic uveal melanoma tumors in the liver tend to have a miliary pattern of spread where there are numerous radiographically evident and microscopically occult metastases in the liver. Therefore, an effective treatment should ideally treat the entire liver and allow for retreatment. None of the embolization or ablation treatments fulfill these requirements nor have any of these techniques been studied in prospective multi-center trials. The PHP procedure utilizing the HEPZATO KIT saturates the entire liver, regardless of the location or imageability of the lesions and most patients are able to undergo multiple treatments.

Please see the full Prescribing Information, including BOXED WARNING for the HEPZATO KIT.

Delcath will hold a business update conference call August 15, 2023, at 8:00 AM Eastern Time to discuss the FDA approval.

Conference Call Information

To participate in this event, dial-in approximately 5 to 10 minutes before the beginning of the call.

Event Date: Tuesday, August 15, 2023
Time: 8:00 AM Eastern Time
Participant Numbers: Toll Free: 1-833-630-1960
International: 1-412-317-1841
Webcast: https://app.webinar.net/rE345LOXL6b

CONFERENCE REPLAY

US Toll Free:	1-877-344-7529
International Toll:	1-412-317-0080
Replay Access Code:	4657227
End Date:	August 21, 2023

Important Safety Information

Patients eligible for HEPZATO should NOT have any of the following medical conditions:

- Active intracranial metastases or brain lesions with a propensity to bleed
- Liver failure, portal hypertension, or known varices at risk for bleeding
- Surgery or medical treatment of the liver in the previous 4 weeks
- Active cardiac conditions including unstable or severe angina or myocardial infarction), worsening or new-onset congestive heart failure, significant arrhythmias, or severe valvular disease
- History of allergies or known hypersensitivity to melphalan or a component or material utilized within the HEPZATO KIT including natural rubber latex, heparin, and severe hypersensitivity to iodinated contrast not controlled by antihistamines and steroids

Most common adverse reactions or laboratory abnormalities occurring with HEPZATO treatment are thrombocytopenia, fatigue, anemia, nausea, musculoskeletal pain, leukopenia, abdominal pain, neutropenia, vomiting, increased alanine aminotransferase, prolonged activated partial thromboplastin time, increased alkaline phosphatase, increased aspartate aminotransferase and dyspnea.

Severe peri-procedural complications including hemorrhage, hepatocellular injury, and thromboembolic events may occur via hepatic intra-arterial administration of HEPZATO. HEPZATO is available only through a restricted program under a Risk Evaluation and Mitigation Strategy called the HEPZATO KIT REMS. Myelosuppression with resulting severe infection, bleeding, or symptomatic anemia may occur with HEPZATO. Additional cycles of HEPZATO therapy will be delayed until blood counts have improved.

Please see the full Prescribing Information, including BOXED WARNING for the HEPZATO KIT.

About Delcath Systems, Inc.

Delcath Systems, Inc. is an interventional oncology company focused on the treatment of primary and metastatic liver cancers. The Company's proprietary products, HEPZATO KIT™ (melphalan hydrochloride for Injection/Hepatic Delivery System) and CHEMOSAT® Hepatic Delivery System for Melphalan percutaneous hepatic perfusion (PHP) are designed to administer high-dose chemotherapy to the liver while controlling systemic exposure and associated side effects during a PHP procedure.

Forward Looking Statements

The Private Securities Litigation Reform Act of 1995 provides a safe harbor for forward-looking statements made by the Company or on its behalf. This press release contains forward-looking statements, which are subject to certain risks and uncertainties, that can cause actual results to differ materially from those described. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Factors that may cause such differences include, but are not limited to, uncertainties relating to: the Company's commercialization plans and its ability to successfully commercialize the HEPZATO KIT; the Company's successful management of the HEPZATO KIT supply chain, including securing adequate supply of critical components necessary to manufacture and assemble the HEPZATO KIT; successful FDA inspections of the facilities of the Company and those of its third-party suppliers/manufacturers; the Company's successful implementation and management of the HEPZATO KIT Risk Evaluation and Mitigation Strategy; the potential benefits of the HEPZATO KIT as a treatment for patients with primary and metastatic disease in the liver; the Company's ability to obtain reimbursement for the HEPZATO KIT; and the Company's ability to successfully enter into any necessary purchase and sale agreements with users of the HEPZATO KIT. For additional information about these factors, and others that may impact the Company, please see the Company's filings with the Securities and Exchange Commission, including those on Forms 10-K, 10-Q, and 8-K. However, new risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. Accordingly, you should not place undue reliance on these forward-looking statements, which speak only as of the date they are made. We undertake no obligation to publicly update or revise these forward-looking statements to reflect events or circumstances after the date they are made.

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