Mersana Therapeutics Presents Preclinical Data Highlighting Potential of XMT-2056 and XMT-1660 in Three Posters at Virtual 2021 AACR Annual Meeting

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CAMBRIDGE, Mass., April 10, 2021 (GLOBE NEWSWIRE) -- Mersana Therapeutics, Inc. (NASDAQ:MRSN), a clinical-stage biopharmaceutical company focused on discovering and developing a pipeline of antibody-drug conjugates (ADCs) targeting cancers in areas of high unmet medical need, today presented preclinical data from XMT-1660, a B7-H4-targeted Dolasynthen antibody-drug conjugate (ADC), and XMT-2056, an Immunosynthen-based STING-agonist ADC at the Virtual 2021 American Association for Cancer Research Annual Meeting being held from April 10-15th.

“The ability of Immunosynthen-based ADCs to activate the innate immune system via STING in tumor cells in addition to tumor-resident immune cells in a targeted manner could offer a significant therapeutic advantage over ADCs that modulate other immune activating pathways. These data demonstrate that XMT-2056 is highly differentiated from other innate immune activating approaches and has the anti-tumor activity and tolerability to support continued development of this novel STING-agonist ADC candidate,” said Timothy B. Lowinger, Ph.D., Chief Science and Technology Officer of Mersana Therapeutics. “Additionally, we presented data showing that XMT-1660 outperformed other B7-H4 ADCs *in vivo.* The inversely correlated expression of B7-H4 and PD-L1 in breast tumors suggests an opportunity for a B7-H4 Dolasynthen ADC to address patients poorly served by checkpoint inhibitors. We expect to complete IND-enabling studies and advance both XMT-1660 and XMT-2056 into the clinic in early 2022.”

“These encouraging data for both the Dolasynthen and Immunosynthen platforms demonstrate the scientific prowess of the Mersana research team and our commitment to discover and develop life-changing antibody-drug conjugates for patients fighting cancer,” said Anna Protopapas, President and Chief Executive Officer of Mersana Therapeutics.

Details of the posters are as follows:

Poster Title: XMT-1660, a B7-H4-targeted Dolasynthen antibody-drug conjugate for the treatment of breast cancer
Poster Number: 907
Session Category: Experimental and Molecular Therapeutics
Session Title: Antibody Technologies

These data show that B7-H4 is a promising target for a Dolasynthen ADC due to its expression and function. B7-H4 is expressed across multiple different tumor types with high unmet medical need, including breast, endometrial and ovarian. XMT-1660 demonstrated robust *in vivo* activity against multiple triple-negative breast cancer models, as well as an ER+/HER2- breast cancer model, all of which express B7-H4.

- In the MX-1 triple-negative breast model, XMT-1660 showed complete, durable regressions of tumors at a DolaLock payload dose of 0.15 mg/kg. In contrast, the DAR-2 and DAR-12 ADCs required twice the payload dose for comparable efficacy. XMT-1660 also showed superior efficacy at matched payload doses in the TNBC patient-derived xenograft model HBCx-24, and in the ER+/HER2- breast cancer PDX model HBCx-19 versus comparators.
- Pharmacokinetics of XMT-1660 as well as the Dolasynthen DAR-2 and Dolaflexin DAR-12 comparator ADCs were evaluated in tumor-bearing mice and all were shown to be highly stable in vivo. Pharmacokinetics and tolerability of XMT-1660 and the Dolasynthen DAR-2 ADC were evaluated in non-human primates at equivalent payload doses. The PK and tolerability profiles were comparable and both ADCs exhibited high stability. These results, together with the superior efficacy of XMT-1660, support the selection of XMT-1660 for further development and for clinical study for the treatment of B7-H4-expressing tumors, such as breast, endometrial and ovarian.

Poster Title: XMT-2056, a well-tolerated, Immunosynthen-based STING-agonist antibody-drug conjugate which induces anti-tumor immune activity
Poster Number: 1738
Session Category: Immunology
Session Title: Immunomodulatory Agents and Interventions

These data suggest that XMT-2056, an Immunosynthen STING-agonist ADC, can overcome the limitations of the current therapeutic approaches, enabling tumor-targeted delivery of a STING agonist with improved efficacy and tolerability over a free IV STING agonist. Anti-tumor activity of Immunosynthen STING-agonist ADCs involves targeted activation of the STING pathway in both tumor-resident immune cells and tumor cells, delivering a one-two punch with the potential to increase the therapeutic index.

- *In vitro* studies show that XMT-2056 has potent STING activity with >100-fold improvement in activity in comparison to the free STING-agonist payload.
- XMT-2056 shows excellent *in vivo* efficacy even after a single IV dose, while having minimal effect on systemic cytokines. A single, low dose administration of XMT-2056 led to sustained tumor regressions in mice in comparison to the IV STING agonist which showed modest activity even at a dose approximately 100 times higher than that of the ADC. In contrast,

when comparing the effect on systemic cytokine levels, the IV STING agonist had significantly higher levels compared to the STING-agonist ADC, which supports the hypothesis that a STING-agonist ADC can target STING activation to the tumor microenvironment, leading to improved anti-tumor activity and a significantly greater therapeutic index.
- *In vitro* and *in vivo* studies demonstrate that STING agonist ADCs are able to activate the STING pathway in both tumor-resident immune cells and tumor cells, offering a potential advantage over other innate immune activating pathways.
- To evaluate the safety profile, XMT-2056 was administered intravenously to non-human primates (NHP) in single and repeat-dose studies at multiple dose levels. XMT-2056 shows favorable pharmacokinetics in NHPs and is well tolerated at a dose level >10-fold higher than required for sustained tumor regression in mice models. Together these data support the clinical development of XMT-2056.

Poster Title: Tumor cell-intrinsic STING pathway activation leads to robust induction of Type III Interferons and contributes to the anti-tumor activity elicited by STING agonism
Poster Number: 1773
Session Category: Immunology
Session Title: Innate Immunity to Tumors

STING pathway agonism induces anti-tumor immunity by upregulating a Type I interferon response within the tumor microenvironment. While systemically or intra-tumorally administered free STING agonists are currently being evaluated in the clinic, these data suggest that a STING-agonist ADC, in which the STING agonist is conjugated to an antibody directed to a tumor antigen, can overcome the limitations of the current therapeutic approaches.

- *In vitro* studies show that while most cancer cell lines do not respond to STING agonism in standard monoculture conditions, Immunosynthen STING-agonist ADCs do activate STING in the same cancer cells in the presence of immune cell-conditioned media, suggesting that the tumor cell-intrinsic STING pathway can be activated in the presence of cues from immune cells.
- Nanostring analysis of human tumor xenografts reveal tumor cell specific induction of type III interferons (IFNs) by tumor cell-targeting Immunosynthen STING-agonist ADCs. *In vitro* studies confirmed the Type III interferon induction at the mRNA and cytokine level. Type III interferon production was markedly reduced in STING knock out cancer cell and immune cell co-cultures, suggesting that the tumor intrinsic STING activation is required for a robust Type III interferon induction in response to STING agonism. In addition, these data show that blocking Type III IFNs with neutralizing antibodies in cancer cell:immune cell co-cultures inhibits the production of key cytokines and cancer cell killing induced by STING-agonist ADC treatment, pointing to a potentially important role for Type III IFNs in anti-tumor immune responses downstream of STING pathway activation in tumor cells.
- Together these data demonstrate that tumor cell intrinsic STING activation leads to a robust type III interferon induction, which contributes to the anti-tumor activity of tumor cell-targeted STING-agonist ADCs. This study supports the further development of Immunosynthen STING-agonist ADC candidates.

About Mersana Therapeutics
Mersana Therapeutics is a clinical-stage biopharmaceutical company using its differentiated and proprietary ADC platforms to rapidly develop novel ADCs with optimal efficacy, safety and tolerability to meaningfully improve the lives of people fighting cancer. Mersana's lead product candidate, upifitamab rilsodotin (UpRi), is a Dolaflexin ADC targeting NaPi2b and is being studied in UPLIFT, a single-arm registration strategy, in patients with platinum-resistant ovarian cancer as well as the expansion portion of a Phase 1 proof-of-concept clinical study in patients with NSCLC adenocarcinoma. XMT-1592, Mersana's second ADC product candidate targeting NaPi2b-expressing tumors, was created using Mersana's customizable and homogeneous Dolasynthen platform and is in the dose escalation portion of a Phase 1 proof-of-concept clinical study. The Company's early-stage programs include XMT-1660, a Dolasynthen ADC targeting B7-H4, as well as XMT-2056, a STING-agonist ADC developed using the Company's Immunosynthen platform. In addition, multiple partners are using Mersana's Dolaflexin platform to advance their ADC pipelines.

Forward-Looking Statements
This press release contains "forward-looking" statements within the meaning of federal securities laws. These forward-looking statements are not statements of historical facts and are based on management's beliefs and assumptions and on information currently available to management. Forward-looking statements include information concerning the Company's business strategy and the design, progression and timing of its clinical trials, the ability of the single-arm UPLIFT cohort to enable registration, and expectations regarding future clinical trial results based on data achieved to date, and the sufficiency of the Company's cash on hand. Forward-looking statements generally can be identified by terms such as "aims," "anticipates," "believes," "contemplates," "continues," "could," "estimates," "expects," "goal," "intends," "may," "on track," "opportunity," "plans," "poised for," "possible," "potential," "predicts," "projects," "promises to be," "seeks," "should," "target," "will," "would" or similar expressions and the negatives of those terms. Forward-looking statements represent management's beliefs and assumptions only as of the date of this press release. The Company's operations involve risks and uncertainties, many of which are outside its control, and any one of which, or combination of which, could materially affect its results of operations and whether the forward-looking statements ultimately prove to be correct. Factors that may materially affect the Company's results of operations and whether these forward-looking statements prove to be correct include, among other things, that preclinical testing or early clinical results may not be predictive of the results or success of ongoing or later preclinical or clinical studies, that the identification, development and testing of the Company's product candidates and new platforms will take longer and/or cost more than planned, and that our clinical studies may not be initiated or completed on schedule, if at all, as well as those listed in the Company's Annual Report on Form 10-K filed on February 26, 2021, with the Securities and Exchange Commission ("SEC"), and subsequent SEC filings. In addition, while we expect that the COVID-19 pandemic might adversely affect the Company's preclinical and clinical development efforts, business operations and financial results, the extent of the impact on the Company's operations and the value of and market for the Company's common stock will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, physical distancing and business closure requirements in the U.S. and in other countries, and the effectiveness of actions taken globally to contain and treat the disease. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons

actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

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