December 8, 2025

TuHURA Biosciences Presents Data Demonstrating the Delta Opioid Receptor (DOR) as a New Target in Overcoming Acquired Resistance to Immune Checkpoint Inhibitors at the 57th ASH Annual Meeting and Exposition

Oral Presentation highlighted new scientific evidence that DOR is expressed on tumor-associated Myeloid-Derived Suppressor Cells (MDSCs), and its inhibition decreases immune suppressing capabilities of MDSCs by downregulating expression of multiple genes associated with MDSC induced immunosuppression

Data presented in the Company's poster demonstrated that the DOR is also expressed on tumor associated macrophages (TAMs) and DOR inhibition appears to reverse TAM mediated T cell suppression with the potential to overcome resistance to checkpoint inhibitor and other cancer immunotherapies

TAMPA, Fla., Dec. 8, 2025 /PRNewswire/ -- **TuHURA Biosciences, Inc.** (NASDAQ:HURA) ("TuHURA"), a Phase 3 immune-oncology company developing novel technologies to overcome resistance to cancer immunotherapy, today announced that its research on the potential role of the Delta Opioid Receptor (DOR) in controlling the immunosuppressive capabilities of MDSCs was presented in an oral presentation at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition that took place on Sunday, December 7 in Orlando, FL. The Company presented these updated results, along with a poster presentation highlighting the effects of DOR inhibition on TAMs, another immunosuppressive cellular component critical to the tumorigenic microenvironment.

In the oral presentation, entitled: *Delta Opioid Receptor (DOR) Expression on Myeloid-Derived Suppressor Cells (MDSCs) Represents a Novel Target to Overcome Resistance to Immune Checkpoint Inhibitors (ICIs),* Dr. Michael Turner, Vice President Immunology at TuHURA Biosciences presented updated data validating DOR expression on MDSCs and further showing that the pharmacological antagonism of DOR reduced the suppressive activity of MDSCs. MDSCs are a heterogeneous population of immature myeloid cells that contribute to creating an immunosuppressive tumor microenvironment (TME) by suppressing anti-tumor immune responses. The study showed that antagonism of the DOR with a specific inhibitor modulated a variety of direct and indirect MDSC-mediated immunosuppressive factors and reversed T cell suppression, suggesting the DOR may be a novel target to reprogram MDSC induced immunosuppression in the TME.

In the poster, entitled: *Delta Opioid Receptor (DOR): A Novel Target for Reprogramming Tumor-Associated Macrophage (TAM) Immunosuppressive Phenotype to Overcome Acquired Resistance and Enhance the Effectiveness of Cancer Immunotherapies*, Dr. Krit Ritthipichai, Director of Immunology at TuHURA Biosciences, presented the results of a study that showed how the DOR is highly expressed in tumor-infiltrating myeloid cells, particularly TAMs, indicating that the TME induces DOR upregulation relative to peripheral macrophages, and that targeting the DOR provides a promising strategy to reprogram suppressive TAMs and MDSCs, alleviate T-cell dysfunction, and potentially overcome resistance to checkpoint blockade and other immunotherapies.

Dr. James Bianco, President and Chief Executive Officer of TuHURA Biosciences, said "Innate immune cells, MDSCs, TAMs, and adaptive regulatory T cells (Tregs) are among the most important cellular components of the body's immune system that provide the ability to regulate inflammation, autoimmunity and immune tolerance. Our discovery of the expression of the DOR on MDSCs and TAMs, and that its activation is coupled to mechanisms by which these cells contribute to immunosuppression, makes the DOR a compelling target for pharmacologic intervention to overcome acquired resistance to cancer immunotherapy. Data demonstrating that the DOR is also expressed on T regs and controls the expression of FOXP3, a critical immunosuppressive gene, provides a shared mechanism by which endogenous opioids, via the DOR, control the immunosuppressive tone of both innate and adaptive immune responses critical in the pathology associated with cancer and autoimmune disease. TuHURA is the first to demonstrate that this single target shares control of the immune suppressive capabilities of these cells and provides us a unique position to exploit pharmacologic modulation of the DOR to overcome resistance to cancer immunotherapy and the treatment of autoimmune and inflammatory diseases."

"The Company has developed a library of highly selective (>1,200 fold) and potent (<1.0 ng/ml) DOR antagonists and is in position to advance our first-in-class immune modulating bi-functional, bi-specific antibody drug conjugates (ADCs). We anticipate our lead ADC candidate to consist of a DOR inhibitor conjugated to our VISTA inhibiting antibody. TuHURA's updates at this ASH meeting demonstrate that elucidating the role of VISTA on macrophages and MDSCs in promoting the progression of myelodysplasia (MDS) to acute leukemia, as well as VISTA's documented role in being central to how leukemia escapes immune recognition, makes it an ideal candidate to link to a DOR inhibitor. Our ADCs have the potential to not only remove the immunosuppressive tone of the TME but to also checkpoint release resting T cells, allowing them to recognize and kill leukemic cells." Dr. Bianco concluded, "We are excited to be at the forefront of these discoveries and look forward to working on the development of a whole new class of ADCs that could meaningfully change the treatment of cancer."

About TuHURA Biosciences, Inc.
TuHURA Biosciences, Inc. (Nasdaq: HURA) is a Phase 3 immuno-oncology company developing novel technologies to overcome primary and acquired resistance to cancer immunotherapy, two of the most common reasons cancer immunotherapies fail to work or stop working in the majority of patients with cancer.

TuHURA's lead innate immune agonist, IFx-2.0, is designed to overcome primary resistance to checkpoint inhibitors. TuHURA has initiated a single randomized placebo-controlled Phase 3 registration trial of IFx-2.0 administered as an adjunctive therapy to Keytruda® (pembrolizumab) compared to Keytruda® plus placebo in first-line treatment for advanced or metastatic Merkel Cell Carcinoma.

In addition to its innate immune agonist product candidates, TuHURA acquired TBS-2025 in its merger with Kineta Inc. on June 30, 2025. TBS-2025 is a VISTA inhibiting mAb asset moving into Phase 2 development in mutNPM1 r/r AML. In addition, TuHURA is leveraging its Delta Opioid Receptor technology to develop first-in-class, bi-specific, bi-functional antibody drug conjugates targeting Myeloid Derived Suppressor Cells to inhibit their immune-suppressing effects on the tumor microenvironment to prevent T cell exhaustion and acquired resistance to checkpoint inhibitors and cellular therapies.

For more information, please visit www.tuhurabio.com and connect with TuHURA on Facebook, X, and LinkedIn.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS
This press release contains certain "forward-looking statements" within the meaning of, and subject to the safe harbor created by, Section 27A of the Securities Act, Section 21E of the Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995. These Forward-looking statements are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and other future conditions. In some cases you can identify these statements by forward-looking words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "could," "should," "would," "project," "plan," "expect," "goal," "seek," "future," "likely" or the negative or plural of these words or similar expressions. Examples of such forward-looking statements include but are not limited to express or implied statements regarding TuHURA's expectations, hopes, beliefs, intentions or strategies regarding the future and include, without limitation, statements regarding TuHURA's Delta Opioid Receptor Technology, its IFx-Hu2.0 product candidate and Phase 3 trial, and its TBS-2025 asset, and any developments or results in connection therewith and the anticipated regulatory pathway and timing of the foregoing development programs, studies and trials. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. You are cautioned that such statements are not guarantees of future performance and that actual results or developments may differ materially from those set forth in these forward-looking statements. Factors that could cause actual results to differ materially from these forward-looking statements are described in detail in our registration statements, reports and other filings with the SEC, which are available on the combined company's website, and at www.sec.gov.

The forward-looking statements and other information contained in this press release are made as of the date hereof, and TuHURA does not undertake any obligation to update publicly or revise any forward-looking statements or information, whether as a result of new information, future events or otherwise, unless so required by applicable securities laws. Nothing herein shall constitute an offer to sell or the solicitation of an offer to buy any securities.

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