



Oncotelic and Sapu Nano Announces New PK Data Demonstrating IV Sapu003 Reduces GI Accumulation of Everolimus up to 67-Fold Compared With Oral Dosing

AGOURA HILLS, Calif., Dec. 03, 2025 (GLOBE NEWSWIRE) -- Oncotelic Therapeutics, Inc. (OTCQB: OTLC) 45% owned Joint Venture, *Sapu Nano* today announced new pharmacokinetic (PK) and tissue-distribution results demonstrating that **Sapu003**, the company's intravenous (IV) Deciparticle™ formulation of everolimus, **substantially reduces gastrointestinal (GI) drug accumulation**, addressing one of the most significant and well-recognized limitations of oral everolimus (Afinitor®). The data indicate that Sapu003 may offer **improved tolerability** while preserving the drug's intrinsic metabolic profile and enabling more consistent systemic exposure.

IV Sapu003 Reduces GI Exposure to Everolimus by 67-Fold Compared With Oral Dosing

New tissue-distribution data show that Sapu003, delivered intravenously, **eliminates the extreme gastrointestinal accumulation** characteristic of oral everolimus. After oral dosing, everolimus reaches **2,448× plasma levels in the stomach, 750× plasma in the small intestine, and 323× plasma in the large intestine**, confirming that the gut is the dominant exposure site for the oral formulation.

In contrast, IV Sapu003 demonstrates **only 36-48× plasma levels** across the same GI tissues, representing a **67-fold reduction in stomach exposure, a 15.7-fold reduction in small-intestinal exposure, and a 7.4-fold reduction in large-intestinal exposure.**

These findings provide a clear mechanistic explanation for the **well-documented GI toxicity of oral everolimus**-including stomatitis, mucositis, abdominal discomfort, and diarrhea.

Presentation information: PS4-06-05. Sapu003: Everolimus for Injection - Pharmacokinetic Rationale for Phase I Evaluation in HR /HER2 Metastatic Breast Cancer. Wen-Han Chang, John Lopp, Sheng-Hao Min, Robert Hoff, Nancy Chang, Tanjina Hoque, Ann Park, and Cynthia Lee.

Potential for Improved Clinical Tolerability and Antitumor Potency

By bypassing the gastrointestinal tract and delivering the drug directly into circulation, Sapu003:

- Avoids the high local GI concentrations associated with oral toxicity
- Produces more consistent systemic exposure
- Enhances drug penetration into tumor-relevant tissues

These PK advantages complement previously reported efficacy findings in which Sapu003 achieved **97-98% tumor inhibition** in glycolysis-addicted xenograft while outperforming paclitaxel.

Management Commentary

"The fundamental challenge with oral everolimus is that the majority of the drug ends up in the gut, leading directly to the GI toxicity that limits its use," said **Dr. Cynthia Lee, VP of R&D**. "These new data show that IV Sapu003 avoids that problem entirely. By reducing GI accumulation by up to 67-fold, Sapu003 has the potential to offer a far more tolerable and clinically versatile version of everolimus."

About Sapu003

Sapu003 is a novel intravenous nanoparticle formulation of everolimus engineered using Sapu Nano's proprietary Deciparticle™ technology. It is designed to overcome the poor bioavailability, intestinal toxicity, and variable patient exposure seen with oral everolimus while enabling reliable, predictable weekly IV dosing.

About the Deciparticle™ Platform

The Deciparticle™ platform is a proprietary nanotechnology engineered to encapsulate hydrophobic molecules as **uniform, sub-20 nm nanoparticles** for intravenous administration. The platform improves systemic exposure, reduces GI deposition, and supports precision delivery while maintaining manufacturability at clinical scale.

About Sapu Nano

Sapu Nano is a clinical-stage biotechnology company developing Deciparticle™ nanomedicine therapeutics designed to optimize the delivery of hydrophobic oncology agents and peptide-based therapeutics. The company operates an integrated ISO-5 cGMP manufacturing facility supporting rapid progression from formulation to clinical trial supply.

For more information, visit www.sapunano.com.

About Oncotelic

Oncotelic (f/k/a Mateon Therapeutics, Inc.), was formed in the State of New York in 1988 as OXiGENE, Inc., was reincorporated in the State of Delaware in 1992, and changed its name to Mateon Therapeutics, Inc. in 2016, and Oncotelic Therapeutics, Inc. in November 2020. Oncotelic is seeking to leverage its deep expertise in oncology drug development to improve treatment outcomes and survival of cancer patients with a special emphasis on rare pediatric cancers. Oncotelic has rare pediatric designation for Diffuse Intrinsic Pontine Glioma "DIPG" (through OT-101) through its 45% joint venture, melanoma (through CA4P), and Acute Myeloid Leukemia "AML" (through OXi 4503). Oncotelic also acquired PointR Data Inc. in November 2019.

Oncotelic acquired AL-101, during the 4th quarter of 2021, for the intranasal delivery of apomorphine. We intend to develop AL-101 for the treatment of Parkinson Disease ("PD"). Over 60,000 new patients are being diagnosed with PD in the United States and currently there are over 1 million patients in the US and expected to increase to over 1.2 million by 2030. In addition, approximately 10 million suffer from this disease globally. <https://www.parkinson.org/Understanding-Parkinsons/Statistics>. AL-101 is also being developed for Erectile Dysfunction ("ED"). ED is the most prevalent male sexual disorder globally. The percentages of men affected by ED are as follows: 14.3-70% of men aged 60 years, 6.7-48% of men aged 70 years, and 38% of men aged 80 years (Geerkens MJM et al. (2019). Eur Urol Focus. pii: S2405-4569(19)30079-3). However, with the increasing administration of PDE5 inhibitors in clinical practice, it was found that approximately 30-35% of ED patients are treatment failures (McMahon CN et al. (2006). BMJ, 332: 589-92). AL-101 is designed to target treatment failure ED patients who do not respond to PDE5 inhibitors. Through similar mechanism of action, AL-101 is being developed for Female Sexual Dysfunction ("FSD"). Female sexual dysfunction is a prevalent problem, afflicting approximately 40% of women and there are few treatment options. FSD is more typical as women age and is a progressive and widespread condition. (Allahdadi, KJ et al. (2009) Cardiovascular & hematological agents in medicinal chemistry, 7(4), 260-269). There is no available drug for the treatment of FSD. In June 2019, the U.S. Food and Drug Administration approved Vyleesi (bremelanotide) to treat acquired, generalized hypoactive sexual desire disorder ("HSDD") in premenopausal women. This is the only available drug treatment. Vyleesi has essentially replaced the only other drug for HSDD - however, it has a long list of drug-drug interactions, including commonly used antidepressants, such as fluoxetine and sertraline. In addition, it has a black box warning regarding its use with alcohol, a combination that has been associated with hypotension and syncopal episodes. Therefore, there is an urgent need for effective therapy against FSD and HSDD.

Oncotelic's Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934 (the "*Exchange Act*") that involve substantial risks and uncertainties. We generally identify forward-looking statements by terminology such as "may," "will," "should," "expect," "plan," "anticipate," "could," "would," "intend," "target," "aim," "project," "believe," "estimate," "predict," "potential," "seek," "indicate," or "continue" or the negative of these terms or other similar words, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements regarding our or our management's expectations, hopes, beliefs, intentions or strategies regarding the future, such as our estimates regarding anticipated operating income or losses, future performance, future revenues and projected expense, including that to fund our clinical and other development programs; our liquidity and our expectations regarding our needs for and ability to raise additional capital; our ability to continue as a going concern; our ability to select and capitalize on commercially desirable product opportunities as a result of limited financial resources; our ability to manage our expenses effectively and raise the funds needed to continue our business; our ability to retain the services of our current or future executive officers, directors and principal consultants; the competitive nature of our industry and the possibility that our products or product candidates may become obsolete or may not generate revenues as expected or at all; our ability to obtain and maintain regulatory approval of our existing products and any future products we may develop; the development of and the process of commercializing AI/Blockchain and other technologies for supporting the development of OT-101 and Artemisinin for COVID-19, OT-101, including development of OT-101, Artemisinin, OXi4503, CA4P and our 2021 in-licensing of apomorphine; the initiation, timing, progress and results of our preclinical and clinical trials, research and development programs; regulatory and legislative developments in the United States and foreign countries; the timing, costs and other limitations involved in obtaining regulatory approval for any product; the further preclinical or clinical development and commercialization of our product candidates; the entering into any corporate transactions to develop our products through partnerships, joint ventures or other corporate transactions; our ability to make a proposed initial public offering between us and our joint-venture partners for the joint venture, statements about future plans related to the operations of the JV, taking the JV into an initial public offering or the success thereof; building and the success of our nanoparticle platform and the related success of launching the platform; the expected valuation of the JV, and therefore a corresponding increase in the valuation of the Company, by virtue of its ownership in the JV; the success of the launch of Pet2DAO, a corporation with a DAO infrastructure, the success of Pet2DAO and the plans surrounding the pet and animal health, the ability for the Company to register the tokens of Pet2DAO, the actual filing of a registration statement and approval of the tokens as registrable securities with the Securities and Exchange Commission ("*SEC*") through a registration statement, the ability of the tokens to be tradable or any value such tokens may have if they become tradable; our ability to obtain and maintain orphan drug exclusivity for some of our product candidates; the potential benefits of our product candidates over other therapies; our ability to enter into and maintain any collaboration with respect to product candidates; our ability to continue to develop or commercialize our products or product candidates in the event any license agreements in place with third parties expire or are terminated; the performance and conduct of third parties, including our third-party manufacturers and third party service providers used in our clinical trials; our ability to obtain and maintain intellectual property protection for our products and operate our business without infringing upon the intellectual property rights of others; the potential liability exposure related to our products and our insurance coverage for such exposure; our ability to form alliances with other third parties to develop the products in our pipeline through partnerships, joint ventures, mergers or acquisitions; the successful development of our sales and marketing capabilities; the size and growth of the potential markets for our products and our ability to serve those markets; the rate and degree of market acceptance of any future products; the volatility of the price of our common stock; the ability to achieve secondary trading of our stock in certain states; the dilutive effects of potential future equity issuances; our expectation that no dividends will be declared on our common stock in the foreseeable future; our ability to maintain an effective system of internal controls; the payment and reimbursement methods used by private or governmental third-party payers; our ability to retain adequate staffing levels; unfavorable global economic conditions; unfavorable global epidemic and pandemic conditions; a failure of our internal computer systems or those of our contractors and consultants; potential misconduct or other improper activities by our employees, contractors or consultants; the ability of our business continuity and disaster recovery plans to protect us in the event of a natural disaster; and other factors discussed elsewhere in this document or any document incorporated by reference herein or therein.

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