Selecta Biosciences Announces Data in Non-Human Primates, Further Validating Multiple Potential Benefits of the ImmTOR™ Platform in Gene Therapy

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- Co-administration of AAV8 and ImmTOR shows first dose benefit of higher and more durable transgene expression, in addition to mitigating the formation of neutralizing antibodies, compared to AAV8 alone –

- Data support rapid advancement of Selecta's gene therapy pipeline, including lead candidate, MMA-101, for the treatment of methylmalonic acidemia (MMA) in collaboration with AskBio, and ornithine transcarbamylase (OTC) deficiency -

WATERTOWN, Mass., Jan. 06, 2021 (GLOBE NEWSWIRE) -- Selecta Biosciences, Inc. (NASDAQ: SELB, "Selecta"), a biotechnology company leveraging its clinically validated ImmTOR™ platform to develop tolerogenic therapies that selectively mitigate unwanted immune responses, today announced preclinical data that validate the ImmTOR platform's potential to enhance the efficacy, safety and durability of adeno-associated viral (AAV) vector gene therapies. In the study, Selecta observed that co-administration of AAV vector and ImmTOR in non-human primates (NHP) enabled higher and more durable transgene expression as well as robust inhibition of anti-AAV8 immunoglobulin G (IgG) and neutralizing antibodies.

The observation that co-administration of AAV vector and ImmTOR leads to higher transgene expression demonstrates the potential for dosing lower levels of AAV gene therapies when combined with ImmTOR—improving patient safety and lowering costs. Further, long-term gene therapy data demonstrate that expression of systemic AAV gene therapies may wane over time, a limitation that ImmTOR has the potential to address. Finally, AAV gene therapies cannot currently be re-dosed due to the formation of neutralizing antibodies to the AAV vector. In this study, ImmTOR mitigated the formation of these neutralizing antibodies in NHPs, thereby potentially allowing for redosing, another key unmet need in the gene therapy field.

"We are encouraged by the promising data announced today, demonstrating ImmTOR's potential to address current limitations in the gene therapy field by both increasing transgene expression levels and durability following the first dose as well as inhibiting the formation of AAV-specific antibodies," said Carsten Brunn, Ph.D., president and chief executive officer of Selecta. "Our findings indicate that ImmTOR potentially enables gene therapy administration at a lower initial dose and could allow for incremental gene therapy redosing, firmly supporting ImmTOR's ability to enhance the efficacy, safety, and durability of these therapies. Our results, along with previous studies supporting ImmTOR's hepatoprotective properties in liver injury models, move us one step closer to transforming the lives of patients and realizing the full potential of gene therapy. We look forward to leveraging these findings in our OTC deficiency and our MMA programs, the latter of which we expect to initiate in the first half of 2021 in collaboration with AskBio."

In the study, researchers evaluated the administration of a single intravenous (IV) infusion of a recombinant adeno-associated serotype eight capsid directing expression of a transgene encoding secreted embryonic alkaline phosphatase (AAV8-SEAP), a widely used reporter gene transgene, either alone or co-administered with ImmTOR in NHP. Five cohorts of NHP each received $2x10^{12}$ vector genomes (vg)/kilogram (kg) of AAV8-SEAP either alone (cohort 1) or in combination with a single dose of 6 mg/kg ImmTOR (cohorts 2 and 3) or three-monthly doses of 3 mg/kg ImmTOR (cohorts 4 and 5). Cohort 3 received ImmTOR admixed with AAV8-SEAP prior to infusion. All other cohorts received sequential infusions of ImmTOR followed by AAV8-SEAP on Day 0. Cohorts four and five received additional doses of 3 mg/kg ImmTOR at day 28 and day 56 of the study, with cohort five also receiving additional low doses of AAV8-SEAP ($0.2x10^{12}$ vg/kg) at day 28 and day 56.

Selecta intends to present these findings at the annual meeting of the American Society of Gene & Cell Therapy (ASGCT) in May.

Key findings include:

- Transgene expression peaked at Day 28 in animals receiving AAV8-SEAP alone (cohort 1). At Day 28, cohorts 2-5 treated with $2x10^{12}$ vg/kg AAV8-SEAP + ImmTOR showed an average of 1.6x higher levels of transgene expression, indicating a substantial first dose benefit of ImmTOR on transgene expression.
- After Day 28, serum SEAP levels in cohort 1 treated with AAV8-SEAP alone dropped precipitously, declining 93.5% by Day 84, whereas cohorts treated with AAV8-SEAP + ImmTOR showed stable expression of SEAP through Day 84, demonstrating ImmTOR's notable impact on durability of transgene expression. At Day 84, cohorts 2-4 treated with ImmTOR plus a single dose of AAV8-SEAP showed an average of 23.3x higher SEAP expression compared to cohort 1. Cohort 5 that received two additional low doses of AAV8-SEAP on Days 28 and 56 showed 36.7x higher transgene expression than cohort 1 on Day 84.
- All ImmTOR-treated cohorts achieved robust inhibition of anti-AAV8 IgG antibodies through day 56. This effect was strengthened with repeat-dosing of ImmTOR at days 28 and 56. Five out of six animals in cohorts 4 and 5 that received three monthly doses of ImmTOR had neutralizing antibody titers of less than 1:5 at day 84, as measured with a cell-based neutralizing assay, while the sixth animal showed a low titer of 1:8. In contrast, all three animals in cohort 1, treated with AAV8-SEAP alone, had neutralizing antibody titers greater than 1:3400.
- Overall, there was a high degree of correlation between Day 84 anti-AAV8 IgG and neutralizing antibody titers across all

animals and all cohorts.

“ImmTOR holds significant promise and could be revolutionary for the gene therapy field,” said Jude Samulski, Ph.D., president and chief scientific officer of Asklepios BioPharmaceutical, Inc. (AskBio). “The data announced today suggest the use of ImmTOR in conjunction with gene therapy has the potential to overcome significant challenges in the field—making these therapies safer and more effective at lower doses as well as allowing for repeat dosing. We are proud to partner with Selecta and look forward to advancing our investigational therapy through clinical development for patients with MMA and their families.”

Selecta, in partnership with AskBio, expects to initiate a Phase 1 clinical trial of MMA-101 and ImmTOR for patients with MMA in the first half of 2021, with preliminary data expected by the end of 2021.

About Methylmalonic Acidemia
Methylmalonic Acidemia (MMA) is a rare monogenic disorder in which the body cannot break down certain proteins and fats. This metabolic disease may lead to hyperammonemia and is associated with long-term complications including feeding problems, intellectual disability, chronic kidney disease and inflammation of the pancreas. Symptoms of MMA usually appear in early infancy and vary from mild to life-threatening. Without treatment, this disorder can lead to coma and in some cases death.

About Ornithine Transcarbamylase (OTC) Deficiency
OTC deficiency is an X-linked genetic disorder caused by genetic mutations in the OTC gene, which is critical for proper function of the urea cycle. Individuals with OTC experience accumulation of excessive levels of ammonia in the blood. The most severe form of the disorder presents within the first few days of life and is characterized by an inability to control body temperature and breathing rate, seizures, coma, developmental delays and intellectual disability. Because the disorder is X-linked, males are most often affected by the severe form of the disease. Less severe forms of the disorder are characterized by delirium, erratic behavior, aversion to high protein foods, vomiting and seizures. Most approved therapies are focused on reducing the amount of ammonia in the blood and are not curative. Currently, the only curative approach is liver transplantation at an early age, which can be associated with severe side effects and complications.

About Selecta Biosciences, Inc.
Selecta Biosciences Inc. (NASDAQ: SELB) is leveraging its clinically validated ImmTOR™ platform to develop tolerogenic therapies that selectively mitigate unwanted immune responses. With a proven ability to induce tolerance to highly immunogenic proteins, ImmTOR has the potential to amplify the efficacy of biologic therapies, including redosing of life-saving gene therapies, as well as restore the body’s natural self-tolerance in autoimmune diseases. The company’s first program aimed at addressing immunogenicity to AAV gene therapies is expected to enter clinical trials in early 2021 in partnership with AskBio for the treatment of methylmalonic acidemia (MMA), a rare metabolic disorder. A wholly-owned program focused on addressing IgA nephropathy driven by ImmTOR and a therapeutic enzyme is also in development among additional product candidates. Selecta recently licensed its Phase 3 clinical product candidate, SEL-212, in chronic refractory gout to Sobi. For more information, please visit www.selectabio.com.

Selecta Forward-Looking Statements
Any statements in this press release about the future expectations, plans and prospects of Selecta Biosciences, Inc. (“the company”), including without limitation, statements regarding the unique proprietary technology platform of the company, and the unique proprietary platform of its partners, the potential of ImmTOR to enable re-dosing of AAV gene therapy, the potential treatment applications of product candidates utilizing the ImmTOR platform in areas such as gene therapy, the ability of the Company and AskBio to develop gene therapy products using ImmTOR and AskBio’s technology, the novelty of treatment paradigms that the Company is able to develop, whether the observations made in non-human primate study subjects will translate to studies performed with human beings, the potential of any therapies developed by the company and AskBio to fulfill unmet medical needs, the company’s plan to apply its ImmTOR technology platform to a range of biologics for rare and orphan genetic diseases, the potential of the company’s intellectual property to enable repeat administration in gene therapy product candidates and products, the ability to re-dose patients and the potential of ImmTOR to allow for re-dosing, the potential to safely re-dose AAV, the ability to restore transgene expression, the potential of the ImmTOR technology platform generally and the company’s ability to grow its strategic partnerships, and other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “hypothesize,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including, but not limited to, the following: the uncertainties inherent in the initiation, completion and cost of clinical trials including proof of concept trials, including the uncertain outcomes, the availability and timing of data from ongoing and future clinical trials and the results of such trials, whether preliminary results from a particular clinical trial will be predictive of the final results of that trial or whether results of early clinical trials will be indicative of the results of later clinical trials, the ability to predict results of studies performed on human beings based on results of studies performed on non-human primates, the unproven approach of the company’s ImmTOR technology, potential delays in enrollment of patients, undesirable side effects of the company’s product candidates, its reliance on third parties to manufacture its product candidates and to conduct its clinical trials, the company’s inability to maintain its existing or future collaborations, licenses or contractual relationships, its inability to protect its proprietary technology and intellectual property, potential delays in regulatory approvals, the availability of funding sufficient for its foreseeable and unforeseeable operating expenses and capital expenditure requirements, the company’s recurring losses from operations and negative cash flows from operations raise substantial doubt regarding its ability to continue as a going concern, substantial fluctuation in the price of its common stock, and other important factors discussed in the “Risk Factors” section of the company’s most recent Quarterly Report on Form 10-Q, and in other filings that the company makes with the Securities and Exchange Commission. In addition, any forward-looking statements included in this press release represent the company’s views only as of the date of its publication and should not be relied upon as representing its views as of any subsequent date. The company specifically disclaims any intention to update any forward-looking statements included in this press release.

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