aTyr Pharma Announces Encouraging Phase 1b/2 Results for Resolaris™ in its First Rare Myopathy Trial

March 30, 2016
First patient trial of a Physiocrine-based investigational new drug
Preliminary analysis shows potential activity signals in three months of treatment
Safety, tolerability, immunogenicity & PK profile supports Resolaris program advancement in FSHD and potentially other rare diseases

SAN DIEGO, March 30, 2016 /PRNewswire/ -- aTyr Pharma, Inc. (Nasdaq: LIFE) a biotherapeutics company engaged in the discovery and development of Physiocrine-based therapeutics to address severe rare diseases, today announced results from a Phase 1b/2 clinical trial evaluating Resolaris ™in adult FSHD (facioscapulohumeral muscular dystrophy) patients. The Company is developing Resolaris, a potential first-in-class protein therapeutic, for the treatment of rare myopathies with an immune component (RMICs). The Phase 1b/2 study was designed to evaluate the safety, tolerability, immunogenicity and pharmacokinetic (PK) profile of Resolaris in adult FSHD patients, the Company's first treated RMIC population. In addition, the study also evaluated the utility of exploratory pharmacodynamic (PD) markers (including MRI measurements to quantitate areas of potential muscle inflammation) and clinical assessments (including patient reported outcomes).

"As the first clinical trial of a Physiocrine-based investigational new drug in patients, our data set provides important insights about the safety, tolerability, immunogenicity and PK profile of Resolaris in a very challenging disease setting, and explores potential PD markers and clinical assessments in FSHD," said John Mendlein, PhD, Chief Executive Officer of aTyr. "It is our vision to provide patients with FSHD and other muscular dystrophies, such as limb-girdle muscular dystrophy (LGMD) 2B, an innovative treatment that potentially modulates immune components and other important aspects of disease progression."

"We whole heartedly thank the FSHD patients, clinical investigators and clinical sites that contributed to a well conducted double-blind, placebo-controlled trial for Resolaris," added Melissa Ashlock, MD, aTyr's Senior Vice President of Translational Medicine and Therapeutics.

In this randomized, double-blind, placebo-controlled trial, Resolaris was studied in three dose escalation cohorts (0.3, 1.0, and 3.0 mg/kg) across four sites and 20 patients. In each cohort, patients were randomized at a ratio of 3:1 to receive Resolaris or placebo. Patients in the first two dose cohorts were dosed weekly over a period of one month, and patients in the third cohort were dosed weekly over a period of three months. As planned, the Company enrolled a total of four patients in the first cohort and eight patients in each of the second and third cohorts. For the second and third cohorts, inclusion criteria included the presence of at least one skeletal muscle in the legs identified by a non-quantitative MRI technique, which is thought to indicate inflammation. The analysis is based on data available through early March 2016.

A number of exploratory PD markers and clinical assessments were conducted to better understand their utility in FSHD. The study was not powered to demonstrate statistically significant evidence of therapeutic utility or a specific activity endpoint. As part of clinical assessments, a validated patient reported outcome measure designed specifically for neuromuscular diseases, the individualized neuromuscular quality of life (INQoL) questionnaire, was utilized in the study. The Company believes that data from this patient reported outcome measure suggest potential improvement at three months of weekly dosing at 3.0 mg/kg in this relatively small clinical trial of FSHD patients.

Results of the INQoL Overall Score are set forth in the table below:

INQoL Overall Score [1]				
(Negative values represent improvement or less disease burden/impact on a patient)				
	Change from Baseline (%) **ITT Population (n=20)**			
Treatment **Duration Group**	**Placebo**	**0.3 mg/kg**	**1.0 mg/kg**	**3.0 mg/kg**

1 Month	4.12 (n=5)[2]	2.77 (n=3)	-1.22 (n=4)[3]	-3.78 (n=6)
3 Months	15.55 (n=2)	NA[4]	NA[4]	-9.90[5] (n=6)

1) The INQoL Overall Score is comprised of a scoring of five Life domains: Activities, Independence, Social Relationships, Emotions and Body Image. Changes were primarily observed in the categories of patient Activities, Independence and Emotions.

2) Placebo for 1 month data include patients from all 3 dose cohorts per the aforementioned eligibility criteria.

3) INQoL Overall Score could not be calculated for two patients in the 1.0 mg/kg cohort due to unreported values.

4) NA is not applicable; only 1 month of dosing.

5) The relative improvement between placebo and the 3.0 mg/kg cohort at three months is 25.5% (p=0.03).

The proportion of patients with improved INQoL Overall Scores is set forth in the table below:

	Proportion of Patients with Improved INQoL Overall Scores			
Treatment Duration Group	**Placebo**	**0.3 mg/kg**	**1.0 mg/kg**	**3.0 mg/kg**
1 Month	2/5	1/3	2/4	4/6
3 Months	0/2	NA[1]	NA[1]	5/6

1) NA is not applicable; only 1 month of dosing.

Manual muscle testing (MMT), which measures muscle strength, was performed across 15 selected muscle groups. The composite MMT score showed approximately 0.5% improvement with Resolaris compared to a 1% decline in the placebo treated patients, indicating no reportable disease progression by this technique in either placebo or test article groups after three months of weekly treatment. An exploratory MRI technique, to quantitate inflammation in a targeted lower limb muscle, did not record differences between placebo and test article groups after three months of weekly treatment. No substantial differences between the placebo and test article groups were observed after three months of weekly treatment in certain exploratory circulating PD markers, however only 2/20 patients had elevated levels above the normal range at screening.

Across all dose groups (0.3 , 1.0 and 3.0 mg/kg), the Company believes the safety, tolerability, immunogenicity and PK profile of Resolaris supports advancement of Resolaris in FSHD and potentially other rare diseases. No serious adverse events were reported by study investigators. Mild to moderate adverse events were observed in both the test article and placebo treated patients. One moderate adverse event in a test article treated patient (a reversible generalized infusion related reaction in the third cohort), which was reported by a study investigator, was reclassified to a serious adverse event by aTyr. This patient was discontinued from dosing at week 11 of the 12 weeks of treatment, but completed the study visits. The PK of Resolaris was generally well behaved across all dose cohorts and throughout the study. Anti-drug antibodies (ADAs) were confirmed in approximately 40% of the dosed patients. ADAs were of low titer and had no significant effect on PK.

"Given the short duration of Resolaris treatment in our first study in FSHD patients, we are encouraged by the observed improvement in patient reported outcomes, in particular in activity and independence domains. While we need to do additional work to extend and confirm these results which are based on a small number of patients, the data represent our first step forward in our efforts to understand the clinical utility of Resolaris in patients with rare myopathies with an immune component (RMICs)," said Sanjay Shukla, MD, MS, Chief Medical Officer of aTyr. "In addition, we believe the safety, tolerability, immunogenicity and PK profile observed in adult FSHD patients provides a solid foundation to advance our ongoing RMIC clinical programs."

aTyr intends to expand its experience with Resolaris in RMIC patients as follows:

- In adult FSHD patients by additional enrollment of patients in a new or existing clinical trial setting at a dose of 3.0mg/kg to build on the data from these first three cohorts and integrating data in the fourth quarter of this year from the Company's ongoing RMIC trials.
- Continuing efforts in 2016 in the Company's ongoing trials comprising:
    - adult LGMD2B patients (the Company's first LGMD2B trial) evaluating the safety, tolerability, immunogenicity, PK, exploratory PD markers and clinical assessments of a different dosing paradigm from the study reported today;
    - adult FSHD patients (as a subset of the ongoing LGMD2B trial) evaluating the safety, tolerability, immunogenicity, PK, exploratory PD markers and clinical assessments of a different dosing paradigm from the study reported today;
    - early onset FSHD patients (potentially the most severe form of FSHD) evaluating the safety, tolerability, immunogenicity, PK, exploratory PD markers and clinical assessments; and
    - adult FSHD patients rolled over from the study reported today in a long-term safety extension study.

About FSHD

Facioscapulohumeral muscular dystrophy (FSHD) is a rare genetic myopathy affecting approximately 19,000 people in the United States for which there are no approved treatments. The primary clinical phenotype of FSHD is debilitating skeletal muscle deterioration and weakness. The symptoms of FSHD develop in a descending pattern, starting with the face and upper body to the lower body and progressing in a "muscle by muscle" fashion. In addition to muscle weakness, FSHD patients often experience debilitating fatigue and chronic pain. The disease is typically diagnosed by the presence of a characteristic pattern of muscle weakness and other clinical symptoms, as well as through genetic testing. Early onset FSHD occurs in individuals who experience symptoms of progressive muscle involvement as juveniles, and some of these patients suffer from a particularly severe form of the disease.

About aTyr Pharma

aTyr Pharma is engaged in the discovery and clinical development of innovative medicines for patients suffering from severe rare diseases using its knowledge of Physiocrine biology, a newly discovered set of physiological modulators. The Company's lead candidate, Resolaris™, is a potential first-in-class intravenous protein therapeutic for the treatment of rare myopathies with an immune component. Resolaris is currently in a Phase 1b/2 clinical trial in adult patients with facioscapulohumeral muscular dystrophy (FSHD); a Phase 1b/2 trial in adult patients with limb-girdle muscular dystrophy 2B (LGMD2B or dysferlinopathies) or FSHD; and a Phase 1b/2 trial in patients with an early onset form of FSHD. To protect this pipeline, aTyr built an intellectual property estate comprising over 70 issued or allowed patents and over 240 pending patent applications that are solely owned or exclusively licensed by aTyr. aTyr's key programs are currently focused on severe, rare diseases characterized by immune dysregulation for which there are currently limited or no treatment options. For more information, please visit http://www.atyrpharma.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Litigation Reform Act. Forward-looking statements are usually identified by the use of words such as "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "seeks," "should," "will," and variations of such words or similar expressions. We intend these forward-looking statements to be covered by such safe harbor provisions for forward-looking statements and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements, including statements regarding the potential of Resolaris, the ability of the Company to undertake certain development activities (such as clinical trial enrollment and the conduct of clinical trials) and accomplish certain development goals, and the timing of initiation of additional clinical trials and of reporting results from our clinical trials reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies and prospects as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, risks associated with the discovery, development and regulation of our Physiocrine-based product candidates, including with respect to observed results not being replicated in subsequent studies or clinical trials or such product candidates not producing therapeutic benefit or causing other unanticipated side effects, as well as those risks set forth in our most recent Annual Report on Form 10-K for the year ended December 31, 2015 and in our other SEC filings. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

SOURCE aTyr Pharma, Inc.

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