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Zacks Small-Cap Research (NOTE)

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# Achieve Life Sciences, Inc. (ACHV: NASDAQ)

## ACHV: ORCA-OL to Start 2Q:24

### Research Note

Achieve Life Sciences, Inc. (NASDAQ: ACHV) provided an update to its December 11th announcement regarding the FDA's desire for additional long-term cytisinicline exposure data to adequately assess safety risk. Despite an initial anticipated treatment duration of six to twelve weeks, cytisinicline could be used for chronic, repeat or intermittent use if a patient relapses. With this possibility guiding its interactions with drug sponsors, the FDA and Achieve have reached an agreement that a single, open-label study evaluating long-term safety exposure of cytisinicline will meet the safety requirement. Details of the arrangement were provided in a February 29th press release and are described further below.

The study will include safety data on at least 300 subjects that have received cumulative cytisinicline treatment for six months. This data will be included with the new drug application (NDA), which we expect in the first half of 2025. Additionally, one year of safety data from at least 100 subjects treated with cytisinicline will be submitted prior to approval. Subjects for the trial will be drawn from the pool of individuals that participated in the ORCA-1, ORCA-2 and ORCA-V1 trials with a preference for subjects who received 12 weeks of treatment. The desired exposure data is cumulative rather than continuous, giving credit to the duration of therapy already received. We anticipate that the minimum 300 subjects could require an additional 14 weeks of treatment to satisfy the 6-month threshold.

To satisfy the safety requirement, Achieve will launch an Ongoing Research of Cytisinicline for Addiction Program, Open Label (ORCA-OL) trial that will recruit from the more than 1,700 subjects who have already participated in Achieve's previous studies. The company may target recruitment of up to 650 subjects to account for an anticipated dropout rate.

**Timing**

Roughly, we expect to see the safety study start in 2Q:24 with enrollment of the target number of subjects by the end of 3Q:24. A cumulative six months of observation could be complete by the beginning of 2025 with an NDA submission complete, along with the first six months of safety data by 2Q:25. The full year of safety data for the final 100 subjects could complete collecting data by mid-2025 and be submitted to the FDA prior to year-end 2025. If Achieve is able to hold to this timeline, the FDA could assign a Prescription Drug User Fee Act (PDUFA) date in 1H:26.

**Cost**

Based on our conversations with management, we anticipate that the incremental cost of the ORCA-OL study will be $20 million.

**Registered Direct Offering and Private Placement**

Along with the details regarding the ORCA-OL trial and the agreement with the FDA, Achieve announced a registered direct offering and private placement. $60.0 million of the financing will be provided immediately and an additional $64.2 million will be available upon achievement of milestones related to NDA acceptance and through exer-

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cise of warrants. Management believes that the amount raised will be sufficient to fund clinical development of cytisinicline via the ORCA-OL trial and NDA submission which is expected in 1H:25.

The registered direct offering will sell 13,086,151 shares at a price of $4.585 per share, which equates to $60.0 million, gross, and $56.2 million, net. In a concurrent private placement, Achieve will issue unregistered warrants to purchase an additional 13,086,151 shares at an exercise price of $4.906 per share. The warrants have a duration that is the earlier of 3.5-years or 30 days after acceptance of an NDA for cytisinicline by the FDA.

Participants in the financing include Propel Bio Partners LLC, Nantahala Capital, and a large, life sciences-dedicated investor. The financing also includes participation from cytisinicline supplier Sopharma and certain members of the company's management team and board of directors. Lake Street Capital Markets and JonesTrading are acting as placement agents. The capital raise is expected to close on March 4th, 2024.

In other financing news, Achieve has reached a non-binding agreement with Silicon Valley Bank which will extend its outstanding loan into December 2025.

**Background to the FDA Agreement and the ORCA-OL Study**

On December 11th, 2023, Achieve filed Form 8-K updating investors on its interactions with the FDA. The company held a pre-new drug application (NDA) meeting with the agency in October regarding cytisinicline, which was followed by additional interaction and written notes from the meeting. Following the receipt of notes and further interaction, Achieve reported that the FDA acknowledged that there was sufficient efficacy data for a submission; however, the agency desired additional long-term exposure data beyond 12 weeks. The rationale for this request stems from the agency's view that smoking cessation drugs are products used in a chronic and intermittent manner due to relapse and subsequent courses of treatment over a lifetime.

During the meeting and the follow up, Achieve pressed the FDA for further details on what would satisfy the need for long term safety data in terms of number of subjects and duration of a study. However, the agency did not respond with specifics and management sought another meeting to determine what would satisfy the agency. Two important elements were outstanding at this point which Achieve was able to define by late February: what data is required and when it can be submitted.

For products intended for chronic use, such as schizophrenia, blood pressure and cholesterol medications, we have seen safety studies require 300 subjects observed for six months and 100 subjects observed for a year. CEO John Bencich also mentioned this as a standard that has been promulgated by the International Conference on Harmonisation of the Technical Requirements for Registration of Pharmaceuticals for Human Use for chronic use products. This organization does not provide guidance but has been relied upon by US, EU and Japanese regulatory authorities to help design clinical trials. As cytisinicline would not likely be used daily for years but rather intermittently, perhaps with one course of therapy per year. The framework mentioned above emerged as the agreed upon structure.

There are several considerations taken into account when determining the size and length of a safety study. The FDA does not explicitly define what is desired or required but rather uses a risk-based approach that considers several elements. Drugs with serious side effects, novelty of the drug and understanding of its mechanism of action, the target population and data available to date are all considered when determining the design of such a study. Other drug characteristics that are considered when designing a long-term safety study include its immunomodulatory function, potential for addiction or abuse, and whether or not it is intended for long term use.

**Partnerships**

As company management has mentioned, Achieve is speaking with potential acquirors and partners for the commercialization of cytisinicline. The company is seeking a partner with a primary care sales force already in place and is actively conducting discussions.

**Summary**

With the February 29th detail regarding the ORCA-OL trial and the $124 million capital raise, there is additional clarity on the path forward for Achieve and cytisinicline. We anticipate an aggressive early effort to launch the ORCA-OL trial and to compile the NDA for submission in 1H:25. Our timeline anticipates a PDUFA date in 1H:26 and approval of cytisinicline for smoking cessation.

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