

Interview Follicum: The results are very exciting and motivate us to start a topical study

Yesterday, Follicum presented top-line results from the First-In-Man scalp study with FOL-005 for stimulation of hair growth. The results confirm that the treatment is well tolerated and show that FOL-005 has the capacity to stimulate hair growth at optimal dosage. BioStock contacted the company's CEO, Jan Alenfall, for further comments about the study and the results, what they mean and what the next step for Follicum will be.

Follicum's primary candidate, *FOL-005*, is developed to stimulate hair growth. A first phase IIa study with the aim to investigate the safety profile and therapeutic effect of four different doses of FOL-005 and placebo on scalp was just completed. The study was conducted in Germany, at the **German Clinical Research Center for Hair and Skin Science (CRC)** in Berlin and at **bioskin** in Hamburg, a full-service CRO specializing in dermatology. For the study, treatment has been administered through injections on the patient's scalp.

By the end of August, all patients included in the trial had completed treatment. Yesterday, the company could present top-line data, i.e. a summary of the most important findings. The study results show that the hair growth increased by an average of 7 hairs per cm² at the highest dose during the study period. In the placebo group, there were no statistically significant change compared to baseline. The study was designed to evaluate the treatment effect versus baseline (individual changes), not versus placebo.

In addition, the study also showed a clear increase in the number of hair follicles in the growth phase compared with the resting phase, in particular at the highest dose level. This positive effect indicates that FOL-005 may lead to further increased long-term hair growth.

Consumer friendliness an important factor

In parallel with the reported study, Follicum has developed a topical formulation of the candidate, i.e. a product that the patient can administer himself to optimize user-friendliness and commercial potential of the end product.

In the press release, the company emphasizes that both the dose and treatment length needs to be optimized to obtain maximum therapeutic effect, and that these aspects will be reviewed prior to the planned phase IIb study with the topical formulation. Follicum also communicates that they are looking for a suitable partner for further development of the FOL-005 project.

" The overall results from this study are very exciting and motivate a clinical trial with the topical formulation where we optimize the dose, dosage frequency and treatment duration on a larger patient population in order to understand the full potential of FOL-005." – Jan Alenfall, CEO Follicum

Jan Alenfall, can you begin by describing the study design, the aim of the study and what results you expected?

- The reported study was the first one where FOL-005 was tested on the scalp of patients suffering from hair loss (alopecia). The study was planned based on the successful results we had previously seen in our first clinical study where FOL-005 was tested on the thighs on healthy volunteers. The study period was the same in both studies, i.e. 3 months, and in

both studies the drug was administered through injections. In the phase IIa-study, we tested four active doses, with 20 to 25 patients in each patient group. The aim was to generate evidence of tolerability and indications of stimulating effect on the hair follicles on the head.

- Experiences from early studies with e.g. Minoxidil and Finasteride show that it is difficult to obtain significant results on increased hair growth in studies with a small patient population since the between-patient-variation is large. It is however very expensive to conduct clinical studies, each additional patient is associated with a significant cost, and it was thus not an option to include more patients in this first scalp study. From published clinical studies we expected that our study would show an increase of between 5 and 10 hairs/cm².
- In small studies of rather short duration, it is important to analyze additional parameters beyond the hair density that was the primary endpoint of this study. Hence, we also studied several secondary endpoints, such as the number of hairs in the growth phase (anagen phase) and in the resting phase (telogen phase) and the increase in hair length. Positive effects on these parameters are at least as important as the effect on hair density. In future pivotal studies, the treatment duration will be at least 6 months in order to observe the maximum treatment effect. It is important to realize that hair growth takes time and that it differs depending on body area.

Could you elaborate somewhat on the results of your Phase IIa study with FOL-005?

- The clinical study confirms that treatment with FOL-005 is well tolerated and that it has a positive effect on hair growth with an increase of 7 hairs/cm², even though the treatment time was rather short. The result is in line with the increase observed after treatment with Minoxidil and Finasteride for much longer time periods. We are therefore very happy to obtain such a result in a small and rather short study. Also, the increase versus baseline was close to reach statistical significance. On the contrary, no statistically significant change for placebo was observed. Currently, we have not tested the final topical formulation, nor do we have the final dosage ready, but the process of optimizing the formulation and dosing regimen is ongoing.
- We also observed interesting results in several of the secondary endpoints, with one of the most important is a significant increase of the hair growth phase (activation of the hair follicles). This suggests that FOL-005 can "alert" or activate hair follicles. Hence, the results showed an increase in both the total number of hairs as well as in the number of hairs in active growth phase which indicate that a larger increase in hair density could be observed with longer treatment periods.
- We also observe that there is a large variation in the data, which is why larger studies with longer treatment and observation periods are necessary. The overall results from this study are very exciting and motivate a clinical trial with the topical formulation where we optimize the dose, dosage frequency and treatment duration on a larger patient population in order to understand the full potential of FOL-005.
- The study with the topical formulation will be very important to not lose pace in our clinical development program and to ensure that we are commercially attractive. We believe that a product that requires injections is not sufficiently attractive to the patient.

What does the results imply for your hair project and what will be the next step going forward?

- The treatment effect on hair density at the highest dose was slightly weaker than in the previous study and no obvious effects were detected at the lower doses. Therefore, we plan to increase the dose, as well as the dose frequency in upcoming studies. In a pivotal study with the topical formulation, we will also extend the treatment and follow-up period.
- Nonetheless, this study clearly stated that we were able to activate the hair follicles, which indicates that hair growth should increase further at a more effective dosage and long-term

treatment. This finding is particularly interesting because a short growth phase is the primary problem of hair follicles in alopecia patients.

- We will inform all companies that have shown interest in FOL-005 about these positive results, and hopefully it will lead to deeper discussions regarding future collaborations.

Follicum also has a project on unwanted hair growth, that has been put on hold in favor of the development of FOL-005 for the stimulation of hair growth. Does the study result have any impact on this project?

- Currently, we lack the capacity to work on this project but may be able to activate it after we have found a commercial partner for FOL-005 to treat hair loss.

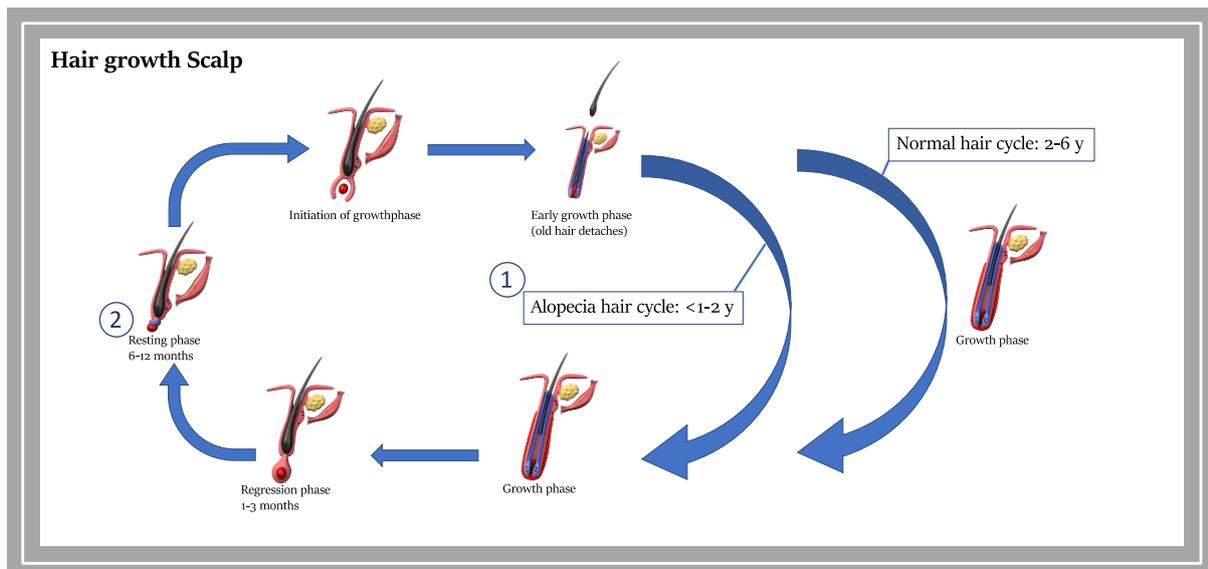
Let's switch perspective. What does the study results imply for Follicum as a company and the value of your project portfolio?

- Today, Follicum has several legs to stand on due to the development of our diabetes program in recent years.
- Our first leg is the original, the project regarding hair regulation where we now see clinical results on scalp for the first time. We can present positive and interesting changes in hair density and other hair growth parameters. We plan to take FOL-005 into the next clinical phase with our new topical formulation to optimize the dose, increase the dose frequency and, if possible, extend the treatment time. We expect to start a topical hair study at the earliest in late fall 2019, and in the meantime find a commercial partner to continue the clinical development of FOL-005. FOL-005 is one of the few clinical phase II development projects in hair growth globally, which is a strength for the company and increases our prospects to find a partner for the project. The clear increase in the number of hairs in growth phase (activation of the hair follicles) in the recently completed study, together with a new patentable topical formulation, is likely to raise interest among international companies with hair and dermatology product portfolios. We will meet some of the companies at the BIO-Europe partnering meeting in Copenhagen next week, and we look forward to the opportunity to present our top-line data and get their feedback.
- Our second leg is the diabetes project, which continues to advance rapidly, and we aim to select a drug candidate early 2019. The experience and the overall knowledge from the hair project will be an advantage when we continue the diabetes project since it is based on a similar peptide family and the development process will be comparable. Through the clinical study, we have shown that we can run a complex phase II project both on time and on budget, which should further increase confidence in the company. We conduct a comprehensive preclinical program in diabetes with very interesting *in vitro* and *in vivo* studies focusing on identifying positive effects on important diabetic complications. We intend to communicate the results as long as we do not compromise our patent application, which will be further strengthened with this data.
- For two years, Follicum has been part of the large SSF diabetes project, which makes our development work more efficient. The recent funding from the **Novo Nordisk Foundation** provides additional resources for the preclinical research with our peptides. Today, we have a constructive dialogue with many major diabetes companies with the goal of initiating scientific collaborations when we have enough unique data on one or more diabetes complications.
- Overall, the study results on hair growth have provided us with additional important information to optimize the clinical program and Follicum has once again proved that we can deliver on time and according to our communicated schedule.

What further milestones can we expect for Follicum in the coming year?

- We plan to file for patent on the topical formulation before the end of the year, as well as further strengthening the diabetes IP. We hope to communicate both *in vitro* and *in vivo* results in the diabetes project within the next 6 months and select a drug candidate in early 2019. The hair study with the topical formulation is scheduled to start in the fall of 2019 at the earliest.

This happens in hair loss



What happens in hair loss is: (1) A reduction in the duration of the growth phase for a large proportion of hair, which results in a shorter hair cycle. This change increases over time. The more advanced hair loss, the greater the proportion of hair follicles in the resting phase. A parallel decrease in the hair diameter occurs, which also results in a visual decrease of hair density. (2) The resting periods before the growth phase occurs become longer, which results in an additional reduction in the number of hairs on the scalp.

On the scalp the normal hair cycle has 3 stages where the longest is the growth phase (anagen), where about 80% of the hair follicles are. This phase is about 2-6 years long. The next phase is called the transition phase and lasts for about 1-3 months. The resting phase (telogen) is 6-12 months and approximately 15-20% of the hair follicles are in this phase. Hairs in the growth phase on our heads thus grow continuously for 2 to 6 years compared to other parts of our body like the eyebrows, eyelashes, arms and legs, where the hairs only grow for up to 45 days.

Hair on other parts of the body goes through the same process as the hair on the head, but the cycle only lasts for about a month. This is why hair on other body parts are so much shorter than head hair. In addition, hair growth rate also differs between body parts. For example, the eyebrows grow at a rate of only 4 mm per month, which could be compared to 10-15 mm per month on the scalp. Therefore, body hair is shorter than scalp hair.

As you grow older, some hair follicles can stop growing which explains why old people more often suffer from hair loss and become thin-haired, and eventually bald. In addition, the length of the growth period differs between individuals, mostly due to genetic factors. All in all, it means that there is a large interindividual variation in hair growth that depends on age, genetic predisposition, nutritional status, stress levels, body area, and more.

In patients with alopecia, the duration of the various phases of the hair cycle has changed. The most important being that the growth phase is shortened and the resting phase is extended as described above. Therefore, it is vital to extend the treatment period of clinical studies to evaluate the full clinical effect of various dosing regimens of a hair stimulating drug candidate.