

Follicum hopes that this Newsletter reaches as many of the company's owners and stakeholders as possible. If you would like to follow or development in the future, we kindly ask you to [register your e-mail address](#) on our website, www.follicum.com. You can also follow us on [LinkedIn](#).

A Christmas message from Follicum

The company has had a very intensive autumn and has finalized a number of important activities that have generated much attention. The key milestones are the successful completion of a new phase II study for stimulating hair growth, and at the same time, new preclinical data has been generated in the diabetes project. The results from the clinical study showed that at the highest dose of FOL-005, hair growth increased by an average of 7 hairs per cm² during the study period. The study also showed that there was a marked increase in the number of hair follicles in the growth phase, particularly at the highest dose tested, whilst there was a clear decrease in the placebo group.

We have continued to develop the manufacturing process for the topical formula that we selected in June. Important work in preparation for the manufacture of FOL-005 prior to clinical trials was carried out in the Autumn, and this work will continue during the first half of 2019 in order to finalize the process well in advance of production for the next clinical study. The formulation complies with our high standards regarding stability and the transportation of FOL-005 to the hair follicle. In addition, the formulation has very attractive cosmetic attributes.

Within the diabetes project, our patented peptides have shown interesting effects in preclinical studies, including effects on release of insulin. The project is advancing rapidly, and in November we filed a new patent application in order to broaden its protection. This additional patent application protects certain new aspects that were discovered during the preclinical studies that have been performed on this class of peptide. Experimental studies also show that our newly optimized peptides have both a protective and a preservative effect on beta cells which are subjected to long-term exposure to high concentrations of glucose. The results are unambiguously positive and demonstrate that these peptide classes have the potential to be a valuable complement in the treatment of diabetes. Our plan is to select a drug candidate at the beginning of 2019, in order to prepare the project for future clinical studies.

At the start of the year, we were able to report the partial mapping of the mechanism of action of our peptides within both the hair and the diabetes projects, since we had identified interesting receptors that appeared to have potential as new therapeutic targets in both areas. This work is important for future discussions with regulatory authorities and with potential partners, and to further develop our products. The work will continue in the coming year, so that we will fully understand how the receptors and these peptide classes work.

Follicum has recently signed an agreement with the Centre for Skin Sciences (CSS) at the University of Bradford, UK, to continue investigation into the mode of action. The aim is to combine *in vitro* experiments with the use of bioinformatics data mining and analysis to study Follicum's different peptide classes. The scope of the project will cover both skin and hair biology, as well as diabetes. The broad experience that CSS brings to the project will have significant impact on our capacity to further understand the mechanism of action of our peptides.

For the hair project, the most important upcoming milestones in 2019 concern the activities initiated for, and the start of a Phase II clinical trial of the topical formulation in patients with hair loss. For our diabetes project, we look forward to additional *in vivo* results of the company's peptides, drug candidate selection, and initial data on effects on diabetic complications in early 2019.

A biological link between hair loss and diabetes

Despite that hair loss and diabetes are two widely different indications, there is a biological link between the two diseases. Research has shown that men may suffer from hair loss in the early stages of diabetes, and that hair loss could be an early sign of type 2 diabetes. Normal hair growth alternates between activity and inactivity in the hair follicles, and a lack of insulin seems to have a negative effect on the transition of the hair follicle into the growth phase. This can result in slower hair growth, or no hair growth at all in diabetics. Our peptide-based drug projects have the potential to treat both of these indications effectively and safely.

Better tissue repair, fewer diabetic complications

The hair growth process is reminiscent of the tissue repair process, and many diabetic complications occur due to the reduced capacity to repair damaged tissue. An improved ability to repair damaged tissue would reduce the risk of diabetic complications, which would be welcomed from a treatment perspective.

Synergies between the hair and the diabetes projects

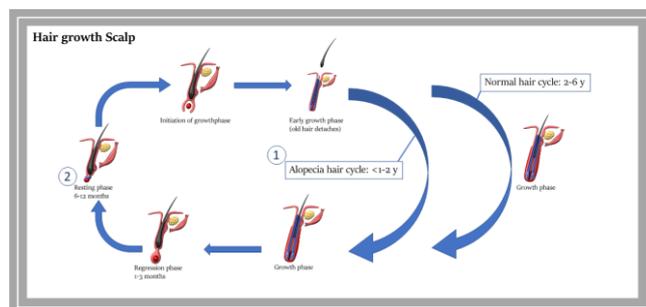
There are clear synergies for the company, in running the two peptide-based projects, at different stages of development. As a result of the extensive expertise and experience of peptide drugs that we have gained since the start in 2011, we are able to rapidly push the diabetes project forward to a stage of development where we will be ready to start a first clinical study of safety and efficacy in diabetes in 2020.

A positive effect on hair growth with an increase of 7 hairs per cm²

In October, we presented new exciting results from the first phase IIa study on the scalp. The study was conducted in Germany, at the German Clinical Research Center for Hair and Skin Science (CRC), Berlin, and at bioskin in Hamburg; a full-service CRO specializing in dermatology. In this study, treatment was administered by injections on defined mini-zones on the patient's scalp.



Positioning of mini-zones on the scalp



Normal and abnormal hair growth cycle in patients with alopecia

The results show that during the study period, hair growth increased by an average of 7 hairs per cm² at the highest dose of FOL-005. This effect was almost of statistical significance compared with hair growth before start of treatment (baseline). In the placebo group, there was no statistically significant effect of treatment. The study was designed to measure the post treatment effect against baseline, and not as a comparison with the placebo group. The increase in hair growth that was

observed is consistent with the findings seen after significantly longer periods of treatment with preparations such as minoxidil and finasteride.

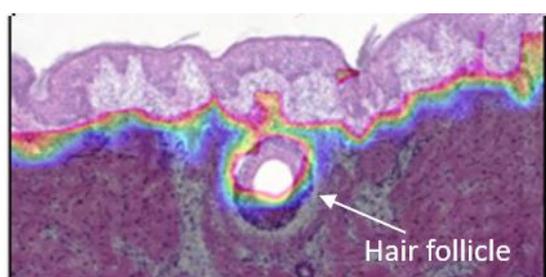
In addition to an increase in the number of hairs, the study also showed a marked increase in the number of hair follicles that were in the growth phase after treatment, especially at the highest dose tested, whilst the placebo group showed a clear decrease. This positive effect indicates that a longer treatment with FOL-005 could further increase hair growth. We are very pleased to be able to present such excellent results after this relatively small and short study. We have now initiated work to prepare for clinical studies using the topical formulation as well as dose optimization.

Results of published clinical studies of established treatments (rows 1-4) for comparison with the phase II-study with FOL-005 (row 5).

Compound	Publication	# subjects	Change in Hair Density	
Minoxidil	D. H. Rushton et al 1989 Quantitative assessment of 2 % topical minoxidil in the treatment of male pattern baldness	47 (12)	6 months 7 hairs	12 months 4 hairs
Minoxidil	Olsen et al 2002 A randomized clinical trial of 5% topical minoxidil versus 2% topical minoxidil and placebo in the treatment of androgenetic alopecia in men	5%: 139 2%: 142	11 months 18.6 hairs 12.7 hairs	
Minoxidil and Finasteride	Rushton et al 2016 Hair regrowth in male and female pattern hair loss does not involve the conversion of vellus hair to terminal hair	Minoxidil: 15 Finasteride: 15	12 months 4 hairs 13 hairs	
Finasteride	D. Van Neste et al 2000 Finasteride increases anagen hair in men with androgen alopecia	93	11 months 7 hairs	
FOL-005	FCS-002, 2018	23	3 months 7 hairs	

A user-friendly topical formulation with good stability and penetration

The work towards the development of a user-friendly formulation continues according to plan. In June, we chose the formulation to be used, and the production of this formulation will now be scaled up and tested in Phase II and Phase III studies prior to registration and launch of the product.



The topical FOL-005 formulation is transported through the layers of the skin, and down to the hair follicle.

There are few drugs in late clinical development for hair growth - FOL-005 is one of them

The market for the treatment of alopecia, i.e. hair loss, is extensive. Annual sales of registered pharmaceuticals reach approximately USD 3 billion globally and in addition, other products are also sold for large sums, that are not classified as drugs. Follicum is continuously working to communicate results and successes to potential partners and we see a strong and growing interest in FOL-005 from many pharmaceutical companies. It is worth noting that there are very few drugs in late clinical development addressing hair growth, and FOL-005 is one of these. At the major partnering meeting

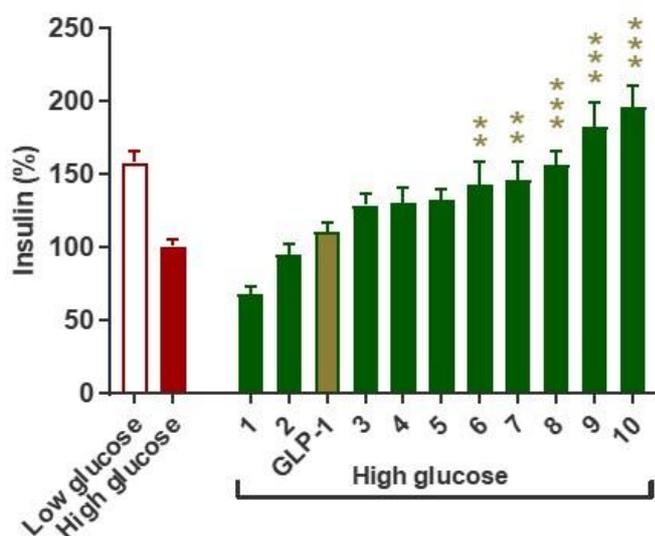
BIO-Europe, which took place in Copenhagen in November, we received a very positive feedback on the study results in discussions with potential partners.

Targeted work to identify factors that can differentiate us from competitors

Our new peptide class stimulates the release of insulin and the results clearly show that it has the potential to be a valuable complement in the treatment of diabetes. In type 2 diabetes, the ability to produce insulin is almost completely eliminated and the levels of insulin are insufficient. The body cannot respond sufficiently to the need for increased insulin production when blood sugar rises after, for example, a meal and in addition, the body's ability to utilize the insulin is impaired. This means that more insulin is needed in order to control blood sugar. There are medicines on the market that help to improve insulin production and lower blood glucose levels, but whilst these treatments are relatively effective, it is only for a limited time. Fluctuations in blood glucose levels create a number of complications in the body such as cardiovascular effects, obesity, and liver and kidney damage. Thus, when the effects decrease and complications arise, additional treatments are needed that can complement the existing arsenal or may be used as an adjunct therapy, for example, to reduce the risks of developing more serious diabetic complications. In 2018, we conducted a number of preclinical studies that show that Follicum's peptides have an insulin-releasing effect that is comparable, or even better than, some existing diabetes preparations. In addition, insulin release is potentiated with increasing glucose levels in *in vitro* studies, which is the ideal scenario for patients with high blood sugar. The potential of the peptides has also been confirmed in glucose tolerance tests where they have a glucose lowering effect in experimental animals. Experimental studies also show that our newly optimized peptides have a protective and preservative effect on beta cells that have been exposed long-term to high glucose concentrations.

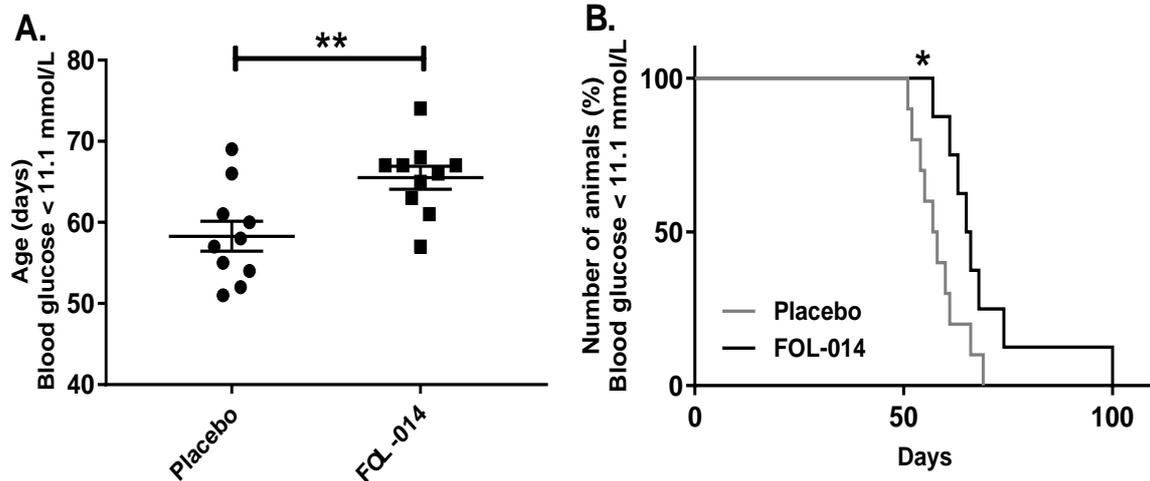
The diabetes market is very large and highly competitive. We therefore work in a targeted fashion to identify factors that can differentiate us from competitors and that can lead to an early partnership. In our international network, we discuss how we can optimize our research in a tailored fashion focusing on limiting medical problems caused by diabetic complications. Since these complications have a major impact on patient health and on costs of healthcare, the goal at Follicum is to develop a treatment that addresses these problems.

During the autumn we have further strengthened our diabetes patent and at the beginning of November, we submitted an updated application to the patent authorities, and at the same time, our first patent was published. The preclinical work is primarily carried out in collaboration with Follicum's researcher network at Lund University.



Experiments with insulin-producing beta cells show that Follicum's peptides maintain beta cell capacity to secrete insulin after prolonged exposure to high levels of glucose, which simulates the physiological situation in diabetic patients. The white bar represents healthy cells and the red bar represents diabetic cells. The green bars (numbered 1-10) show that treatment of diabetic cells with different Follicum peptides restores the ability of the diseased cells to secrete insulin. The stars () on the bars indicate any statistically significant difference against the control (high glucose).*

Furthermore, our preclinical results show that the peptides have the capacity to delay the onset of Type 1 diabetes in an animal model. It is clear from the results that the peptide seeks out, and then remains in the pancreas, which is beneficial for an insulin regulating drug since the pancreas is the hub of insulin production in the body. Current work includes dose optimization as well as studies to determine the mechanism of action of Follicum's peptides in Type-1 diabetes. The work is conducted in close collaboration with an expert group at the diabetes centre at Lund University.



Treatment with FOL-014 significantly extends the time to disease in a Diabetes type 1 model.

The next milestone in the diabetes project will be to select a drug candidate, at the beginning of 2019, followed by a Phase I study that will start in 2020. The goal is to develop a diabetes project that will be attractive to global partners.

Participation in an International Diabetes Project

Since 2017, Follicum has been part of a comprehensive diabetes project led by scientists at Lund University, whose work is funded by the Swedish Foundation for Strategic Research. In addition to Follicum, Novo Nordisk, Johnson & Johnson Innovation and Pfizer participate in the project. This provides us with valuable contacts and opportunities to network at the highest international level. We are also very pleased that the Novo Nordisk Foundation once again awarded funding to Professor Jan Nilsson's research team at the Clinical Research Centre at Lund University, this time the sum of 1.4 million Swedish crowns was awarded to carry out preclinical diabetes studies using Follicum's peptides.

We are also very pleased about the addition of resources to our team, in the form of a postdoctoral position, which we secured in December through our participation in the International Diabetes Consortium. The consortium has financed 5 post-doctoral positions, in order to further strengthen the research. Out of a total of 11 applicants, Follicum's project has been awarded one of these five positions. The aim is to further strengthen the research on the potential of Follicum's peptides for future treatment of diabetes. The post-doctoral position is 100% funded by LUDC-IRC and is a two-year full time position. The work proposed will be to study in detail the mechanism of action of our peptide classes. A postdoctoral researcher is a person who performs advanced research after completing a doctorate.

Finally, I would like to thank you for your interest and support in the process of developing Follicum into a leading international company within hair and diabetes research. We have many interesting

and exciting milestones that will build additional value in the company ahead of us in the coming year – the start of the new Phase II clinical trial in patients with hair loss, additional *in vivo* results on the company's diabetes peptides, the choice of drug a candidate within diabetes, as well as data on effects of the peptide classes on diabetic complications being some of the most important.

Merry Christmas and a Happy New Year!

Lund 18th December 2018

Jan Alenfall, VD