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Dr. Geert Cauwenbergh is Managing Partner of Phases123 LLC, a New Jersey based “think-tank”, consulting and advisory firm for biotech and pharmaceutical companies. Phases123 LLC is primarily focused on support of private start-up companies and small to medium size health care companies (organizational- & business development, R&D strategy & planning, corporate strategy & financial planning, investor- & public relations).

Until February 2019, Geert Cauwenbergh has been President and CEO of Phio Pharmaceuticals a NASDAQ-listed biotechnology company (PHIO: NASDAQ) that is developing self-delivering interference RNA (RNAi) for immuno-oncology and adoptive cell transfer therapy. Prior to his involvement in Phio Pharmaceuticals he also founded or co-founded several other privately held companies such as Phases123, Aramis Pharma, Legacy Health Care and Anethon. Through his consulting firm, Dr Cauwenbergh held positions as Chairman & CEO of RHEI Pharmaceuticals (China), managing director of the Center for Medical Innovation (Belgium) and Executive Chairman of ECI Biotech (USA).

Prior to founding Phases123 and Aramis LLC, in 2002, Dr Cauwenbergh was Founder, Chairman and CEO of Barrier Therapeutics (BTRX: NASDAQ), a biopharmaceutical company with focus on dermatology drug development. Barrier was acquired by Stiefel Laboratories in 2008, at a moment that the company reached annual revenue of \$45 million.

Between 1994 and 2002 Geert held various senior management positions in the Johnson & Johnson Global Consumer Organization and was member of a number of boards within the family of companies of Johnson & Johnson. From 1979 – 1994, Dr Cauwenbergh held various positions in Janssen Pharmaceutica in Belgium, the last one as global Clinical Director for R&D in dermatology and infectious diseases

Dr. Cauwenbergh is currently a member of the Board of Directors of Phio Pharmaceuticals (USA) and Legacy Health Care (Switzerland). Over the past 18 years he has been Board member of several private and public companies, including Moberg Pharma, a public dermatology OTC company in Sweden, Phosphagenics, a public delivery platform technology company in Australia, and Cutanea Inc, a US based subsidiary of Maruho, a Japanese dermatology company. Previously he has held Board positions in Intercept (Public - USA), DARA Biosciences (Public - USA), Upstream Biosciences (Public - Canada), Alto Pharmaceuticals (Canada), Ablynx (Public - Belgium) and Euroscreen (Belgium). He currently also serves as Advisor for Economic Diplomacy for the Belgium in the USA.

Dr Cauwenbergh has authored > 100 publications, and received his Doctorate in Medical Sciences from the Catholic University of Leuven, Faculty of Medicine, where he also completed his masters and undergraduate work. In 2004 Dr. Cauwenbergh was inducted in the New Jersey High Tech Hall of Fame.

Abstract

“Management of Hair Loss by Stimulating Bcl2 Protein in the Scalp”

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Abnormal hair loss patterns are among the most common complaints observed globally by hundreds of millions of people. Diseases associated with abnormal hair loss include androgen dependent male pattern balding, female pattern balding (not androgen dependent), diffuse hair thinning (e.g. in systemic lupus erythematosus), patchy auto-immune hair loss (e.g. alopecia areata), chemotherapy induced alopecia and various others.

Often, therapy for treatment of hair loss disorders has been monodirectional. Only few treatment approaches have attempted to tackle the various underlying issues that can contribute to hair loss and hair growth. Drugs used today to fight hair loss and promote hair growth often do not consider the hair follicle as an organ/entity that can be affected by several molecular biological factors that cause premature hair loss or shedding. Some of these factors involve perifollicular inflammation, breach of the immune privilege of the skin/hair follicle, premature onset of the catagen phase, shortening of the anagen phase, altered microcirculation. As a result, it is reasonable to assume that a more pleiotropic therapeutic approach might result in better outcomes for several forms of hair loss.

In the past 12 years some solid work has been done with a quadruple botanical extract, Coacillium, that has targeted a pleiotropic approach to hair and scalp diseases. Very often, small molecules and biological drugs have a single, well defined, mechanism of action; and such a mono-factorial approach can indeed result in sometimes excellent results in certain diseases. The new regulations, introduced by FDA and EMA for the development of botanical drugs, have established a framework to evaluate botanical drugs and extracts, also allowing for a pleiotropic approach to disease management thanks to the multi-components nature of plants. The development of Coacillium is an example of such a pleiotropic approach.

This botanical drug, based on a specific combination of 4 extracts (*Allium cepa*, *Citrus limon*, *Theobroma cacao*, *Paullinia cupana*), has demonstrated to control inflammation through, among other things, its anti-oxidant effects. It has shown to reduce ICAM and E-selectin, helping to restore impaired immune privileges of the hair follicle. In a biopsy study in volunteers with androgenic alopecia, Coacillium demonstrated histologically to increase Ki67 and collagen synthesis. In these same volunteers, scalp biopsies indicated significant reductions in Bcl2, indicating that loss of protection against apoptosis in the hair follicle can shorten the anagen phase and accelerate telogen; whereas after 3 months of topical use of CG210, hair had started to regrow, and Bcl2 levels in those parts of the scalp had returned almost back to normal, as observed in those same healthy volunteers.

These mechanistic findings have also been evaluated in clinical studies for male pattern and female pattern baldness, chemotherapy induced alopecia and pediatric alopecia areata.

- In patients in France with male pattern baldness it was demonstrated that the anagen/telogen ratio significantly improved during the course of a 3 months treatment.
- In Greece, in women with female pattern baldness, similar effects were confirmed in a placebo controlled clinical study, over 6 months.
- In Japan, patients who had stagnated hair growth after a year on oral finasteride therapy, experienced enhanced hair thickness when they added topical use of Coacillium to oral finasteride as compared to a topical placebo that was added in a control group.
- Female patients undergoing chemotherapy in Japan that were treated with a higher dose of Coacillium, regrew more hair and faster after chemotherapy than a cohort of patients not using the product.
- In a pivotal double-blind placebo-controlled Phase 2/3 study in moderate to severe pediatric alopecia areata (25% to 99% SALT score), conducted in Germany and France (cohorts of 6 patients with 2 on placebo and 4 on Coacillium), a blinded interim review of the first 9 cohorts (i.e. 54 patients – 36 on Coacillium and 18 on Placebo) showed that 31 (57%) had improved (on average 41% improvement in SALT score) versus 17 (32%) worsening, and 6 patients dropped-out after their first visit. On average, patients enrolled in the trial had a SALT score of 53% at baseline and had been suffering from AA for 22 months. Considering the low response rate that is historically seen with placebo in this condition, this study may well be underway to establish in a rigid double-blind placebo controlled pivotal study the therapeutic potential of Coacillium for the management of alopecia areata.
- Across all studies, side-effects were mild, local and transient only.

In conclusion, it appears that Coacillium, a botanical drug, seems to be able to beneficially affect various types of hair loss disorders. The pleiotropic effect of this botanical drug, restoring anti-apoptotic levels of Bcl2, while at the same time suppressing inflammation, restoring the immune privileges of the hair follicle and boosting collagen deposition around the follicle, seems to partially reset and restore the biology of that hair follicle, resulting in hair growth patterns returning close to normal, with unparalleled safety.