Cellestia Biotech AG

A new targeted cancer therapy blocking Notch pathway signaling with a novel mode of action by selective inhibition of the transcription complex in the cell nucleus is approaching clinical development

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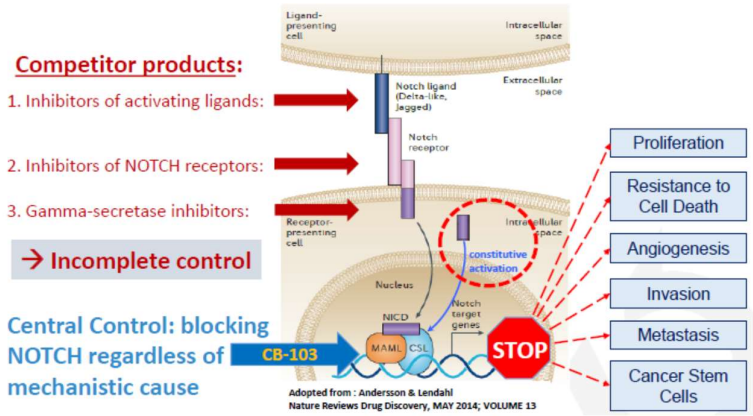
Cellestia Biotech AG Technologiepark Basel Hochbergerstrasse 60C 4057 Basel SWITZERLAND	Founded in: 2014 CEO: Michael Bauer, PhD No. of employees: 5 Type of Ownership: private Primary stock exchange: N/A

September 2016: Created by two scientists at the École Politechnique Fédérale de Lausanne (EPFL) in 2014 and joined by experienced drug development and business professionals in 2015, Cellestia Biotech AG is developing oral medication along with companion diagnostics for Notch dependent hematological malignancies and solid tumors. Venture Valuation (VV) interviewed the CEO, Dr. Michael Bauer in Basel, Switzerland.

VV: **What is the difference of your new mode of action Notch inhibitor compared to other compounds targeting the Notch signaling pathway?**

Bauer: CB-103 is a unique, first-in-class compound, targeting the transcription complex in the cell nucleus, the most downstream event in the Notch signaling cascade, whereas several pharmaceutical and biotech companies are targeting the Notch pathway on the cell surface, with monoclonal antibodies-based treatment against Notch activating ligands and receptors, as well as small molecule gamma-secretase inhibitors. (See image below).



While Notch is a clinically validated target, our competitors' compounds do not work in tumors driven by constitutive activation that is independent of receptor-ligand interaction and caused by genetic changes of the Notch genes leading to its continuous activation.

With our new mode of action targeting the Notch pathway centrally, our approach is the only method to control and block the signaling cascade regardless of molecular cause, by targeting the Notch transcription activation complex in the cell nucleus. The Notch signaling pathway, when aberrantly activated, leads to tumorigenesis and promotion of tumor growth. CB-103 is the only inhibitor that works at the gene transcription level, the convergence point of a complex, multi-factorial pathway.

Another difference is that CB-103 is a patient friendly oral medication formulated for immediate release after ingestion. The monoclonal antibody treatment approach, which some competitors are developing, requires frequent injections or infusions by medical professionals.

VV: **Who owns the project and what is the patent status?**

Bauer: Cellestia´s know-how is based on approximately 10 years of academic research and Cellestia has a world-wide exclusive license agreement on our invention from the EPFL Technology Transfer Office.

The PCT (Patent Cooperation Treaty) application was filed in 2012 in the EU, USA, Canada, Australia, Brazil, China, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, and Russia. The patent has already been granted in the USA and Singapore. Additional countries will follow in due course.

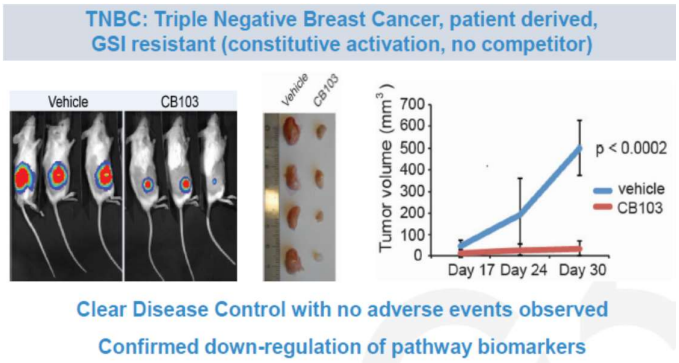
VV: **Your clinical development program is focusing on breast cancer and leukemia?**

Bauer: We have conducted research studies on a wide range of different cancer cell lines as well as in-vivo proof of concept demonstrated in patient derived triple-negative breast cancer (TNBC) and T-cell acute lymphoblastic leukemia (T-ALL).

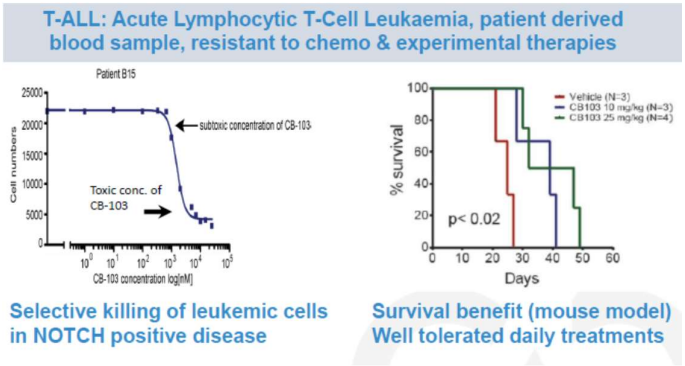
In clinical development we intend to focus on some key indications such as TNBC and T-ALL. However, an important element of our clinical program will be to identify the most promising indications, by selection of patients with confirmed Notch activation in their cancer. To that end, we will include Notch positive patients in a variety of hemato-oncological and solid tumor indications in our clinical development like leukemia, several lymphoma sub-types and numerous solid tumor indications (breast, melanoma, colorectal, lung, etc.). We have already set up a collaboration network with leading clinics and oncologists in Europe.

One key indication is TNBC, which represents around 20% of all breast cancers, and a sub-population within TNBC suffers from Notch driven cancer due to constitutive activation, for which no targeted treatment is available. Without having efficacious treatment options, this sub-population of TNBC is considered an orphan drug indication.

This image shows impressive disease control of TNBC tumor, achieved by treatment with CB-103 in a patient derived tumor model, with constitutive activation, compared to untreated vehicle control. In such cancers with its growth driven by Notch pathway activation, gamma-secretase inhibitors or Notch targeting antibody drugs do not work.



For leukemia, CB-103's effectiveness has been confirmed in blood samples derived from children who suffered from Notch positive T-ALL. The charts below demonstrate the anti-leukemia efficacy of our drug in a blood sample of a patient resistant to various chemotherapy regimen and other therapies. The data (left graph) confirm single-agent activity of CB-103 against the leukemia cells in the blood sample, without showing a toxic effect on normal blood cells from a patient, who died at the age of 3 years after failure of all available therapies. Using the transplanted into animal model, a clear survival benefit is demonstrated, as result of treatment with CB-103 (right graph).



In addition to monotherapy, CB-103 has been proven in pre-clinical tests to significantly enhance chemotherapy as well as other targeted therapies.

VV: **You are preparing for Phase I combined with Phase 2a clinical studies early 2017.**

Bauer: We have already achieved three levels of pre-clinical proof of concept: in-vitro cell cultures, in-vivo animal models, and the above mentioned ex-vivo human patient blood incubations.

The first-in-human Phase I-IIa clinical studies will be carried out in collaboration with Vall d'Hebron University Hospital and Institute of Oncology in Spain, a leading oncology research center in Europe, as well as with other leading clinics in Germany, Netherlands and Switzerland.

We are already working in close partnership with Vall d'Hebron University Hospital and Institute of Oncology to develop a diagnostic approach to enable the selection for our clinical studies of patients with tumor cells with confirmed Notch pathway activation, therefore having a higher chance to respond to CB-103 treatment.

At present, we are completing the preclinical development program. Having now "green lights" in all aspects, such as manufacturing, formulation and toxicology safety investigations, we are preparing for the initiation of our clinical development program in 2017.

VV: **How is your fund raising going?**

Bauer: In 2016 we successfully raised the funds to conduct the preclinical development program. Now we are in the process of starting discussions for Series A of approximately 10 million USD, and eventually including Series B of approx. 20 million USD with institutional investors (e.g. venture capital), private equity investors, and global pharmaceutical / biotech companies. These proceeds will be used to conduct the clinical development program.

We are also, already at this early stage, in discussions to evaluate opportunities for partnering or entering co-development activities with pharma companies, who are interested in adding value to their drug development pipeline / portfolio with our technology.

Recent transactions have demonstrated a significant industry interest in anti-cancer medicines targeting the Notch signaling pathway to complement the pipeline by the ability to target this important oncogenic pathway. This interest is particularly driven by recent research confirming that Notch activation is a major resistance mechanism that renders available therapies ineffective or drives relapse after initial response to treatment.

VV Comments after the interview:

The Notch signaling pathway is a very complex, multi-factorial cell to cell communication mechanism. Since 1914 when the appearance of a notch in the wings of the fruit fly was observed by John S. Dexter in the U.S., many researchers have contributed to reveal a highly complex cell signaling system.

Almost 100 years later, Cellestia has become the first company offering a "silver bullet" therapeutic solution to block tumorigenesis caused by an aberrantly activated Notch signaling pathway, regardless of mechanistic cause. Its lead development compound, CB-103, is close to complete pre-clinical development and will enter clinical development in 2017, offering a great hope for cancer patients with Notch positive tumors for whom no Notch-targeting therapy is available. With this new therapy, Cellestia is addressing a currently unmet medical need and therefore rapidly advancing the project to clinical stage.

According to Cellestia, it is estimated that over 250,000 people are newly diagnosed with a Notch positive cancer every year in the seven major markets. The global market related to Notch dependent cancers is estimated to exceed 10 billion USD. By leveraging its proprietary therapy combined with a companion diagnostic approach, Cellestia is well-positioned to become a leader in the Notch specific anti-cancer therapy.

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