

Partnering opportunity - Innovative health products

Biohit Oyj was established in 1988 and has been a publicly listed Finnish company since 1999. Biohit is a global hightech and biotech company driven by solid basic research and innovations, headquartered in Helsinki, Finland. On the focused niche markets Biohit is the global market leader in electronic pipettes, and the world's leading Original Equipment Manufacturer (OEM) of liquid handling products. Consequently, many OEM customers such as bioMerieux, 3M and three Johnson & Johnson Group companies complement their diagnostic test systems with Biohit's innovative solutions and technologies.

In addition to Liquid Handling (LH) division, Biohit has during the last seven years invested heavily in the development of the diagnostics products and has established a new Biohit HealthCare Division. The company's diagnostic products can be combined with its LH products to offer comprehensive analyzing systems and laboratories for research and clinical diagnostics.

Biohit is now seeking strategic partners for its diagnostic division. A new independent company, Biohit HealthCare will be comprised of the diagnostic products, related innovations, new products and technologies/know-how.

Biohit HealthCare (BHC)

BHC is focusing on the diseases of the gastrointestinal tract. In this area Biohit has carried out solid basic research in collaboration with leading scientists and has produced (r)evolutionary innovations with investments of over € 20 million. Biohit has unique solutions for reliable diagnosis of dyspepsia (25–40 % of the population), *Helicobacter pylori* (*H. pylori*) infection (over 50 % of the population) and atrophic gastritis with related risks (2–10 % of the population) as well as risks of the complications of gastroesophageal reflux disease (over 20 % of the population). These solutions (patents and patents pending) promote the development of safe and cost-effective evidence-based and preventative medicine.

BHC's diagnostic product range includes several immunoassay tests, quick tests, and monoclonal antibodies for diagnostic and research applications (www.biohit.com / Diagnostics / Literature and Brochures). These products, which together produce valuable information and diagnoses of diseases of the gastrointestinal (GI) tract and some other diseases, have been divided into the following product palettes.

Diagnostic Palettes for GI Tracts:

- GastroPanel innovation (www.gastropanel.net) is a patient-friendly examination technique for patients with GI disorders such as dyspepsia, *H. pylori* infection, atrophic gastritis and gastroesophageal reflux disease. The innovation is based on the measurement of various biomarkers from a single blood sample (Pepsinogen I,

Pepsinogen II, Gastrin-17, *H. pylori*, IgA & IgG antibodies). The next revolution in medicine is that pharmaceutical products will be created and used in tandem with diagnostic tests like GastroPanel to promote evidence based medicine and to help save people from unnecessary diseases caused by GI disorders.

- GastroView innovation (www.gastroview.com, www.gastroprofile.com) is the same as GastroPanel, excluding the Gastrin-17 test. GastroPanel and GastroView provide possibilities to rationalize the endoscopy practice, to select and prioritize patients for gastroscopy and biopsy specimen examination. These innovations may reduce the number of gastroscopies radically. The global market potential would be in excess of €4,0 billion.
- The GastroSoft program supplies a patient report of the GastroPanel and GastroView results. The reports produced by GastroSoft are based on clinical studies comparing the results of GastroPanel examinations with results from gastroscopy and biopsy specimen examinations.
- GastroMate Analyzers (under development), a fully automated Point of care (POC) analyzing system for immunoassay panels and tests, such as GastroPanel and GastroView. The market potential of the analyzer and consumables (e.g., immunoassay cassettes) may exceed one billion euros.
- GastroPanel laboratories: Four different-sized comprehensive laboratories for microplate immunoassay tests, such as GastroPanel and GastroView (www.biohit.com / Diagnostics / Biohit Diagnostics Product Catalogue, p. 23). There is no estimate of the market potential.

Quick Tests and some other tests:

- *H. pylori* Quick Test gives results in 1–2 minutes.
- Lactose Intolerance Quick Test offers results in 20 minutes and is, similarly to *H. pylori* Test, to be combined with every professionally performed gastroscopy and biopsy specimen examination (no estimate of the market potential).
- Fecal Occult Human Blood Quick Test for the screening of colorectal cancer (no estimate of the market potential).
- Immunoassay Tests for Celiac Disease Panel and Inflammatory Bowel Disease Panel (the market potential might be close to €10 million).
- SLE (Systemic *Lupus erythematosus*) immunoassay Test. A combination of the Biohit SLE test with an anti-dsDNA test is recommended as the panel of choice in differentiation of SLE from rheumatoid arthritis. The SLE test could also be used as an aid for assessing the activity of SLE (the market potential might be close to €50 million).
- Cellular Fibronectin (cFn) Tests for the detection of cFn in plasma and in other body fluids for diagnosis of reactive conditions (1), such as gastrointestinal cancer (2). An example diagnosis of the risk of preterm birth during pregnancy by analysis of cFn levels in body fluids (under evaluations (3), the market potential might be close to € 500 million, (4) below). Serum cFn determination by the cFn ELISA (ready) and cFn POC quick blood test (under development) can also be valuable in clinical and

emergency practice to improve the risk/benefit ratio of thrombolytic treatment of stroke patients. In addition, stroke patients can be divided by the cFn ELISA in a low and a high risk group. There are approximately one million strokes/ a year in Europe, of which 20% will get another stroke within a year. Consequently, there is need to check all the stroke patients two times a year. The market potential of the cFn ELISA and POC tests may exceed €500 million.

(1) The cFn- immunoassay blood test aims to complement the GastroPanel examination. If the GastroSoft-program, which interpretes the results of the test panel, indicates an increased risk of gastric cancer and the serum level of cFn is elevated, it may indicate that the patient suffers from gastric cancer or is at a high risk of it. If the interpretation provided by GastroSoft is normal but the level of cFn is elevated the treating doctor should look for cancer elsewhere in the gastrointestinal tract. If the result of the GastroPanel and the level of cFn are normal it is unlikely that the patient suffers from gastric cancer.

(2) Yläupa S. (1996). *The Development of a Method for Quantification of Cellular Fibronectin EDAcFn and Its Clinical Applications*, Ph.D. Thesis, University of Helsinki.

(3) In collaboration with Biohit Oyj., The Department of Obstetrics and Gynecology, Kuopio University Hospital (Kuopio, Finland) is evaluating Biohit's cFn test. The clinical study is conducted by Professor Seppo Heinonen, and it's purpose is to determine the dynamics of cFn concentration in swabs from the posterior fornix during pregnancy and the process leading to delivery. The results are compared with commercial oncofetal cFn quick test (Adeza, Sunnyvale, CA, USA), and the goal is to determine the accuracy of Biohit's quantitative cFn test in the assessment for risk of preterm delivery.

(4) In 1988 – 1989 two founders of the US based start-up company Aspen visited Biohit. Since these visits Biohit provided for some years its cFn MAB's to Aspen company, now with the new name Adeza and owned by Cytyc. – See Adeza and its market value at www.cytyc.com / Corporate / Press releases: Feb 12, 2007 Purchase Price of Approximately \$450 Million Adeza to Be Acquired by Cytyc for \$24 Per Share. Adeza's product is the cFn MAB- based test system for the risk of preterm birth during pregnancy (Luzzi V, Hankins K, Gronowski AM. Accuracy of the rapid fetal fibronectin TLi system in predicting preterm delivery. Clin Chem 2003; 49: 501-2). The sales of this Adeza's POC cFn quick test is approx. \$50 million and the global market potential estimate is \$500 million.

Microplate instruments

BHC completes microplate immoassay kits with some microplate instruments, soft ware and pipettes for working as comprehensive analyzing systems (5). CEO of Biohit, Professor Osmo Suovaniemi's innovations, such as vertical measurement principle, have revolutionized microplate analyses worldwide and have been utilized extensively and successfully since the 70's (www.google.com / search: "*Osmo Suovaniemi vertical measurement principle*" and "*the King of Patents Osmo Suovaniemi in Finland 2002*"). These innovations have become global laboratory and industrial standards. They also resulted in the rapid and massive development of reliable and safe non-radioactive microplate immunoassays. Today most of analyzers and analyzing systems in research and clinical laboratories are based on the vertical measurement principle and can be used with GastroPanel and GastroView as well as with any other microplate immunoassays.

(5) Suovaniemi O. (1994). *Automated Instrumentation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors*, Ph.D. Thesis, University of Helsinki.

Related new product and technology/know-how palette

Acetaldehyde eliminating product palette:

- XyliCyst chewing gum eliminates carcinogenic and addictive acetaldehyde from the saliva of smokers (the market potential may exceed €500 million).

- BioFilter eliminates carcinogenic and addictive acetaldehyde from smoke of tobaccos (no estimate of the market potential).
- BioCyst capsules (food additives under development) eliminates carcinogenic acetaldehyde formed in achlorhydric stomach. Achlorhydria caused by atrophic gastritis or proton pump inhibitors (PPI) makes the person susceptible to the colonization of the stomach with microbes representing the normal oral flora. In consumption of sugars, which are parts of most balanced meals, the oral bacteria can elicit the production of acetaldehyde by fermentation in the stomach. Also ingested alcohol can be metabolized to acetaldehyde by these same microbes. Cysteine that dissolves from BioCyst capsules in the stomach forms a stable complex with acetaldehyde and makes it thereby inactive. In practice, the forthcoming BioCyst capsules should be used in connection with eating by individuals who are diagnosed to have atrophic gastritis and achlorhydria, or even by those under long-term use of PPI medication. The market potential for BioCyst may be substantial, even billions of euros because of the high number (500 million) of people with atrophic gastritis and PPI-users, as well as because of the increasing awareness of carcinogenic acetaldehyde.
- BioFood method eliminates carcinogenic acetaldehyde from some food products (e.g., yogurt and beer). There is no estimate of the market potential.

Technology and know-how palette:

Technologies and know-how as well as products (patents and patents pending) are available for licensing and collaboration (e.g. GastroPanel applications for automated non-microplate immunoassay analyzers). Monoclonal antibodies, *E. coli* strains, DNA Probes, *in situ* tests, Cox-2 and SNP analysis:

- Clones and monoclonal antibodies for histopathological tumor diagnosis and for use as basic components in diagnostic test kits
- Technology and capacity for producing HPV-, EBV- and CMV DNA Probes
- *E. coli* strains for producing HPV-, EBV- and CMV DNA Probes
- HPV *in situ* Typing and Screening Tests (ready but not marketed)
- EBV and CMV *in situ* Typing Tests (ready but not marketed)
- Cyclooxygenase (COX-2) as a tumor marker. Patents pending (a stand by project).
- Single Nucleotide Polymorphisms (SNP) analysis (a stand by project). Patents pending.

Collaboration opportunities with pharmaceutical industries

In medicine, it is obvious that good diagnostics go hand-in-hand with proper treatment. The business world as well as Food and Drug Administration (FDA) regulators are increasingly building this understanding into product development by supporting co-development of new drugs with development of diagnostics. This new development and the combination of the GastroPanel diagnostics with the PPI treatment of gastroesophageal reflux disease as well as with the antibiotics and PPI treatment of *H. pylori* infection would promote the safe and cost-effective evidence-based and preventative medicine. This will substantially reduce the costs of health care as well as prevent diseases, promote wellbeing and even save from unnecessary deaths.

Opportunity Criteria

Biohit has successfully carried through the major part of the long R&D-stage of the above mentioned diagnostic product palettes and is now on the verge of global breakthrough. For this purpose Biohit HealthCare (BHC) is looking for strong strategic partners from pharmaceutical industries, diagnostics and financial units to create a dream team of diagnostics or diagnosis and drugs. The partners should be willing to complete and strengthen their present and future product platforms with BHC's present and future diagnostic products and, when appropriate, with Biohit's liquid handling products.

Biohit's target is that the new BHC company, to be established, for example, on joint venture basis, will have enough financing (a private placement) and that the partner(s) will bring also and especially global marketing/sales skills as well as worldwide distribution networks. Biohit's target is that Biohit HealthCare will become a public company within 2–3 years.