



## Strong Potential: Transforming the way medicines work

Alpha Deal Group considers BioLingus GmbH, as a unique opportunity to benefit from strong and growing biological market. The Company has developed first-in-class novel drug delivery technology that allows oral (sublingual) administration of peptides, biologicals and immune-therapies. The technology has been tested in both animal and human studies and has proven to be able to match subcutaneous injections in its effectiveness for delivering compounds. The Company's investment in the development of novel drug delivery technology has been recognized by the pharmaceutical industry. It is exploring partnerships with other pharmaceutical companies to further exploit the potential of its technology and transform current standard practices in the administration of peptides and proteins.

### Investment Highlights

- BioLingus has developed a novel proprietary platform for sublingual delivery of macro molecules such as peptides and proteins for chronic diseases and immune-therapies.
- Sublingual delivery also known as 'under the tongue' delivery means that the drugs diffuse into the blood through tissues under the tongue, rather than via gastrointestinal (GI) tract, resulting in superior absorption and bioavailability.
- BioLingus's main focus is on metabolic diseases such as diabetes and inflammatory diseases such as arthritis.
- In the metabolic space, BioLingus is using its technology to develop sublingual formulations of exenatide, liraglutide (new) and the combination product of insulin+exenatide
- In the anti-inflammatory space, BioLingus is focusing on the development of sublingual IL-2 for auto-immune disease, including type-1 diabetes, psoriasis and arthritis.
- BioLingus technology is differentiated along critical success factors such as: sublingual delivery instead of "oral via GI tract"; use of chronically safe / GRAS Excipients; relative low cost product, with long shelf life and scalable process.
- Sublingual delivery benefits include: ease of administration; fast onset of action (under the tongue there is a thin layer of epithelial cells and a strong blood flow, so drugs are taken up quickly into the body); room temperature storage of drugs (unlike injectable solutions that must usually be refrigerated); and avoidance of needles, needle stick injuries and blood borne virus infections.
- These benefits are particularly relevant in developing countries, where warm conditions can degrade the drugs and vaccines.

## BioLingus GmbH

### BUY SIDE PORTFOLIO SELECTION

Name	<b>BioLingus GmbH</b>
Industry	<b>Biotechnology</b>
Employees	<b>n/a</b>
Founded	<b>2014</b>
Headquarter	<b>Hergiswil, Switzerland</b>
Website	<a href="http://www.biolingus.ch">www.biolingus.ch</a>

#### Business Overview

- BioLingus has developed a technology for the development of oral (sublingual) delivery of macro molecules such as peptides and proteins for chronic diseases, including Diabetes I & II
- The Company has its own patent protected technology for the next 20 years
- Patents have been granted in the US, Australia, China, Japan, Russia, Canada, Mexico, Brazil, Thailand. In 2017, patents were granted to Europe, Malaysia and Indonesia
- BioLingus Technology is a micro-encapsulation process which uses the proprietary technology to create microcapsules, which can be formulated in different formulations, such as sublingual tablets

#### Key Developments

- **October 2017:** Successful pharmacodynamic studies with sublingual liraglutide
- **July 2017:** Awarded Best European CEO Biotech – Europe and Most Innovative Biotech company – Europe, by the CEO Monthly Magazine
- **March 2017:** Successful development of novel liquid (drop) formulation, which will allow very precise and personalise dosing

#### Management

- Yves Decadt, Chief Executive Officer
- Didier Coquoz, Chief Development Officer
- Thomas S.Y. Ko, Chief Scientific and Technology Officer
- Ken Pang: Medical Director

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## Sublingual Technology for Diabetes and Metabolic Disorders

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BioLingus is currently developing the following treatments for diabetes and metabolic disorders

- Oral (sublingual) formulation of exenatide
- Oral (Sublingual) formulation of liraglutide (new)
- Oral (Sublingual) formulation of insulin+exenatide ("insulin+")
- Oral (Sublingual) formulation of IL-2 for early onset of diabetes Type I

### Diabetes type II:

- Type II diabetes mellitus (DM) is an incurable chronic metabolic disorder that affects approximately 10% of the population. Type II DM is estimated to account for over 90% of all types of diabetes and is growing globally
- Over 175 million people are estimated to have undiagnosed Type II DM which is largely a consequence of unhealthy eating, irregular or no exercise
- In addition, 35.3% of people are estimated to have pre-diabetes, which is defined as having a glycated haemoglobin of 5.7% to 6.4% in patients not previously diagnosed with diabetes. This is equivalent to a population of approximately 7 million in the UK alone and represents a significant growth over the rate of 11.6% established in 2003
- Obesity is a major risk factor for pre-diabetes

*While the BioLingus development of sublingual exenatide, insulin+ and IL-2 was already ongoing since the previous report, we focus in this report on the new development related to sublingual liraglutide.*

### Liraglutide sublingual

**Liraglutide, like exenatide, is a "GLP-1 analogue" developed and marketed by Novo Nordisk. Sales in 2016 were around \$3bn.**

- Liraglutide is an acylated glucagon-like peptide-1 agonist (GLP-1 agonist) derived from human GLP-1-(7-37), a less common form of endogenous GLP-1, and was originally approved for the **treatment of Type II diabetes mellitus** by the EMA in July 2009 and the FDA in January 2010
- The drug was first developed for *sub-cutaneous delivery* by Novo Nordisk Pharmaceuticals and has been marketed exclusively by

them globally although generic forms (injectables) are under development by various companies including Teva

- It is marketed globally with the brand name Victoza for type II diabetes and, more recently, Saxenda - a separate strength for the treatment **of obesity**
  
- Importantly, liraglutide – unlike other GLP-1 agonists – is indicated for the treatment of obesity and, since July 2017, as an adjunct for the management of cardiovascular risk factors. Both of these indications could effectively treble the market potential for liraglutide globally
  
- **In summary:**
  - o BioLingus Sublingual Liraglutide represents a significant opportunity in terms of sales growth; it offers a significantly more preferable way of delivering liraglutide to patients
  - o Liraglutide's current sales is around \$3bn and is expected to double in the next 5 years
  - o BioLingus Sublingual Liraglutide is anticipated to have relatively low production costs and, consequently, a relatively high profit margin
  - o In patients with such mild indications (obesity, NASH, prediabetes), the preference of an oral treatment versus an injection will be more pronounced as compared to patients with diabetes
  - o Because all the above, it is expected that BioLingus may take a substantial share of the future GLP-1 analogue market

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## Sublingual Technology for Inflammatory Diseases

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In the anti-inflammatory space, BioLingus is focusing on the development of sublingual IL-2 for auto-immune diseases, including type-1 diabetes, peanut allergy, psoriasis and arthritis.

In this report, we focus more on the psoriasis development.

### Developing a needle-free treatment for psoriasis

BioLingus is working on developing a needle-free treatment for psoriasis. Sublingual delivery provides an advantage because it allows for more direct delivery to the lymphatic system, providing both the benefit of not requiring injections and the advantage of increasing the efficacy of some formulations.

**Psoriasis:** Psoriasis is a common, chronic, immune-mediated disorder that causes epithelial cells to build up and form scales and itchy, dry patches. The disease typically affects patients outside of their elbows, lower back, knees or scalp. Psoriasis can be associated with further serious health conditions, such as diabetes, heart disease and depression. In severe cases, people can develop psoriatic arthritis, which can lead to painful inflammation in the joints. According to WHO, psoriasis affects 1.5% to 5.0% of the population in most developed countries. To address these needs, a number of new, highly effective injection-based drugs have hit pharmacy shelves in recent years. However, there is an ever-increasing need for developing ways to improve both convenience and adherence to these medications by turning injections of biological molecules into pills.

**Current Standard treatment of care for psoriasis:** Although there is currently no cure for psoriasis, several treatment options are available for patients to reduce inflammation and clear some symptoms. Mild forms of the disease are treated with topical agents, moderate forms with phototherapies, and severe forms with systemic agents. Injectable biologic therapies, such as the TNF- $\alpha$  and IL-12/23 inhibitors are also used to treat moderate-to-severe plaque psoriasis. Leading biologic treatments approved for treatment of psoriasis including Adalimumab (Humiria), Etanercept (Enbrel), and Infliximab (Remicade) have long dominated the psoriasis market. However, these compounds have started to face some stiff competition as new drugs have emerged.

Recently, there has been a wave of new injectable biologics targeting interleukin-17 (IL-17). In July, Leo Pharma received permission from the European Commission to market Kyntheum (brodalumab), an antibody that blocks the IL-17 receptor, to treat moderate-to-severe plaque psoriasis. Brodalumab, which was originally developed by AstraZeneca, is also being marketed in the US under the name Siliq by Valeant. Some

major players have their own versions of an IL-17 antibody. For example, Novartis' Cosentyx (secukinumab) and Eli Lilly's Taltz (ixekizumab) are both approved to treat plaque psoriasis both in the US and the EU. In July, Janssen received FDA approval to use another drug, Tremfya (guselkumab), an antibody that selectively inhibits IL-23 to treat moderate-to-severe plaque psoriasis. In head-to-head studies with both its own drug, Stelara, and Humira, researchers found that patients on Tremfya achieved clearer skin. Janssen is currently in the midst of conducting series of phase III trials with the antibody for psoriatic arthritis, as well as another head-to-head study with the anti-IL-17 antibody, Cosentyx. Boehringer Ingelheim and AbbVie have partnered to develop their own anti-IL-23 antibody to treat psoriasis as well as other immune conditions, such as Crohn's disease and asthma.

#### Comparison of leading immune modifying drugs for psoriasis

Brand name	Manufacturer	Generic name	Mode of administration	Dosing schedule	Price*
Enbrel	Amgen	Etanercept	Subcutaneous	Twice a week	\$4,000 per four syringes of 50mg
Stelara	Janssen	Ustekinumab	Subcutaneous	Dosing at day 0, then 4 weeks, then every 12 weeks	\$9,000 per syringe (45mg/0.5ml)
Humira	AbbVie	Adalimumab	Subcutaneous	Every 2 weeks	\$4,150 per 2 syringes of 40mg/0.8ml
Cosentyx	Novartis	Secukinumab	Subcutaneous	once a week for 5 weeks, once a month thereafter	\$8,300 per 2 syringes of 150mg/ml

Source: Alpha Deal Group. Note: \*Retail price.

**Psoriasis market size:** According to Global Data, the psoriasis market is forecasted to rise from \$6.6bn in 2014 to over \$13.3bn by 2024, driven by the availability of new therapies, increased uptake of biosimilar drugs where available and expansion of existing therapies across the globe. Small molecule and biologic drugs targeting IL-17 and IL-23 are expected to lead the way.

## Investment Thesis

**BioLingus is making tremendous progress in the execution of its strategy to become a leading player for oral (sublingual) delivery of peptides and proteins for chronic diseases.**

### Sublingual Delivery of Therapeutic Biologicals

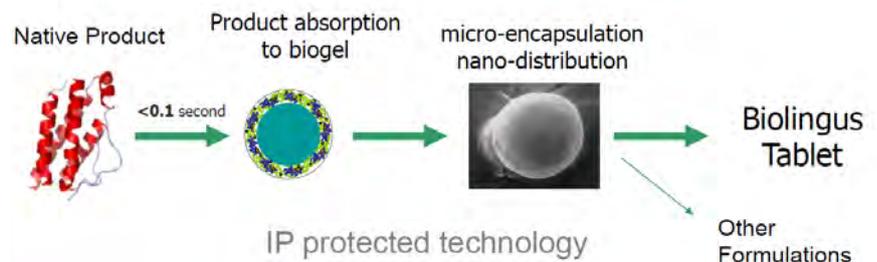
BioLingus is a Swiss biotech company spearheading the development of oral (sublingual) delivery of peptides and proteins. The Company focuses on the development of its own products for the treatment of chronic diseases, such as diabetes and inflammatory diseases. A particular area of interest is also mucosal immunotherapy, as sublingual administration allows for targeting the lymphatic system directly.

Lead product are the oral version of the diabetes drug exenatide liraglutide and the combination insulin+exenatide. BioLingus actively seeks to develop other oral biologics with partners.

### Breakthrough Technology Platform

BioLingus has developed and owns patented protected technology for sublingual delivery macromolecules, such as peptides, proteins, novel protein scaffolds, nucleotides, domain antibodies, vaccines and immunotherapies (BioLingus Technology). The BioLingus Technology is the result of more than a decade of research and development on different types of molecules which have resulted in optimised and stable formulation, robust process, and innovative custom built equipment engineering of the granular design.

At the basis of the BioLingus Technology is a micro-encapsulation process which uses the proprietary technology to create microcapsules, which can be formulated in different formulations, such as sublingual tablets. The micro-encapsulation process has been modified and optimised for sublingual delivery of bioactive molecules proteins and is protected by propriety patents.



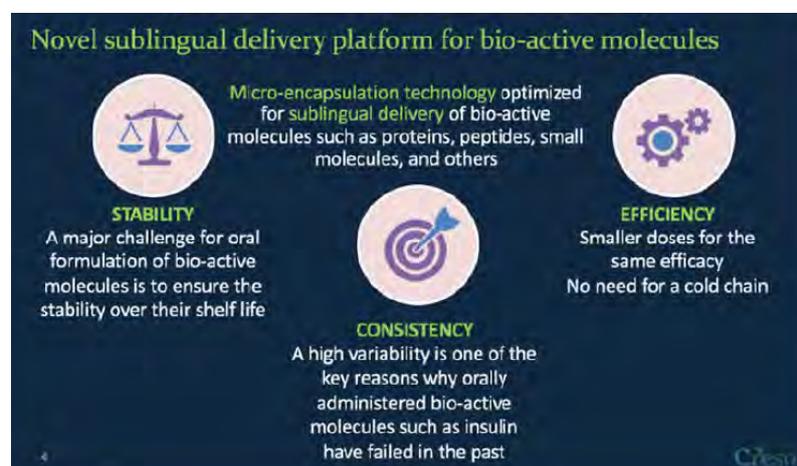
Source: BioLingus, Alpha Deal Group

BioLingus Technology has been tested in both animal and human studies and has proven to match subcutaneous injections in its effectiveness for delivering compounds. In other words, the same drug can be given in an oral form without the anguish of injections.

In the past year, BioLingus has successfully developed a liquid form of its formulation, which allows for very precise and personalized dosing.

## BioLingus Technology Differentiation

The BioLingus Technology is not only achieving the protein stabilization with commercially acceptable bio-availability and low variability, but also is differentiated along critical success factors (which were reasons for failure of other technologies in the past). Under the Company's sublingual delivery technology, the drug diffuses into the blood through tissues under the tongue, through the oral cavity (not via the GI (gastrointestinal) tract). The buccal mucosa offers a near ideal non-invasive portal through which natural products can enter directly into the blood stream. Its large surface area provides direct access to a rich network of blood vessels, offering the potential for rapid absorption of medications into the circulatory system. Using this route the delivery method avoids the gastrointestinal and the respiratory systems. The technology uses chronically safe / GRAS ("Generally Recognised As Safe under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act) inactive substances; and is a relatively low cost product with long shelf life and a scalable process.



Source: BioLingus, Alpha Deal Group

Sublingual delivery by itself is not new; it has been used in industry for small molecules. However, what is new is that the Company has redeveloped it for biological molecules. It opens the door for non-invasive delivery of many biological molecules that have so far only been taken by injections. For instance, in diseases such as diabetes and inflammatory disease, many patients have to take daily injections, as it is the only way to get their medicines administered. For some of those patients, the Company's technology may significantly improve the quality of their daily lives.

**Technology Differentiation (vs other companies in field)**

	BioLingus	A1	A2	C1	C2	D	E	G	H	O	R	R
<b>Oral Route</b>												
No GI targeting	V	-	V	-	-	-	-	V	-	-	-	-
Buccal	V	-	V	-	-	-	-	V	-	-	-	-
Sublingual	V	-	V	-	-	-	-	-	-	-	-	-
<b>Composition</b>												
GRAS / chron. safe excipients	V	?	?	?	?	?	?	?	?	?	?	?
No protease inhibitors	V	?	?	?	?	?	?	?	?	-	?	?
No modification API	V	V	V	V	V	V	V	-	V	V	V	V
<b>Other</b>												
Sublingual Immune Therapy	V	-	-	-	-	-	-	-	-	-	-	-
No device needed	V	V	V	V	V	V	V	-	V	V	V	V
Cost-Effective	V	V	V	V	V	V	V	V	V	V	V	V
Protein stabilization	V	?	?	?	?	?	?	?	?	?	?	?
User-friendly	V	V	V	V	V	V	V	-	V	V	V	V
Commercialized product	V	-	-	-	-	-	-	V	-	-	-	-

Source: BioLingus, Alpha Deal Group

**Experienced Team with Significant Experience**

BioLingus management team has over 75 years of combined experience in global pharmaceutical industry. Yves Decadt is CEO and Co-Founder of BioLingus. He has more than 25 years of global pharmaceutical experience in technical/scientific, business development roles and as CEO. He has served as CEO of Stragen Pharma and VP Business Development at SkyePharma, both in Switzerland. Yves has worked almost 20 years at Johnson and Johnson, in different roles and countries. Didier Coquoz, Chief Development Officer, is a 20+ years seasoned pharma R&D executive (VP R&D and CEO) and serial biotech entrepreneur with experience in North America and Europe. He has been instrumental in the development/regulatory management from drug candidate up to phase III and registration of close to 30 biologics, monoclonal antibodies, peptides, cell-based therapeutics, NCEs, of which 4 reached the market world-wide. Thomas SaiYing Ko, Chief Scientific and Technology Officer, is a pharmaceutical formulation specialist with 35 years of proven technical and commercial success. He has special skills in systemic delivery of biologically active peptides or protein for the treatment of chronic diseases without injections. He is also inventor of a number of patents. We believe this management team is fully capable of executing and growing its business into a formidable and influential player within the drug delivery technology space over the coming years.

Dr Ken Pang has joined BioLingus in 2017 as Medical Director. Ken (MBBS (Hons), BMedSc, FRACP, PhD) is a practising physician scientist. Clinically, Ken graduated as the valedictorian of his medical school class at Royal Melbourne Hospital in Australia, before completing his specialist training in pediatrics. Scientifically, Ken completed his PhD at the University of Melbourne in immunology and genomics, and subsequently undertook postdoctoral studies as a Fulbright Scholar in the Department of Molecular and Cellular Biology at Harvard University, where he also completed a Business Development Fellowship within the

Office of Technology Development. Ken's academic output includes 39 peer-reviewed publications that have been cited >8000 times and have appeared in journals such as *Science*, *Immunity*, *Genome Research*, and *Molecular Psychiatry*.

### **Actively Looking for Partnerships and Funding**

As part of its strategy to secure the necessary resources to further exploit its technology and advance its pipeline for the benefit of patients, BioLingus continues to pursue discussions with potential industry partners. The Company also plans to raise additional funds to advance its own projects, develop partnering projects as well as for supply and manufacturing.

We believe that, as compared to typical new molecule development, BioLingus has a) relative low development costs b) relative low risk and time to exit and c) can be applied to many high value drugs.

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