STATUS REPORT

XINTELA

XINTELA – INTEGRINS MARKING THE FUTURE

INTRODUCTION

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After many years of hype and expectations, modern regenerative medicine therapies are now numerous and are being delivered to patients in several indications. However, the next generation of cell therapies is evolving and showing progress, and Lund-based biotech Xintela is in the forefront of the development with its integrin marker technology platform, XINMARK. The marker technology is utilized to identify and select high quality stem cells for the development of the therapeutic stem cell platform XSTEM. The main focus for XSTEM is Osteoarthritis and Covid-19 related ARDS. Moreover, XINMARK is also used for the development of targeted antibody-based therapies to aggressive cancers.

Product development based on many years of research

The founder and CEO of Xintela, **Evy Lundgren Åkerlund**, initially discovered the cell surface protein integrin $\alpha 10\beta 1$ as a marker on cartilage cells over 25 years ago. Later discoveries showed that integrin $\alpha 10\beta 1$ is also present on the cell surface of mesenchymal stem cells, and that it is highly expressed on certain aggressive tumours, including glioblastoma. The discovery of integrin $\alpha 10\beta 1$ now forms the basis for the company's marker technology platform, **XINMARK**, used by Xintela in its product development.

Unique stem cell platform XSTEM

Xintela is using its marker technology to identify and select high quality allogeneic mesenchymal stem cells, XSTEM. With this approach, Xintela is able to demonstrate identity and purity of its stem cell product, and maintain consistency over time, which is very important from a quality and regulatory point of view in the development of cell-based therapies. The selection of high-quality stem cells also gives several functional advantages.

Osteoarthritis

The company's first indication for XSTEM is osteoarthritis (OA), a degenerative disease of the joints resulting in gradual breakdown of joint cartilage. Around 15 per cent of the population suffer from OA globally, which makes it one of the most common human diseases.

There are no approved treatments for OA that can halt or cure the disease, and today's treatments can only offer symptomatic relief. Xintela's first stem cell product for treatment of OA, XSTEM-OA, has the potential to become a disease modifying treatment in a market estimated to grow to USD 10 billion by 2024.

Veterinary medicine

Xintela's marker technology for stem cell therapy development can also be applied in veterinary medicine to treat dogs and horses suffering from OA. The prevalence of canine OA is as high as 20 per cent in North American dogs over one year of age. The market for stem cell treatments of OA in dogs is steadily growing and is expected to reach USD 218 million in 2026.

Covid-19/ARDS

Within the stem cell area, Xintela is also evaluating XSTEM for the treatment of Covid-19 related Acute Respiratory Distress Syndrome (ARDS), a life-threatening condition affecting many Covid-19 patients. Swedish innovation agency Vinnova granted Xintela SEK 1 million for a preclinical study of XSTEM-ARDS in this particular indication. Xintela has recently announced promising results from the ongoing study.

INTRODUCTION

Large hidden value in Xintela´s GMP facility

On the premises in Lund, Xintela has built their own GMP facility to produce stem cells for their upcoming clinical trials in OA, as well as future clinical and animal health applications.

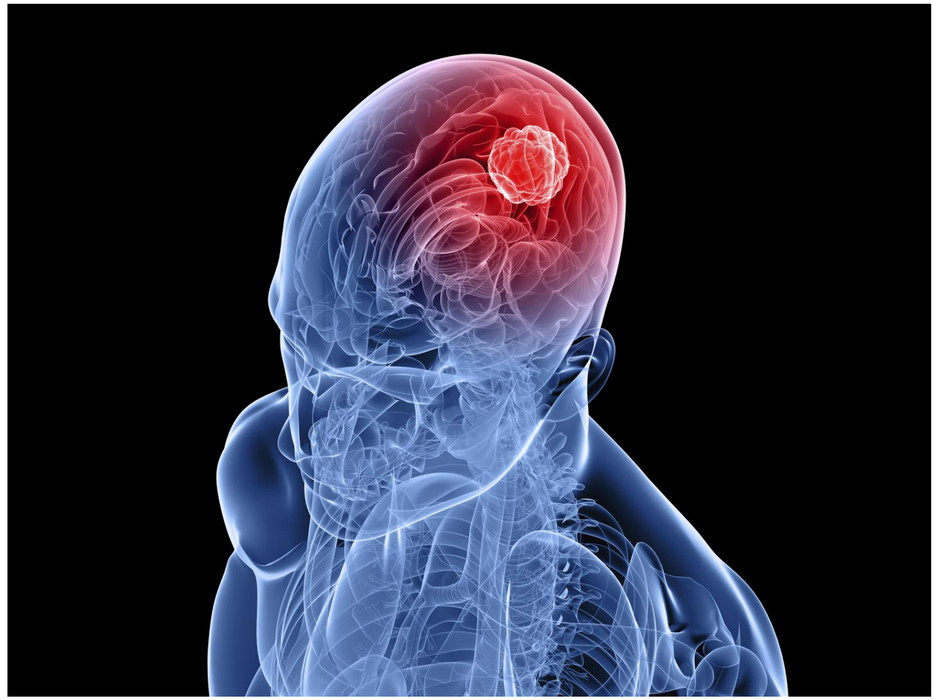
Having access to their own GMP facility and full control over the manufacturing process provides several strategic benefits for the company. In a global environment, where the number of new advanced therapies under development are rapidly increasing, the demand for qualified GMP facilities for these type of products is rapidly increasing. Therefore, the GMP facility increases Xintela's attractiveness as a future partner since Xintela can not only provide a unique therapeutic stem cell technology, but also the manufacturing capacity.

Moreover, the knowledge of GMP production built by Xintela internally could potentially also open up for another type of attractive business model that may generate large revenues – contract manufacturing.

Oncology – targeting aggressive cancer forms

Xintela has also discovered that their marker integrin α10β1 is highly expressed in several aggressive cancer forms, making it an attractive therapeutic target for these aggressive cancers. Therefore, the company is developing an antibody-based therapy, XINMAB, targeting integrin α10β1, and the first indications that are being explored are glioblastoma and triple negative breast cancer (TNBC), two areas of high unmet medical need. The company has reported promising preclinical in vivo results, demonstrating that their treatment concept holds great promise.

The targeted antibody therapy is also being evaluated for other aggressive cancers such as lung cancer, prostate cancer and pancreatic cancer.



SAMMANFATTNING PÅ SVENSKA

Markörteknologi

Xintela är ett av bolagen som ligger i framkant av nästa generations cellterapier och nya riktade cancerbehandlingar. Bolaget grundades av Evy Lundgren-Åkerlund 2009 och baserar sig på hennes forskning och upptäckt av cellyteproteinet och markören integrin α10β1 .

Upptäckten utvecklades under många år av forskningarbete till XINMARK, Xintelas unika teknologi som ligger till grund för stamcellsplattformen XSTEM, samt används för att utveckla antikropps-baserade terapier mot aggressiva cancerformer.

XSTEM för behandling av artros

Inom stamcellsterapi har Xintela utvecklat XSTEM-OA, Xintelas selekterade stamceller för behandling av artros i människor. Bolaget kommer att inleda kliniska studier på patienter med knäartros under 2021. Det medicinska behovet av artrosbehandlingar är stort eftersom det inte finns några sjukdomsmodifierande behandlingar. Marknaden OA-behandlingar växer och väntas vara värd 10,1 miljarder USD år 2024.

XSTEM för behandling av Covid-19 relaterad ARDS

Inom stamcellsområdet erhöll Xintela i våras bidrag från Vinnova om att utvärdera XSTEM som en potentiell behandling av Covid-19-patienter som utvecklat det livshotande tillståndet akut andnödssyndrom (ARDS). Bidraget finansierar en preklinisk undersökning vars resultat förväntas under Q4 2020. Huvuddelen av studien är genomförd och resultaten hittills visar en tydlig förbättring av lungfunktionen och att stamcellerna kan vända det kritiska ARDS-tillståndet.

GMP-anläggningen

Xintela har byggt upp en egen GMP-anläggning i sina lokaler på Medicon Village i Lund. Bolaget avser att här tillverka XSTEM för de kommande kliniska studierna och även veterinärprodukter när det blir aktuellt.

Att äga och ha tillgång till sin egen GMP-anläggning skapar en rad ekonomiska och strategiska fördelar. Inom cell- och genterapi råder det särskild brist på den här typen av produktionsanläggningar då utveckling av nya cellterapier ökar kraftigt.

Onkologi – aggressiva cancerformer

Xintela har även upptäckt att ett högt uttryck av integrin α10β1 i flera aggressiva cancerformer. Bolaget utvecklar därför XINMAB, en riktad behandling med antikroppar som binder till integrin α10β1, i form av funktionsblockerande antikroppar och s.k. antibody-drug conjugates.

Huvudfokuset med XINMAB just nu är glioblastom och trippelnegativ bröstcancer (TNBC), två typer av aggressiv cancer med ett stort medicinskt behov. Lovande prekliniska resultat har meddelats av bolaget inom glioblastom-projektet och under sommaren 2020 annonserades att TNBC kommer att bli nästa fokusområde inom onkologi. Dessa indikationer har ett stort marknadsvärde, inom glioblastom finns även möjlighet till orphan drug designation-status. Marknaden för TNBC-behandlingar väntas växa till 2,1 miljarder USD till 2025, medan marknaden för glioblastombehandlingar beräknas uppgå till 3,3 miljarder USD år 2024.

Onkologiprogrammet har potential att utökas till andra aggressiva cancerformer som exempelvis prostatacancer, lungcancer och bukspottskörtelcancer.

UPCOMING TRIGGERS

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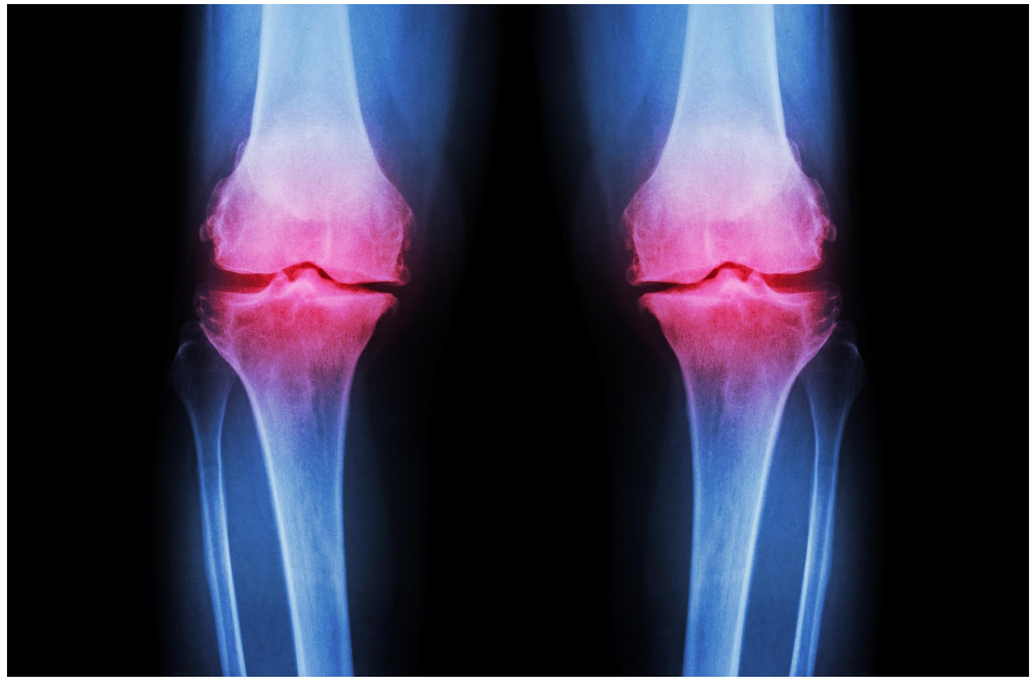
Key milestones

- Approval from the Medical Products Agency for production of XSTEM in the GMP facility
- Final results from preclinical study evaluating Xintela's stem cell therapy for Covid-19 related ARDS (Acute Respiratory Distress Syndrome)
- Initiation of clinical phase I/II study with XSTEM-OA in patients with knee osteoarthritis
- Partnership in veterinary medicine for the development and commercialisation of stem cell therapy for animals
- Production of antibody candidate and perform safety/tox studies in the oncology project
- Partnership within the oncology project for clinical development and commercialisation



THE COMPANY IN BRIEF

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Xintela was founded in 2009 by Evy Lundgren-Åkerlund and is based on her research from Lund University and in the company Cartela.

Xintela is headquartered at Medicon Village in Lund, Sweden. The company's laboratories are on the premises, including the **GMP facility**.

The company's largest shareholder is **The** Bauerfeind Group, one of the largest orthopaedic equipment companies based in Germany, and has global prescence.

Xintela's management and board of directors are also shareholders of the company.

Market	Nasdaq First North Growth Market	Number of shares	57 542 856
Ticker	XINT	Share price 2020-10-29	SEK 3.12
ISIN	SE0007756903	Market cap 2020-10-29	SEK 179 533 711

Largest shareholders as of 2020-08-31*	No. of shares	Capital/votes (%)
Deutsche Bank AG, W8IMY	12 705 255	22,08
Evy Lundgren-Åkerlund	4 273 250	7,43
Avanza Pension	3 097 607	5,38
Nordnet Pensionsförsäkrings AB	2 117 942	3,68
Pär Åke Odentoft*	1 966 101	3,42
Fredrik Olsson	1 030 000	1,79
A M Karlsson i Kvicksund AB	1 000 000	1,74
Kerstin Monsén	953 654	1,66
AB Svedala Finans	894 052	1,55
Jan Ivar Nordqvist	882 704	1,53

*including legal entities associated with the person

THE COMPANY IN BRIEF – MANAGEMENT TEAM

Evy Lundgren-Åkerlund, PhD, Assoc. Prof.
Xintela's founder and CEO/CSO. Extensive experience in biomedical research and development. Has previously held senior positions in both academia and industry. Founded Cartela AB and was CEO and Head of Research from 2000-2007. Was Director of Operations/CEO of Ideon Bioincubator/Lund Life Science Incubator from 2008-2012.
Holds 4 273 250 shares

Gregory Batcheller, LL.M., J.D, BSc (Economics)
Chairman of the board since 2011
Extensive experience in pharmaceuticals, biotech and medtech.
Current assignments: Chairman of the Board of Saga Diagnostics AB, Monocl AB and Immune Biotech Medical Sweden AB. Partner of Business Research Life Sciences Ltd. CEO of Stanbridge Corporation BVBA. Advisor to Aquilion AB.
Holds 608 300 shares

Gunnar Telhammar, MSc Business Economics
CFO since 2013.
Has held several positions as CFO, both in Sweden and abroad, and has been operating through his own consulting firm BioFinans AB for over 15 years.
Current assignments: CEO of BioFinans AB, CFO of AcouSort AB (Publ) and ImmuneBiotech AB. Member of the board of Targinta AB (Publ).
Holds 73 466 shares

Thomas Areschoug, Ph.D.
CBO, appointed in August 2020.
Has extensive experience from biomedical R&D and business development in life science, most recently in a leading role at Business Sweden.
Holds 12 500 shares.

Peter Ekolind, MBA.
COO, appointed in August 2020.
Has extensive experience of marketing, sales and leadership in several global pharmaceutical companies in various senior positions such as marketing- business area- and country manager. He has also been CEO of Getinge Sverige AB and Avidicare AB.
Holds 100 000 shares

THE COMPANY IN BRIEF – MEMBERS OF THE BOARD

Gregory Batcheller, LL.M., J.D, BSc (Economics)
Chairman of the board since 2011
Experience: Extensive experience in pharmaceuticals, biotech and medtech.
Current assignments: Chairman of the Board of Saga Diagnostics AB, Monocl AB and Immune Biotech Medical Sweden AB. Partner of Business Research Life Sciences Ltd. CEO of Stanbridge Corporation BVBA. Advisor to Aquilion AB.
Holds 608 300 shares

Sven Kili, M.D.
Board member since 2014
Experience: Extensive experience in cell therapy. Sven is a surgeon with orthopaedic specialist training with many years' experience of successful development and commercialisation of cell and gene therapy products from senior positions in the pharmaceutical industry, including Genzyme, Sanofi Biosurgery and GlaxoSmithKline.
Current assignments: Sven is a Board member as well as Chief Medical Officer (CMO) of Xintela. Sven is also Chairman of the Board of Sven Kili Consulting Ltd, and Board member of CCRM and SCB and on the Scientific Advisory Board of LGC.
Holds 330 424 shares

Karin Wingstrand, Pharmacist
Board member since 2014
Experience: Advisor to the life sciences industry. Previously employed as Global head of AstraZeneca's Clinical Development, and Global head of AstraZeneca's Pharmaceutical and Analytical Research and Development.
Current assignments: Board member of Mevia AB, T-bolaget AB, Aqilion AB, Xbrane Biopharma AB, Histolab Products AB, Winkon holding AB and Integrum AB.
Holds 60 000 shares

BUSINESS MODEL

PRODUCT DEVELOPMENT - OVERVIEW

Xintela is using its marker technology platform XINMARK to develop novel products in two areas – cell therapy and oncology.

Cell therapy

In the field of cell therapy, Xintela has used its unique marker technology XINMARK to identify and select high quality therapeutic stem cells to develop the stem cell platform XSTEM. One important benefit of Xintela's selection method is that it leads to homogeneous and consistent high quality stem cell preparations and thereby provides a mechanism to show identity and purity of the stem cell preparations. This provides key regulatory benefits in the development of stem cell products and a clear competitive advantage compared to Xintela´s competitors.

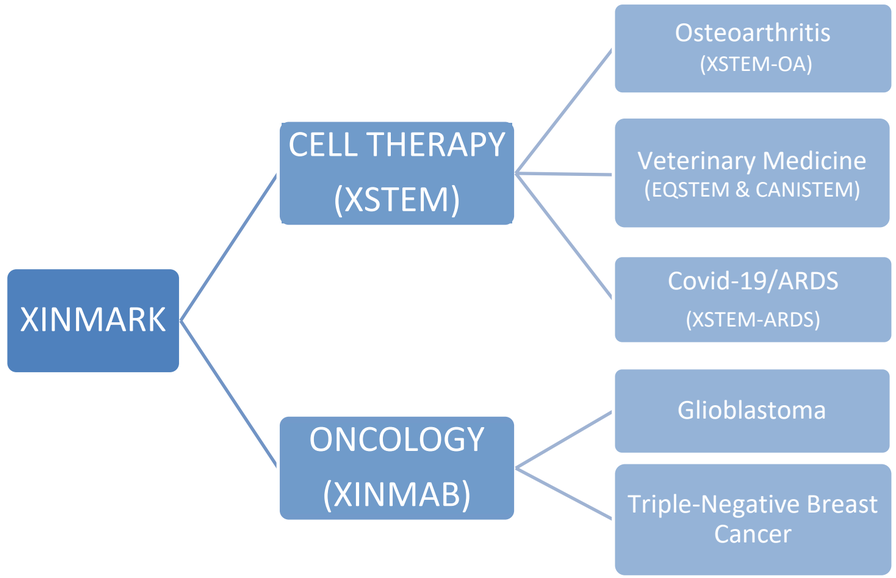
Moreover, Xintela is using adipose tissue as the source of stem cells, which is beneficial from an ethical point of view. With an allogeneic approach, stem cells from one donor can be used to treat multiple patients, which significantly lowers the production costs and ultimately the price for the treatment compared to autologous stem cells products.

The first therapeutic focus regarding XSTEM is the treatment of OA in humans, but the company is also evaluating XSTEM for treatment of Covid-19 related ARDS. Xintelas stem cell platform is also used in veterinary medicine for the development of stem cells therapies for OA in dogs and horses.

Oncology

Within the oncology field, Xintela is using XINMARK to develop a targeted antibody-based therapy, XINMAB, to aggressive cancers with high unmet medical need, including glioblastoma and triple-negative breast cancer (TNBC).

The oncology business is currently run by Xintela, but the company aims to spin out the oncology business to its wholly owned subsidiary Targinta.



BUSINESS MODEL – CELL THERAPY (OA)

Osteoarthritis (OA)

Xintela's initial focus within the cell therapy field is the treatment of osteoarthritis – a degenerative joint disease that results in gradual breakdown of cartilage and other joint tissues, which is both painful and debilitating. The most commonly involved areas are fingers, knees, hips, feet or the neck and lower back.

Although OA occurs in people of all ages, it is most common among the elderly. As a matter of fact, the disease is the primary cause of pain and chronic disability after the age of 65. It is estimated that a 15 per cent of the population worldwide above 60 years suffer from OA. Today, there are no treatments that can halt the progression or cure OA and the patients are only offered drugs that provide symptom relief, i.e from pain and inflammation.

XSTEM-OA

The company's stem cell product for the treatment of osteoarthritis is called XSTEM-OA and is injected into the affected joint with the aim to stop further development of osteoarthritis, regenerate the cartilage and bone, and reduce the need for joint replacement surgery. XSTEM-OA has several biological advantages, such as increased homing to damaged cartilage, increased differentiation capacity, and immunomodulatory capacity to decrease the inflammatory response commonly seen in OA. Thus, XSTEM-OA has exciting potential to be developed as a disease-modifying OA drug (DMOAD).

Positive preclinical in vivo studies

Studies in a validated horse model for post-traumatic OA have shown that Xintela's selected stem cells are safe and that they have a positive effect on the articular cartilage and underlying bone following cartilage damage. The treated joints had significantly less cartilage damage and less bone sclerosis in the injury site compared to controls.

Production of XSTEM-OA and initiation of phase I/II study

Xintela has recently established its own GMP facility for production of XSTEM-OA for clinical trials. Once the manufacturing license has been granted, production of XSTEM-OA will begin and a phase I/II clinical trial with XSTEM-OA can be initiated.

The clinical study will be conducted in Australia on patients suffering from knee OA. The plan is to initiate the study in 2021 and once the study is completed, Xintela's ambition is to enter a partnership to continue clinical development and commercialisation of XSTEM-OA.

POSITIONING AND COMPETITIVE LANDSCAPE – CELL THERAPY (OA)

Current therapies in OA

Osteoarthritis is the most common joint disease in humans which in turn means that the global market is huge. Indeed, the global market for OA therapy is expected to grow from USD 6.8 billion in 2019 to USD 10.1 billion by 2024, with an annual growth of 8.1 per cent. Part of the forecasted growth is due to a growing elderly population and rising levels of obesity in most countries.

The current therapy options only treat the symptoms of OA by relieving pain and reducing inflammation. The most commonly used OA treatments are NSAIDs, e.g. Ibuprofen and Naproxen, opioids, and intra-articular corticosteroid injections. The final option, if all other treatments do not provide any benefit, is to undergo surgery to the replace the affected joint.

Benefits with Xintela's XSTEM-OA

An expected trend in the OA market is a shift from symptom addressing drugs to novel DMOADs such as cell and gene based therapies and other treatments with disease-modifying potential, as well as anti-NGF (nerve growth factor) therapies for better pain relief.

There are a number of ongoing clinical studies on stem cell-based treatments of OA, including a phase III study with Stempeucel (**Stempeutics,** India), RYONCIL which is in phase II (**Mesoblast,** Australia) and Progenza which is in phase I (**Regeneus,** Australia).

An advantage of XSTEM-OA is that it is composed of a homogenous preparation of high-quality selected stem cells, providing both functional and quality advantages. Xintela's selected stem cells assure a consistent high quality between donors, high differentiation and immunomodulatory capacity, and improved homing to the damaged cartilage.

Market potential of XSTEM-OA

The valuation expert company **Xplico** conducted an analysis of the market potential and value of XSTEM-OA intended for Xintela's internal use. It was assumed that moderate and severe knee OA patients is the target market for XSTEM-OA, and that 6 million patients is treated in the US, Japan and EU5 (UK, France, Germany, Spain and Italy). However, since the competition from generic OA treatments will most likely remain high, a future market share of anti-NGFs and novel disease modifying OA treatments is assumed to be around 10 per cent of the total OA drug market.

Assuming a peak market share of 25 per cent for XSTEM-OA in this segment and prices per patient of USD 15 000 in the US and USD 7 500 for the EU and Japan, peak sales per year of XSTEM-OA for treatment of knee OA is estimated to potentially USD 1.4 billion. The risk-adjusted net present value (rNPV) of the project for knee OA is estimated to approximately USD 50 million for the US, Japan and 5EU together.

POSITIONING AND COMPETITIVE LANDSCAPE – CELL THERAPY (OA)

A need for disease-modifying OA drugs

XSTEM-OA is being positioned as a potential disease modifying alternative in an industry dominated by treatments focusing on managing the symptoms. There are currently no DMOADs on the market, i.e. a drug that would stop or even reverse the progression of OA. The rules for reimbursement in DMOAD and cell therapy may be unclear which may create challenges for DMOADs, including XSTEM-OA.

Another promising DMOAD and an interesting competitor to Xintela is Samumed's SM-04690, which is an intra-articular injection (small molecule) for knee OA. A previous phase IIa study of SM04690 has demonstrated positive effects on knee OA pain, physical function, and medial joint space width compared to placebo.

An additional interesting competitor to Xintela's XSTEM-OA is Kolon Life Science's Invossa, which received market approval in South Korea in 2017 as the world's first allogeneic cell/gene therapy for OA. However, the approval was revoked in May 2019 due to lack of efficacy and mis-labelling. The phase III clinical trial for Invossa in the US was suspended by FDA, but is now resumed.

Inadequate pain relief and anti-NGFs

More than half of all treated OA patients fail to achieve adequate pain relief, which means that there is a need for alternative analgesics to reduce the pain in OA patients. Anti-NGF (anti-nerve growth factor) antibodies are believed to have the potential to address this need in moderate-to-severe OA patients.

The major anti-NGF players are Pfizer/Eli Lilly's tanezumab, which received FDA fast track designation in June 2017, and Regeneron/Teva's fasinumab. Tanezumab has previously been the most commercially and clinically attractive anti-NGF, but Tanezumab showed mixed results in its second phase III study presented in September 2019. The study gave no statistically different outcome in the primary endpoint (overall assessment, pain and physical function).

BENCHMARK DEALS- CELL THERAPY (OA)

Deals in the OA space

Several licensing deals involving new drugs in the OA space have been struck during the last 7 years. Given the need for more effective therapies and the projected market growth driven by developing DMOADs and anti-NGFs, several new license deals are likely to be announced in the coming years.

Date	Licensee	Licensor	Candidate/drug	Phase	Territory	Total deal value (USD)	Upfront (USD)
6 Oct 2020	Novartis	Merck	M6495	I	Worldwide	530 M	59 M
25 Nov 2018	Mundipharma	Kolon Life Science/TissueGene	Invossa	III	Japan	594 M	27 M
14 Dec 2017	Flexion Therapeutics	GeneQuine Biotherapetuics	GQ-203/FX201	Preclinical	Worldwide	65 M	2 M
28 Jul 2017	Servier	Galapagos	GLPG1972/S201086	Ib	Worldwide excl US	341 M	7 M
23 Jul 2013	Transition Therapeutics	Elli Lilly & Co	TT-601	Preclinical	Worldwide	130 M	Not disclosed

BUSINESS MODEL – CELL THERAPY (OTHER PROJECTS)

Veterinary medicine

Xintela's marker technology can also be used in veterinary medicine to select and quality assure stem cells from animals for the treatment of OA, which is common in both companion animals and horses.

In North America, the OA prevalence is reported at 20 per cent of all dogs over 1 year of age. As the number of pet dogs is estimated to be approximately 90 million in the US, and almost as many in Europe, the market for stem cell treatments for dog OA is substantial and has been estimated to about USD 185 million by 2022, and USD 218 million by 2026.

A stem cell treatment for OA within animal health also enables Xintela to enter a large global market where the regulations are not as comprehensive as in human medicine, which enables a significantly faster entry on the market resulting in substantial early revenue for Xintela.

Covid-19/Acute Respiratory Distress Syndrome (ARDS)

Xintela is also evaluating XSTEM for the treatment of Acute Respiratory Distress Syndrome (ARDS), a life-threatening lung condition that can affect Covid-19 patients. Symptoms on ARDS include severe shortness of breath, laboured and rapid breathing, low blood pressure and tiredness. The syndrome occurs when fluid builds up in the air sacs (alveoli) in the lungs which keeps the lungs from filling with enough air, which deprives the organs of oxygen.

In Scandinavia, the reported incidence of ARDS has been 17,9 cases per 100 000 person-years. However, the incidence has most likely increased significantly due to the Covid-19-pandemic.

Current ARDS treatment

A patient with ARDS will probably be admitted to an intensive care unit and placed on a ventilator to facilitate breathing. The underlying cause of ARDS should also be treated. For example, antibiotics might be needed if a bacterial infection is the cause. However, there is no effective treatment for ARDS, and patients are only offered oxygen therapy, i.e. oxygen mask or mechanical ventilator, and fluid management. The global market for ARDS devices is anticipated to reach USD 16.9 billion by 2027, expanding at a CAGR of 7.2 per cent from 2020.

XSTEM-ARDS has the potential to improve ARDS

In May 2020, Xintela was awarded a grant (SEK 1 million) from the Swedish Innovation Agency Vinnova to finance a preclinical study in a pig ARDS model to evaluate XSTEM for the treatment of ARDS (XSTEM-ARDS). The study is conducted in collaboration with the Cardio-thoracic surgery clinic, Skåne University Hospital in Lund and Lund University.

On October 26th 2020, Xintela reported promising results from their ongoing preclinical study with XSTEM-ARDS. The treatment had so far shown a positive therapeutic effect with a clear improvement of lung function and reversal of the critical ARDS condition in the pig model. This means that XSTEM-ARDS has the potential to improve the severe condition in ARDS patients, which can shorten intensive care time and reduce mortality.

BUSINESS MODEL – THE GMP FACILITY

Outsourcing is a strong trend in the pharmaceutical industry, and estimates indicate continued growth in the coming years. The market for contract development and manufacturing organisations (CDMOs) has been valued at USD 69 billion, and forecasted to grow by8.1 per cent annually, and by 2025 the market is expected to reach USD 109 billion in total turnover.

The CDMO market is fragmented, ranging from small specialised facilities to worldwide one-stop-shop-companies. The demand for manufacturing capability is particularly strong within regenerative medicine, with a rapidly growing number of new advanced therapies under development. This puts Xintela's GMP ready facility in an interesting spot.

A strategic asset

For companies reaching clinical trials, the usual solution is to employ a CDMO or a contract manufacturing organisation (CMO) for the production of the drug candidate according to Good Manufacturing Practices (GMP) for the trials, a quality standard needed to produce drugs for clinical trials as well as commercial production. However, this is normally very expensive and leaves the company fully dependent on its manufacturing partner.

As there still are few CMOs that have the capacity and knowledge to produce cell therapies according to GMP, Xintela identified the need to set up its own facility to produce XSTEM. The company recognised several strategic benefits, such as full control and flexibility in the manufacturing process, shorter lead times, reduced costs, and staff expertise in GMP production and workflows.

Having full access to a GMP certified laboratory does not only imply significantly lower costs in the manufacturing process, but also puts Xintela on the map as an attractive partner for future collaborations.

Applying for approval in Q4 2020

The manufacturing facility is prepared for GMP certification, Xintela plan to apply in Q4 2020 for approval for GMP manufacturing of XSTEM for the coming phase I/II trial. Final inspection by the Swedish MPA is expected in the beginning of 2021 and an approval will be a major milestone for Xintela. The GMP facility will also be able to produce stem cells for the veterinary products.

Demand for GMP facilities is rising

British research firm **Results Healthcare** published a report on the market for CDMOs in 2019. They confirm the strong trend and the fragmented market with room for different sized facilities and companies allowing for various specialised operations as well as large capacity facilities. So does **Deloitte** in their insights report "2020 Global life sciences outlook", published in January 2020.

The demand is coming from companies in all stages, from discovery to marketed products. Cell- and gene therapies constitute the fastest growing sub sector of the CDMO market. Companies are actively searching for spaces and facilities to acquire, but the availability of such objects is highly limited.

BUSINESS MODEL – THE GMP FACILITY

Acquisitions in the field

In 2019, **Catalent**, a global CDMO based in the US, acquired **Paragon** and their facility to produce viral vector for gene therapy, GMP plasmids and lentivirus vectors, for USD 1.2 billion.

The same year, **Thermo Fisher** acquired American firm **Brammer Bio**, a CDMO specialist in cell and gene therapies, for USD 1.7 billion. Although these deals are at the top end of the spectrum, several other mergers and acquisitions have been made in this space since.

In this context facilities with GMP authorisation are rare assets. Should Xintela decide to sell, the company would be able to a collect a significant premium for their asset, far above booked value.

A business on its own

Another strategic alternative for Xintela could be to run the facility as a separate business unit, for other companies to hire. Initial investments would be required, but the facility would probably quickly become profitable given the strong demand for GMP production facilities in cell- and gene therapies. GMP certification is a high entry barrier and encompasses not only equipment, quality assured work processes, but a great deal of the value lies in a qualified staff and expertise, as well as processing and implementing GMP standards.

Valuation of the GMP facility

Having established the facility, there are multiple of hypothetical options including contract viral vector or plasmid manufacturing, fill-finish operations, GMP cell banking or CAR-T-manufacturing.

Based on this possibility, cell- and gene therapy consultant **Dark Horse Consulting** conducted a valuation of the GMP facility intended for Xintela's internal use. With suite fees for GMP processes equivalent of Xintela's capacity roughly in the scale of USD 300 000 per month per cleanroom and estimated gross margins of around 40 per cent - the facility would eventually be generating an EBITDA of about USD 5.2 million per year.

Typically, CDMOs are valued at 10-15 times EBITDA, according to Results Healthcare, although Catalent paid 20 times EBITDA for their gene therapy specialist and so did Thermo Fisher in their acquisition of Brammer Bio.

The multiple range of 10-15 times EBITDA, implies a valuation of Xintela's GMP facility of approximately USD 50 – 70 million.

BUSINESS MODEL - ONCOLOGY

In oncology, XINMARK is used to develop an antibody-based targeted therapy, XINMAB, for aggressive cancers with high unmet medical need. Xintela develops two types of antibody-based drugs: function blocking antibodies and Antibody- Drug Conjugates (ADC), in which a cell toxin is linked to the antibody. The antibodies target the company's marker, integrin α10β1, which is highly expressed in aggressive cancer types, including glioblastoma and triple-negative breast cancer. Importantly, the expression of integrin α10β1 is restricted in normal tissue.

Antibody-Drug Conjugates

The Antibody-Drug Conjugates (ADC) exert their therapeutic effect by targeting and binding to the target on cancer cells, integrin α10β1, triggering uptake of the ADC and delivery of the cytotoxin that has a killing effect on the cancer cells.

Function blocking antibodies

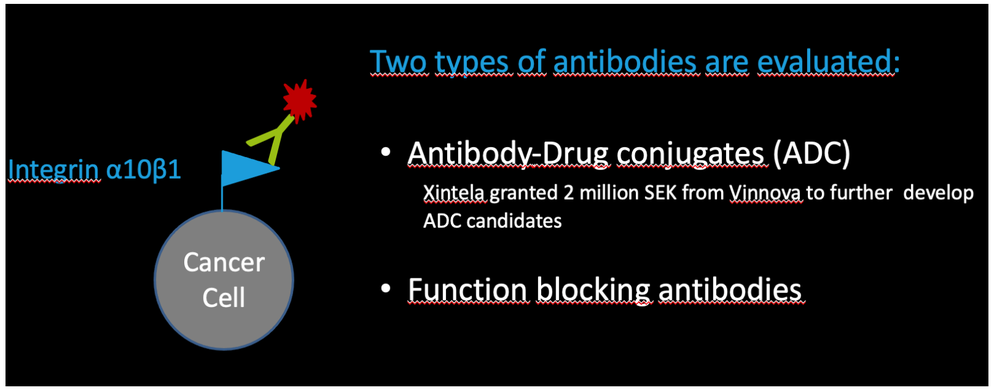
Function blocking antibodies to integrin α10β1 on cancer cells block certain functions related to the integrin. Thereby, the antibodies can inhibit the function of certain cancer cells and suppress the growth of the tumour.

Several indications

The antibody-therapies are developed to target aggressive cancers forms and Xintela's current focus is set on Glioblastoma and Triple-negative breast cancer (TNBC). Research has also demonstrated that Xintelas integrin target is expressed also on other aggressive forms of cancer, including prostate cancer, lung cancer and pancreatic cancer, which means that the treatment can potentially be expanded to other cancer indications as well.

targinta

Targinta is Xintela's fully owned subsidiary. The strategy is to find a development partner or to out-license oncology projects after their preclinical programme. Spin-out of Targinta is prepared and will be conducted when future financing and development strategy is decided.



BUSINESS MODEL - ONCOLOGY

Glioblastoma

Xintela develops therapeutic antibodies for targeted treatment of glioblastoma (also known as IV glioma), the most common and aggressive form of brain tumour in adults. Glioblastoma develops from glial cells (supportive tissue) and is rapidly growing and commonly spreading into nearby brain tissue. Glioblastoma has a generally poor prognosis and high resistance to current therapies - surgery, radiation and chemotherapy and a few drugs. The average survival time with current treatments is only 15 months, and 4 months without treatment.

In Europe and USA alone, 25-30 000 people are affected by glioblastoma per year. The global market value in 2024 for glioblastoma treatments has been estimated to reach approximately USD 3.3 billion.

Xintela's goal is to treat the cancer more directly and effectively than with current treatment, thus extending the patient's survival as well as improving quality of life for patients affected by glioblastoma.

In 2019, Xintela published preclinical findings from cell studies and animal models showing that an ADC targeting integrin $\alpha 10\beta 1$ has a killing effect on glioblastoma cells both in vitro and in an orthotropic animal model. In 2020, Xintela also reported that function-blocking antibodies significantly suppress the growth of glioblastoma tumours in vivo, further validating the target for therapeutic use.

In June 2020, Xintela was granted preliminary approval from the European Patent Office for the antibody treatment of glioblastoma and other brain tumours using the company's target molecule integrin $\alpha 10\beta 1$.

Triple-Negative Breast Cancer (TNBC)

In June 2020, Xintela announced that the next focus within the oncology programme will be triple-negative breast cancer (TNBC), the most aggressive form of breast cancer which often causes metastases and relapses. TNBC does not have any of the receptors that are commonly found in breast cancer - oestrogen and progesterone receptors and HER2. This makes TNBC more difficult to treat since most hormone therapies target one of these three receptors.

Approximately 170 000 people are diagnosed with TNBC per year globally, which corresponds to 10-15 per cent of all diagnosed breast cancer. The global market value for TNBC treatments is estimated to USD 2.1 billion by 2025.

Xintela's decision to focus on triple-negative breast cancer is based on positive preclinical results with function blocking antibodies in cell experiments and in a validated tumour volume model.

POSITIONING AND COMPETITIVE LANDSCAPE – ONCOLOGY

Glioblastoma

There is a great need for a better and more effective treatment since glioblastoma has a generally poor prognosis and low response to current therapies. The treatment usually involves surgery followed by chemotherapy and radiation, and sometimes high doses of steroids to reduce the amount of symptoms. The primary objective of surgery is to remove as much of the tumour as possible without injuring the surrounding brain tissue. However, it can be difficult to remove the tumour entirely since glioblastoma often invades surrounding tissue with tumour cells.

Current approved drugs

There are currently three drugs specifically approved for glioblastoma – temozolomide, Avastin (bevacizumab) and Gliadel (carmustine wafer). Temozolomide is often given in combination with radiotherapy which gives significant increase in survival rates with only a few side effects. Merck's Temozolomide is generic since 2016 and it achieved peak sales of USD 1 billion per year before losing patent protection. This provides an indication of the commercial opportunity associated with a new treatment for glioblastoma.

Drugs under development

There are currently around 10 drugs in the late stages of development as a treatment for glioblastoma, but only a few appear to be relevant competitors. Additionally, some late stage projects have been halted during the past couple of years. For example, Abbvie's project of developing the ADC ABT-441 (depatuxizumab mafodotin) has been terminated because of lack of survival benefit.

Bristol-Myers Squibb's Opdivo (nivolumab) has also showed disappointing clinical outcome since it failed to show improved survival in several clinical phase III studies, which means that the probability of an approval for Opdivo for treatment of glioblastoma is low.

Another drug that failed during development is Celldex Therapeutics' peptide vaccine Rintega (rindopepimut), which failed in phase III.

XINMAB's market potential – Glioblastoma

The valuation expert company **Xplico** conducted an analysis of the market potential and value of XINMAB for treatment of glioblastoma, intended for Xintela's internal use. The target patient group was assumed to be newly diagnosed glioblastoma patients and recurring glioblastoma patients for second line treatment. The prevalence was estimated to 12 751 patients in the US, 2 651 in Japan and 17 565 in EU5 (France, Germany, Italy, Spain and the UK), with an annual growth rate of 1.2 per cent. Of these, about 76 per cent were actively treated. Since Glioblastoma is a rare disease, Xintela can potentially apply for orphan drug designation which can give the company exclusive marketing and development rights for XINMAB.

Under the assumptions that 75 per cent of the glioblastoma patients express the integrin target, a treatment price of close to USD 100 000 per patient per year, and a peak market share of 30 per cent, XINMAB could reach peak market sales of USD 400 million per year in the US, Japan and 5EU for the treatment of glioblastoma. The risk adjusted net present value (rNPV) of the project was estimated to potentially USD 34 million.

POSITIONING AND COMPETITIVE LANDSCAPE – ONCOLOGY

Triple-negative Breast Cancer

Triple-negative breast cancer is considered to be more aggressive than other types of breast cancer and it usually comes with a rather poor prognosis, mainly because there are fewer treatment options than for other types of breast cancers. This is because the cancer cells do not have the oestrogen or progesterone receptors or enough of the HER2 protein to able to treat it with hormone therapy or targeted drugs work. Instead, TNBC is usually treated with a combination of surgery, radiation therapy and chemotherapy.

Drugs under development

There are several drugs under development with the aim to find better treatments than current standard treatments for TNBC. This also means that there are several drugs that may constitute as competitors for Xintela's treatment. Some of the drugs are even in the late stages of development, while some drugs have already been approved. Even if the TNBC pipeline has several products in development, there are no direct competitor with the same technology as Xintela.

In March 2019, FDA approved Roche's immune checkpoint inhibitor Tecentriq (atezolizumab) in combination with chemotherapy for patients with TNBC.

Another immunotherapy that has been approved by FDA is AstraZeneca and MSD's Lynparza (olapariab). Earlier this year, FDA also approved Immunomedics Trodelvy (Sacituzumab govitecan) as an antibody-drug conjugate (ADC) for the treatment of patients with triple-negative breast cancer.

XINMAB's market potential - TNBC

The valuation expert company Xplico conducted an analysis of the market potential and value of XINMAB for the treatment of TNBC for Xintela´s internal use. It was assumed that there are approximately 80 000 diagnosed TNBC patients in stage I-IV receiving drug treatment in the US, EU5 (France, Germany, Italy, Spain and the UK) and Japan, with an annual growth of 0.8 per cent.

Under the assumptions that 70 per cent of TNBC patients express Xintela´s integrin target, a peak market share of 20 per cent and prices of USD 100 000 per patient per year, the peak sales of XINMAB for treatment of TNBC was estimated to potentially reach USD 1.2 billion in these markets. The risk-adjusted net present value (rNPV) of XINMAB for treatment of TNBC was estimated to approximately USD 27 million.

BENCHMARK DEALS - ONCOLOGY

Deals within oncology

Several licensing deals have been struck during the last couple of years regarding preclinical/early clinical assets within oncology based on antibodies (including ADCs). The total deal value ranges from USD 165 to 830 million with upfront payments ranging between USD 10-120 million.

Deals within glioblastoma and Triple-Negative Breast Cancer

There are few licensing deals with announced deal terms in glioblastoma and TNBC. Most deals cover other indications as well. However, Merck has recently unveiled a substantial licensing deal for Seattle Genetics' ADC ladiratuzumab vedotin (LV) for treatment TNBC. Seattle Genetics will receive a USD 600 million upfront payment and Merck will make a USD 1.0 billion equity investment in 5.0 million shares of Seattle Genetics common stock at a price of USD 200 per share. In addition, Seattle Genetics is eligible for progress-dependent milestone payments of up to USD 2.6 billion. The project is currently in clinical phase II trials.

Another recent example of a licensing deal is the agreement between Jounce Therapeutics and Celgene for the development and commercialisation of JTX-8064. The license agreement was signed in July 2019 and under the agreement Jounce will receive USD 50 million in license fee upfront and USD 480 million in milestone payments. The project is in preclinical phase.

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IP-SITUATION

IP-SITUATION

Strong and broad patent portfolio

Xintela's technology platform is protected by a large number of patents in key markets such as Europe, USA, Australia, Canada, Japan and China. Xintela's IP position encompasses patents protecting its inventions around integrin α10β1, including the use of antibodies directed to the integrin marker in several applications areas, e.g. antibody treatment of glioblastoma, as well as product patents.

Xintela has an active IP strategy and continuously files new patent applications covering commercially relevant uses, methods and products generated in the R&D pipeline. In June this year, Xintela announced that the European Patent Office (EPO) had issued a preliminary approval ("Intention to grant") for the patent application related to the antibody treatment of Glioblastoma and other tumours of the brain using the company's target molecule integrin α10β1. The EPO recently informed Xintela that they will grant the patent on November 11th 2020.

On October 29th 2020, Xintela announced that they have received an "intention to grant" from the European Patent Office for a patent which will protect its stem cell product XSTEM, and the use of these stem cells for prevention and treatment of degenerative joint diseases such as osteoarthritis, and other related disorders. The intention to grant concerns the patent called "XSTEM/Stem Cell Product" on the following slide.

Expiration dates

Noteworthy is that two of Xintela's older patents will expire within the next years (2023 and 2024). However, for the company's other patent families more than 15 years of patent term remains. There is also a possibility of patent extension (Supplementary Protection Certificate/Patent Term Extension) for up to 5 years for the products that have received market approval from the regulatory authorities.

XACT patent

Xintela's US patent application "XACT for chondrocytes" protects the use of the company's cell surface markers - integrin α10β1 and integrin α11β1. The method can determine the quality and purity of chondrocyte preparations. The US Patent and Trademark Office (USPTO) has issued a Notice of Allowance for the XACT patent application, which means that they intend to grant the patent.

IP-SITUATION

The following table presents Xintela's IP portfolio, which consists of seven patent families that protects various aspects of Xintela's technology platform.

Filing for a PCT application means that the application is preliminary examined via World Intellectual Property Organization (WIPO). The company can thus obtain protection in several jurisdictions/territories with a single filing. There are currently 153 member jurisdictions/territories, including the US, China, Japan and Europe (EPO).

Patent family number	Patent family	Status	Estimated patent expiry
WO 03/106492	"Stem cell marker patents" – Marker for stem cells and its use	Granted	2023
WO 2004/089990	"Antibody patents" -New monoclonal antibody capable of binding integrin α10β1	Granted	2024
WO 2016/133449	"Brain tumour patents" - "Detection and treatment of malignant tumours in the CNS"	Pending in national phase Granted by EPO	2036
WO 2018/033596	"Marker for Neural Stem Cells"	Pending in national phase Granted in South Africa	2037
WO 2018/138322	"XSTEM/Stem Cell Product"	Intention to grant by EPO	2038
WO 2019/002547	"XACT for chondrocytes" - Quality assurance of chondrocytes	Pending in national phase Granted in USA	2038
WO 2020/212416	"Aggressive cancer forms"	PCT	2039

FINANCIAL STATUS

FINANCIAL STATUS

In July 2020, Xintela completed a share issue of SEK 40.5 million before costs. The issue was oversubscribed by 291 per cent, no guarantors were used. Along with the new shares, a warrant was also issued with subscription in November. Potentially, the warrant could add another SEK 32 million to the cash balance, further strengthening the financial position.

The newly added funds will be used for the cell therapy area, including applying for a manufacturing license, expanding the production team, preparing for the clinical trial in knee OA with XSTEM-OA and investigating new indication areas.
The acquired capital will also be used for the continuation of the preclinical studies in glioblastoma and TNBC to prepare for clinical studies and partnering activities, as well as investigation of other indications for XINMAB.

Warrants in November

The warrant of series 2020:1 was issued in connection with the rights issue during summer 2020, and could add another SEK 32 million to the company, assuming full subscription at SEK 1.92 per share.

The subscription period for the warrant starts on November 4th and ends on November 18th 2020. The subscription price will be determined by 70 per cent of the volume weighted average price of the shares during the period October 19th to October 30th with a minimum subscription price of SEK 1.92 per share.

Bridge loan

In may 2020, Xintela signed an agreement with investor Gerhard Dal to raise a bridge loan in two tranches totalling SEK 18.9 million. Tranche 1 of SEK 8 million was repaid on July 30th and the second tranche of SEK 10.9 million is due January 31st, 2021. The loan can be converted into shares, should the lender choose to do so. In that case, the subscription price will be at 12.5 per cent discount to the volume weighted average price during the 15 days prior to the calling of the conversion.

Added funding in 2020	MSEK	
Rights issue	40,5	
Potential funding		**Subscription period**
Warrant series 2020:1	32	4th – 18th November 2020

Financial calendar	Date
Interim report Q3 2020	27 November 2020

BIOSTOCK’S COMMENTS

BIOSTOCK'S COMMENTS

The unique marker technology platform XINMARK, together with a strong IP-situation, has put Xintela in the forefront in the development of novel stem cell therapies and targeted antibody treatments in oncology, with focus on diseases of high unmet medical need and significant market potential.

Within cell therapy, Xintela's marker technology platform is utilised to identify and select high quality stem cells for the development of the therapeutic stem cell platform XSTEM. The XSTEM platform clearly differentiates Xintela from its competitors as it enables the company to demonstrate identity and purity of its stem cell product, and maintain consistency over time, which is very important from a quality and regulatory point of view in the development of cell-based therapies. In addition, XSTEM also provides several functional advantages.

Xintela´s first stem cell product, XSTEM-OA, will enter into phase I/II clinical studies in knee osteoarthritis (OA) patients during 2021 and has exciting potential to be developed as a disease modifying OA treatment (DMOAD) in a rapidly growing market. The risk adjusted value of the project for knee OA is estimated to approximately USD 50 million.

Veterinarian products for treatment of OA in animals are also carrying significant value, including a market for cell therapies to dog OA worth around USD 200 million globally.

XSTEM is currently also being evaluated for treatment of Covid-19 related ARDS. Xintela recently announced promising results in their preclinical ARDS study that eventually could lead to a novel therapy for a serious lung complication where there currently are no effective treatments available.

A key asset in Xintela's operation is the GMP facility that soon will be authorised to manufacture XSTEM-OA for the upcoming clinical study in knee OA. Having access to their own GMP facility will significantly lower the total risk in the stem cell project. Flexibility and control, time management and staff expertise are some of the strategic and financial benefits of the GMP facility.

The facility makes the company an attractive partner in future collaborations. Xintela could also consider to run the facility as a CMO entity, with potential to realise substantial cash flows and profitability given the strong demand for GMP facilities in the cell and gene therapy space. Estimates indicate a value of the GMP facility of approximately USD 50 - 70 million.

In oncology, Xintela's antibody technology XINMAB has shown promising preclinical data in the treatment of aggressive cancer types. Initial focus areas are glioblastoma and TNBC, two indications with a high unmet medical need. The treatment concept could also be evaluated in other aggressive cancer forms, such as lung cancer, prostate cancer and pancreatic cancer. The risk adjusted values of the glioblastoma and TNBC projects have been estimated to potentially USD 34 and 27 million, respectively.

The progress of Xintela's projects and investment in the GMP facility, has built substantial value in the company.

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