Xintela

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Approaching major milestones

Xintela's Q321 report provides key updates on the company's pipeline and business plans. Lead programme XSTEM-OA will begin patient enrolment in early 2022, with the aim of showing disease-modifying osteoarthritis drug (DMOAD) properties. A second clinical study, assessing XSTEM in difficult-to-heal venous leg ulcers, is planned for mid-2022 and offers a potentially faster path to market. Subsidiary Targinta has advanced towards preclinical development following selection of a drug candidate (TARG10) for triple negative breast cancer (TNBC) with spin-off formalities picking up speed. We expect several potential inflection points for Xintela in coming months, albeit contingent on sufficient and timely fund-raising.

XSTEM approaching the clinic in osteoarthritis

A Phase I/IIa study assessing XSTEM in patients with moderate knee osteoarthritis (OA) is expected to enrol the first patient in early 2022. Three different doses will be assessed in up to 54 patients with an 18-month observation period (six monthly safety and efficacy evaluation). The primary goal is to establish the drug's safety, but preliminary efficacy will be another key component evaluated.

Expanding the XSTEM opportunity to wound healing

Following encouraging results in a preclinical animal study in wound healing, Xintela has decided on venous leg ulcers as the next target for XSTEM. A clinical study is planned for mid-2022 and will evaluate the safety and healing potential of XSTEM over a 10-week period. Successful development could allow the company access to a potential $4.8bn market (by 2026) and a likely faster route to market.

Drug candidate finalised for TNBC

Subsidiary Targinta has transitioned to preclinical development with the selection of TARG10, a function-blocking antibody, as its drug candidate for TNBC. An antibody-drug conjugate (ADC) is likely to be announced as the next candidate during Q122, according to the company. With a new board in place and preclinical development underway, we expect spin-off formalities to continue to gain speed.

Access to funds crucial to development plans

At current normalised annual burn rates (c SEK55m), Xintela's funds (SEK15.9m cash plus a SEK9m short-term loan raised post-period) would fund operations into Q122. Timely financing would be key to deliver on the pipeline plans.

Historical financials

Year end	Revenue (SEKm)	PBT (SEKm)	EPS (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/17	0.0	(21.9)	(0.79)	0.0	N/A	N/A
12/18	1.6	(26.3)	(0.83)	0.0	N/A	N/A
12/19	5.7	(38.1)	(1.10)	0.0	N/A	N/A
12/20	14.9	(36.6)	(0.68)	0.0	N/A	N/A

Source: Company filings

Price	SEK2.07
Market cap	SEK184m

Share price graph

Share details

Code	XINT
Listing	Nasdaq First North Growth
Shares in issue	89.1m
Net cash at 30 September 2021	SEK15.9m

Business description

Xintela is a Swedish preclinical-stage biotechnology company with focus on stem cell-based therapies and oncology, based on its proprietary integrin marker technology platform. Its lead candidate is XSTEM-OA, ar MSCs based treatment for osteoarthritis (OA), expected to commence Phase I/IIa trial enrolment in early 2022. XSTEM is also being evaluated in venous leg ulcers with clinical trials expected to commence in mid-2022. While the veterinary OA business is seeking out-licensing opportunities following proof of principle, the oncology business is being primed for a spin-off under subsidiary Targinta.

Bull

- Unique technology platform with first-in-class potential.
- Serving markets with high unmet need and significant commercial opportunity.
- Scope for expansion into other musculoskeletal, wound healing and oncology indications.

Bear

- Difficulty securing funding for clinical trials.
- Challenges in finding partners/out-licensing opportunities.
- Regulatory hurdles in different geographies.

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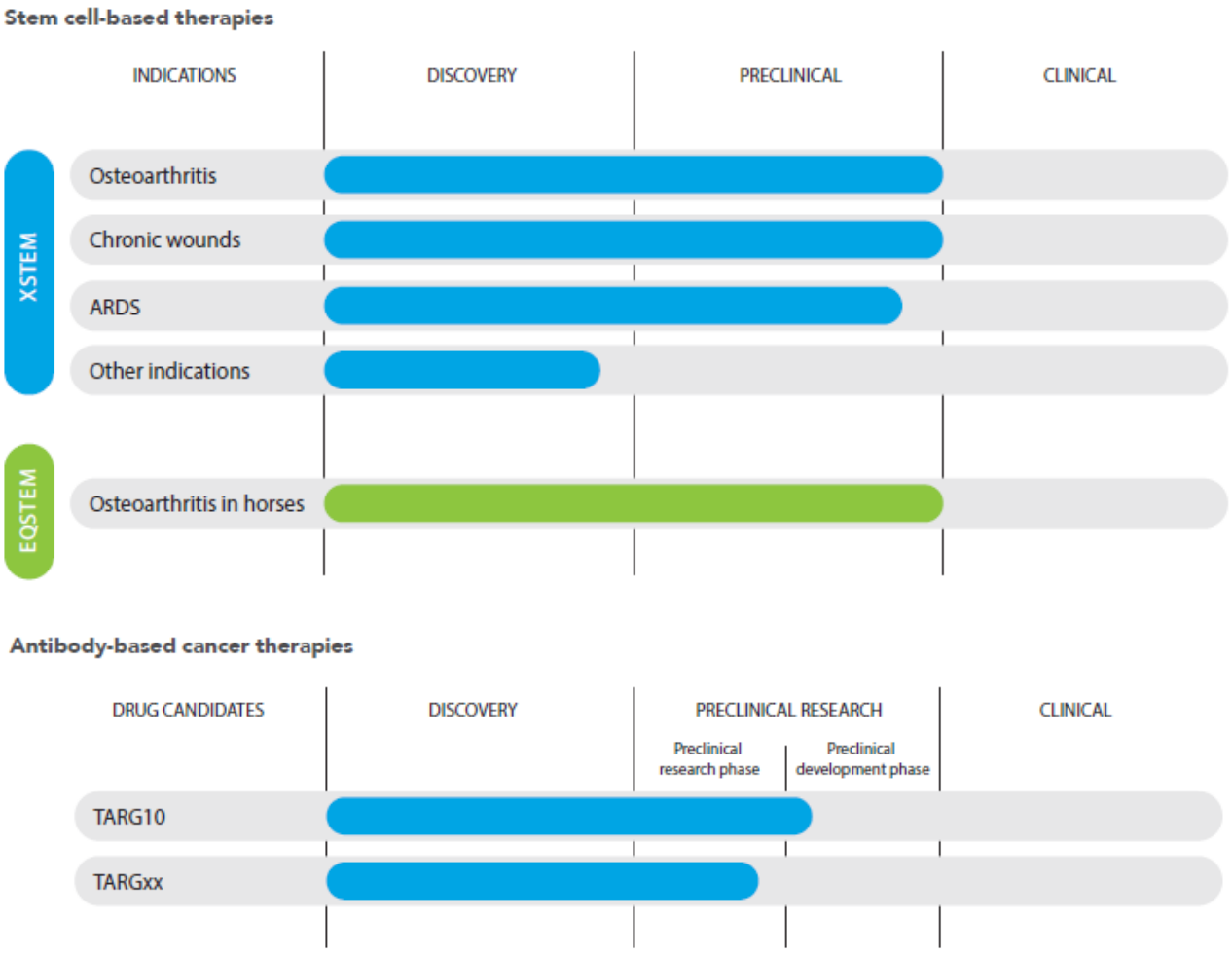
Xintela's pipeline

Xintela uses its proprietary integrin α10β1 biomarker platform to target indications in the stem-cell regenerative space as well as solid tumours. Within the regenerative stem cell space, the company's biomarker platform allows it to select a homogeneous preparation of α10β1 expressing allogeneic mesenchymal stem cells (MSCs) forming the stem cell therapy platform XSTEM. In the oncology area, early studies by Xintela indicate that the α10β1 biomarker is expressed in a number of 'aggressive tumours', which can then potentially be targeted by antibodies developed by the company. Exhibit 1 presents the company's development pipeline across targeted indications.

Exhibit 1: Xintela's pipeline



Source: Company filings

XSTEM-OA poised for clinical transition

Xintela's lead programme XSTEM-OA is set to commence patient recruitment in early 2022. The trial will be conducted in Australia (the rationale behind the selection of Australia as the study destination is discussed in our initiation report), and in preparation Xintela, in July 2021, incorporated an Australian subsidiary, Xindu, and has contracted with local contract research organisation (CRO) Greenlight Clinical to conduct the company's first in-human trials using its stem cell product XSTEM. Xintela's goal is to out-license the asset following completion of the trial (proof-of-concept).

The company's Q321 report provides some additional information on the logistics and design of the upcoming study. Stem cells for the trial have been manufactured in the company's own GMP manufacturing facility and will be shipped to Australia in December 2021. We see this aspect as a key advantage for Xintela, affording it greater flexibility and control over the manufacturing process (reduced risk of delays) and potentially reducing both time and cost associated with the production. The facility remains a key asset for Xintela, and the company aims to, in the longer term, utilise the resource to manufacture stem cells for partnered products and potentially as a contract manufacturer for other advanced therapy medicinal products (ATMPs).

The XSTEM-OA study will be a combined Phase I/IIa clinical trial assessing XSTEM in patients with moderate knee OA (grades II–III in the official Kellgren and Lawrence system; grade IV is the most severe) and will recruit up to 54 patients who will receive an injection directly in the affected knee joint. Three different doses will be tested (details unavailable) and patient progress will be monitored for a total of 18 months, with safety and efficacy evaluations every six months. While the primary objective of the study would be to prove the safety of XSTEM, the company would be seeking preliminary efficacy data to support its goal of demonstrating DMOAD properties (effectively reversing cartilage damage/regenerating cartilage) for its drug. As a reminder there are currently no approved DMOADs on the market although several clinical trials are underway. The potential global OA therapeutics market opportunity is assessed to be $11bn by 2025 although the sub-segment targeted by Xintela remains highly competitive. Nonetheless, we believe that any new therapies approved with a DMOAD tag could make noticeable inroads into the market.

Exploring the wound-healing opportunity

Following encouraging results from its preclinical pig model study analysing XSTEM's wound healing capabilities (conducted in collaboration with The Burn Center at Linköping University Hospital), the company has broadened XSTEM's clinical development to include difficult-to-heal venous leg ulcers (VLUs), the most common type of difficult-to-heal wounds. While detailed datasets from the preclinical study have not been publicly disclosed, the company has indicated that treatment with XSTEM aids healing and the newly formed tissue closely resembled 'normal skin' and also led to less scarring compared to transplanted skin cells. Xintela plans to initiate Phase I/IIa clinical studies in VLUs in association with the Linköping team in mid-2022 evaluating safety and preliminary efficacy of XSTEM over a 10-week period.

Venous leg ulcers market potential

Normal wound healing is characterised by four overlapping phases: haemostasis, inflammation, proliferation, and remodelling. Most wounds follow this progression when treated with standard wound care. Difficult-to-heal wounds (defined as wounds that fail to heal within three months), however, fail to progress past the inflammatory stage, leading to prolonged and persistent wounds. Difficult-to-heal leg ulcers (CLUs) are described as wounds below the knee, persisting for over six weeks with no tendency to heal after three or more months. The condition affects 1% of the adult population and 3.6% of people older than 65 years of age, and is associated with a significant economic burden for the healthcare system. It is estimated that 2–4 % of the total healthcare budget in industrialised countries is related to costs for care and treatment of difficult-to-heal wounds. The common causes are venous disease, arterial disease and neuropathy, with VLUs, the targeted indication for Xintela, accounting for c 70% of all CLUs.[1]

A VLU is an open skin lesion of the lower leg or foot that is caused by improper blood circulation. Dysfunctional blood valves or obstructed veins in the legs can hamper efficient blood flow back to the heart, leading to the blood pooling in the veins. This puts pressure on the capillaries that carry blood to the different layers of skin and also damages the tissue and prevents it from receiving

1 Shubhangi Vinayak Agale, Chronic Leg Ulcers: Epidemiology, Aetiopathogenesis, and Management, *Ulcers*, vol. 2013

oxygen, nutrients and cells required for wound healing. Over time, this can result in an open wound. Current standard of care treatment includes compression therapy and dressings, which may be combined with pentoxifylline and aspirin therapy. Despite this, only 60% of the wounds heal by three months and once healed, 75% of wounds recur within three weeks. A substantial 60% of VLUs turn into chronic wounds,[2] highlighting the significant unmet need in the space.

The global VLU treatment market size stood at $2.95bn in 2018 and is estimated to grow to $4.84bn by 2026 (CAGR of 6.4%), with compression therapy accounting for 61.7% of the market share. While newer treatment options such as growth factors and skin substitutes are being increasingly used to stimulate wound healing, the market remain underserved. MSC based therapies have been explored in recent times in both preclinical and small clinical studies as therapeutics for chronic wounds and have been shown to reduce inflammation and scarring[3] (attributed to their immunomodulatory properties, regenerative potential and paracrine effects). However, larger-scale clinical trials are required, where the heterogeneity of MSC preparations remains a major roadblock. Xintela's XSTEM platform promises a more 'homogeneous' selection of MSCs courtesy of its α10β1 biomarker platform and could be favourably placed to overcome this potential shortcoming. Moreover, given the relatively short expected study duration, data from the upcoming Phase I/IIa trial are expected to be released prior to the OA study, potentially creating an earlier monetisation opportunity for the company.

Taking EQSTEM forward

On 27 October 2021, Xintela announced that it would continue the development of the EQSTEM (MSC product for horses, equivalent to XSTEM in humans) to beyond the proof-of-principal stage originally planned for the programme. The company indicated plans to meet with the European Medicines Agency (EMA) to determine additional study requirements for EQSTEM's approval in the European market. The additional studies will be conducted in collaboration with Professor Casper Lindegaard at the Department of Veterinary Clinical Sciences (University of Copenhagen), the same team that recently conducted the preclinical study assessing the therapeutic impact of EQSTEM on lameness[4] in horses with OA after a joint injury. According to the company, the study results showed that an injection of EQSTEM in a joint with OA after a joint injury significantly reduced the lameness of the horses compared to untreated horses with a similar injury. Given the high prevalence rate of OA in equine animals (c 25%) and the scarcity of effective therapeutic options, the market remains attractive for Xintela. A veterinary stem cell product also faces a less rigid regulatory environment and a potential shorter route to the market, creating another opportunity for early revenue generation as compared to XSTEM-OA.

Targinta progressing towards key milestones

The major development during the period for Xintela's wholly owned oncology focused subsidiary Targinta has been the selection of TARG10 (function-blocking antibody expected to inhibit certain functions related to the integrin α10β1, such as tumour cell viability, migration and proliferation, although the exact mechanism has not yet been specified by the company) as its drug candidate for TNBC, transitioning the oncology programme into preclinical development. As a reminder, within the oncology domain, Xintela is employing its biomarker technology to develop antibody based targeted therapies for aggressive tumours, with an initial focus on TNBC and glioblastoma (GBM). The antibodies will target Xintela's in-house biomarker integrin α10β1, which the company asserts is highly expressed in aggressive tumours. In addition to function-blocking antibodies such as

2 Robst, S., Weller, C.D., Bobbink, P. et al. Prevalence and incidence of venous leg ulcers—a protocol for a systematic review. *Syst Rev* 10, 148 (2021)

3 Otero-Viñas M, Falanga V. Mesenchymal Stem Cells in Chronic Wounds: The Spectrum from Basic to Advanced Therapy. Adv Wound Care (New Rochelle). 2016

4 The degree of lameness is a measure of the degree of pain and impaired function in the injured joint.

TARG10 (that can inhibit unspecified cancer cell functions such as proliferation and migration), the company is also developing ADCs, which work by attaching a cytotoxin to the antibody, which is then delivered to the tumour. The ADC would be seeking integrin α10β1 expressing cells, believed to be highly localised in the tumour site(s) and a candidate is likely to be announced in Q122. The goal is to enter into commercial agreements immediately after conclusion of preclinical development of the selected assets. Both the integrin α10β1 cancer target and the antibodies are patent protected, strengthening the company's intellectual property and potentially enhancing Targinta's attractiveness to prospective partners, in our opinion.

Targinta's spin-off preparations are also picking up speed with separation from Xintela nearly complete, as highlighted in the company's Q321 report. Targinta has been operating independently out of its own premises and has a separate management and board in place, following the appointment of Per Norlén as CEO (effective September 2021) and a new board in October 2021. Xintela's board plans to convene a general meeting before end-2021 (market conditions permitting) to decide on the stock-dividend of Targinta in accordance with the Lex Asea rules.[5] The dividend will be distributed amongst Xintela's shareholders in the form of shares in Targinta in proportion to their shareholding in Xintela. The aim is to list Targinta shortly after the dividend. We believe that the spin-off could support the company's efforts to unlock value in both these promising but diverse therapeutic areas and see the upcoming separation as a major catalyst for Xintela.

Q321 results

Xintela's Q321 operating loss stood at SEK10.8m, up c 53% y-o-y from SEK7.1m in Q320, driven by higher R&D expenses related to preclinical activities. R&D expenses made up the bulk of the cost structure (79%) and were reported at SEK10.4m in Q321, up 17% y-o-y over the Q320 figure of SEK8.9m. The net loss for the quarter was SEK10.9m, up from SEK8.3m in Q320.

Xintela ended the quarter with a net cash balance of SEK15.9m. In November 2021, the company raised SEK9m as a short-term bridge loan, but we note that the duration is fairly brief (repayment due no later than 28 February 2022; monthly interest rate of 1.4%) and expect the funds to be utilised to support Targinta's spin-off formalities. 9M21 free cash flow stood at SEK52.5m (operating cash flow of SEK51.8m plus SEK0.7m net capex). Excluding the SEK10.9m loan repayment in Q121 gives a normalised cash burn of c SEK41.6m for the first nine months of 2021 (c SEK55.5m annualised). At this run-rate Xintela's net cash balance provides a fairly short cash runway (into the beginning of 2022) for the company. This may be adequate to conclude the spin-off of Targinta, but we expect a need to raise further funds by early 2022 to proceed with the Phase I/IIa trials for XSTEM-OA and conduct the studies planned for other indications. The company has indicted that it is working to secure various forms of long-term financing (including partnerships, project financing, equity capital raising, grants or loans) for both Xintela and Targinta.

5 Lex Asea is a tax law concept for tax-free dividends of subsidiaries to the shareholders of the parent company in accordance with the rules of Swedish tax law.

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