

# TiGENIX

(a limited liability company (NV/SA) incorporated under Belgian law with its registered office in Leuven, Belgium)

## Offering of up to €40 million newly issued shares

The offered shares are offered to retail investors in Belgium and pursuant to a private placement to institutional investors in Belgium and elsewhere in Europe

The lead managers will be granted an over-allotment option, exercisable as of the listing date until 30 days following the closing date of the offering, for a number of shares up to 15% of the shares offered in the main offering at the final offering price, for the sole purpose of allowing the lead managers to cover over-allotments, if any. The shares covered by the over-allotment option will all be new shares of TiGenix

The offering and distribution of this prospectus are subject to certain restrictions  
See "certain restrictions on the offering and the distribution of this prospectus",  
beginning on page 35

INVESTING IN THE SHARES INVOLVES A HIGH DEGREE OF RISK

### Risk Factors

Investing in the shares that TiGenix is offering and that are described in this prospectus involves substantial risks. Before making an investment in the shares, prospective investors should carefully read the entire prospectus and should give particular attention to the risk factors set forth in the section "Risk Factors", starting on page 21. At present, none of the TiGenix products have been commercially launched. TiGenix' products are at varying stages of development and it may never have a product that is commercially successful. Regulatory approval of TiGenix' unapproved products as medicinal products may be delayed, not obtained or, in the case of approved products not maintained. Furthermore the market acceptance and third party reimbursement of TiGenix' products is uncertain. TiGenix may be unable to compete effectively against new technologies or competitors that could develop products that may be cheaper, more effective or safer than TiGenix' products. Since its incorporation in February 2000, the Company has not been profitable and has generated operating losses. **Under IFRS, the annual accounts of the Company as per December 31, 2006 show losses for the financial year 2006 in the amount of €8.2 mio, i.e. 56% of the Company's total equity as per January 1, 2006.** ING Belgium NV/SA, one of the lead managers in connection with this offering, is one of the main shareholders of TiGenix

Listing on the Eurolist by Euronext Brussels of all existing shares in TiGenix,  
all new shares as well as all shares to be issued upon exercise  
of the over-allotment option and warrants



PiperJaffray

*Lead managers*

**PETERCAM**

*Co-lead manager*

Prospectus dated February 27, 2007



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## SUMMARY

*This summary should be read as an introduction to the prospectus. It contains selected information about TiGenix and the offering. It does not include all the information that may be important to investors. This summary should be read together with the more detailed information and the consolidated financial statements and notes thereto included elsewhere in the prospectus. It should also be read together with the matters set forth under “Risk Factors”. Any decision to invest in the shares offered herein should be based on consideration of the prospectus as a whole. No civil liability will attach to the Company or its board of directors with respect to this summary, including any translation thereof, except if the summary is misleading, inaccurate or inconsistent when read together with the other parts of the prospectus. Where a claim relating to the information contained in a prospectus is brought before a court, the plaintiff investor might, under the applicable national legislation, have to bear the costs of translating the prospectus before the legal proceedings are initiated.*

## CERTAIN DEFINITIONS AND EXPRESSIONS

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Throughout this summary and elsewhere in the prospectus, certain terms and expressions are used. Unless the context in which these terms and expressions are used does not so permit, or unless these terms or expressions are defined differently, they should be read and understood as follows:

- a reference to the “Company” or “TiGenix” should be read as a reference to TiGenix NV/SA, a limited liability company (*naamloze vennootschap – NV / société anonyme – SA*) organized and existing under the laws of Belgium, with registered office at Technologielaan 3, 3001 Leuven (Heverlee), Belgium, and registered with the register of legal entities (*rechtspersonenregister – RPR / registre des personnes morales – RPM*) (Leuven) under company number 0471.340.123;
- a reference to the “shares” should be read as a reference to the shares in the Company;
- a reference to the “board of directors” should be read as a reference to the board of directors of the Company;
- a reference to the “statutory auditor” should be read as a reference to the statutory auditor of the Company.

## BUSINESS SUMMARY

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TiGenix is a late-stage biomedical company that focuses on innovative local treatments for damaged and osteoarthritic joints. The Company is exploiting the power of regenerative medicine to develop durable treatments, validated through controlled clinical trials, for these indications. The Company's lead product for cartilage repair, ChondroCelect, has successfully completed a randomised Phase III clinical trial and will be launched in Europe and/or in the United States, if and when all necessary regulatory approvals have been obtained. To the best of the Company's knowledge, ChondroCelect is the first cell-based medicinal product that has generated positive data in randomised controlled clinical trials for this indication and as such the Company expects the product to be well positioned for regulatory approval.

Based in Leuven, Belgium, TiGenix was founded in 2000 by Prof. Dr. Frank P. Luyten, rheumatologist and renowned scientist, and Gil Beyen, bioengineer and MBA, and CEO of the Company since its inception. The Company is built on technologies developed at both the Katholieke Universiteit Leuven and the Universiteit Gent and its scientific background lies in its expertise in the developmental biology of cartilage, bone and other connective tissues. The insights that the scientific founders gained into the biology of cartilage, namely how a stem cell transforms into a healthy cartilage cell and what happens when this cartilage cell gets injured or degenerates into an arthritic cell, led to the development of a technology platform focused on finding solutions that address specific musculoskeletal problems.

The lead indication among these is cartilage damage, which is a debilitating affliction affecting the mobility and functioning of patients. Western societies are characterised by ageing populations that place

an increasing emphasis on high quality of life and life-long mobility, and, as such, cartilage problems represent a large and growing unmet medical need. Current therapies do not provide satisfying, long-term durable repair and the Company believes there is a need for more effective treatments for cartilage damage. TiGenix' lead product, ChondroCelect, uses the patient's own cells as a basis for a quality-controlled product for cartilage repair, characterised by its biological potency. The Company has identified a specific set of genetic markers to identify potent cartilage-forming cells. These cells can form good cartilage when reimplanted into the patient's joint, which is critical in preventing degeneration of the joint and the development of osteoarthritis ("OA").

In January 2007, the Company entered into a strategic partnership with Fidia Advanced Biopolymers ("FAB"), based in Italy. FAB has developed a biological scaffold on which the ChondroCelect cells can be seeded to form a three-dimensional (3D) implantable construct. The combined product will enable arthroscopic implantation, which should facilitate the handling of the product for orthopaedic surgeons.

In addition, the Company' researchers are working to address more advanced stages of OA as well as to effect the repair of other tissues, such as meniscal tissue. The Company has recently identified novel cell culture methods that have the potential to further enhance the potency of its cell-based products. This opens the possibility of addressing larger cartilage defects and, in combination with the implantable 3D biomaterial, to treat more advanced and osteoarthritic joint surface lesions.

The Company believes that its main competitive strengths are:

- **Clear focus on a major unmet medical need.** The Company has a clear and singular focus on joint disorders and OA, which are among the largest and fastest growing disease areas in Western societies, due to the ageing demographic of those societies<sup>1</sup>. To date, no satisfactory medical solution exists for the treatment of cartilage damage or OA, making them indications with major unmet medical needs.
- **Leading cellular technology platform.** The Company has developed a leading cellular technology platform to identify and characterise cell populations with specific biological functions, through a combination of its core cell culture and genetic marker technologies. The platform enables the Company to further develop such cellular medicinal products which have a predictable *in vivo* behaviour.
- **ChondroCelect trial represented a first in class.** ChondroCelect, the Company's lead product for cartilage repair, has successfully completed a randomised Phase III clinical trial in which it demonstrated clear structural superiority combined with clinical non-inferiority over microfracture, currently the most common procedure for repairing cartilage damage.
- **Solid regulatory expertise.** Due to the novel nature of the field, regulations surrounding the approval of cell-based therapies are still in the process of being finalised. The Company anticipated such a rapidly changing regulatory environment and so developed solid regulatory expertise.
- **Access to leading biomaterials.** Through its strategic partnership with FAB and its distribution agreement with Geistlich (a Swiss developer and manufacturer of collagen-based biomaterials for use in medical applications), the Company has access to proven biomaterial solutions which can be used to facilitate the implantation of its ChondroCelect product, thus increasing the product's ease of use.
- **Innovative treatments in the pipeline.** The Company's in-depth know-how of the biology of stable cartilage formation and the signalling pathways associated with OA forms the basis of the ChondroCelect product platform. It also offers the potential to broaden the product's applications towards osteoarthritic joints, as well as to develop similar products for the repair of other

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<sup>1</sup> World Health Organisation. The Bone and Joint Decade: Consensus Document ([www.boneandjointdecade.org](http://www.boneandjointdecade.org)).



musculoskeletal tissues such as meniscus, for which applications are currently being examined by the Company.

- **Solid intellectual property.** The Company has built a strong intellectual property portfolio consisting of patents and trade secrets surrounding the Company's genetic markers, cell culture methods and stem cell technology. The two core patents have been granted in Europe, while several others are pending. In addition, the Company has recently identified, and filed a patent application on, novel cell culture methods that can further enhance the potency of its cell-based products.
- **Experienced management team.** TiGenix' management team contains a strong mix of highly experienced professionals with a track record in the biomedical and pharmaceutical fields

Between its inception in February 2000 and September 2003, the Company raised approximately €1 million in two seed rounds. In September 2003, the Company closed a second financing round of €12 million. During this round, four institutional venture capital (VC) companies invested in TiGenix' (ING Belgium NV/SA, Auriga Ventures II FCPR, Fagus NV and Capricorn Venture Fund II NV). In November 2005, TiGenix completed a third financing round of €16 million, with both existing and new investors. In this last round, international investors from the United States (HSS Ventures Inc.) and Japan (ITX Corporation) were among the new investors. Other sources of funding in the first years include two technology grants by the Flemish government, as well as income from licences and research collaborations.

## CORPORATE GOVERNANCE

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At the closing date, the board of directors of the Company will consist of maximum nine (9) members. See section 4.2.4 of chapter 4.

The statutory auditor of the Company is BDO ATRIO Bedrijfsrevisoren - BDO ATRIO Réviseurs d'Entreprises CVBA/SCRL, represented by Luc Annick.

The Company has adopted a corporate governance charter in accordance with the recommendations set out in the Belgian Code on Corporate Governance (the "Code") issued on December 9, 2004 by the Belgian Corporate Governance Committee. The Company's board of directors intends to comply with the Belgian Code on Corporate Governance, but believes that certain deviations from its provisions are justified in view of the Company's particular situation. These deviations include, but are not limited to, the following:

- Article 6.1. of the Code: as there is only one executive director (the Chief Executive Officer, or "CEO") and there is no management committee, the Company has not drafted specific terms of reference of the executive management.
- Article 7.4. of the Code: only the independent directors shall receive a fixed remuneration in consideration of their membership of the board of directors and their attendance at the meetings of committees of which they are members. They will not receive any performance related remuneration, nor will any option or warrants be granted to them in their capacity as director. However, upon advice of the nomination and remuneration committee, the board of directors may propose to the shareholders' meeting to deviate from the latter principle in case in the board's reasonable opinion the granting of options or warrants would be necessary to attract independent directors with the most relevant experience and expertise.
- Article 8.9. of the Code: only shareholders who individually or collectively represent at least 20% of the total issued share capital may submit proposals to the board for the agenda of any shareholders' meeting. This percentage is in line with Article 532 of the Belgian Company Code (relating to the convening of a shareholders' meeting) but deviates from the 5% threshold provided by the Code.

The board of directors of the Company will review its corporate governance charter from time to time and make such changes as it deems necessary and appropriate.

## OFFERING SUMMARY

<b>Company</b> .....	TiGenix NV/SA, a limited liability company ( <i>naamloze vennootschap – NV / société anonyme – SA</i> ) organised and existing under the laws of Belgium, with registered office at Technologielaan 3, 3001 Leuven (Heverlee), Belgium, and registered with the register of legal entities ( <i>rechtspersonenregister – RPR / registre des personnes morales – RPM</i> ) (Leuven) under company number 0471.340.123.
<b>Lead managers</b> .....	ING Belgium NV/SA, with registered office at Marnixlaan 24, 1000 Brussels, Belgium, and Piper Jaffray Ltd., having its principal place of business at One South Place, London ECM2M 2RB, United Kingdom.
<b>Co-lead manager</b> .....	Petercam NV/SA, with registered office at Sint-Goedeleplein 19, 1000 Brussels, Belgium.
<b>Underwriters</b> .....	ING Belgium NV/SA - Piper Jaffray Ltd. - Petercam NV/SA
<b>Syndicate members</b> .....	ING Belgium NV/SA - Piper Jaffray Ltd. - Petercam NV/SA
<b>Financial service</b> .....	The financial service in Belgium will be provided by ING Belgium NV/SA.
<b>Offering</b> .....	<p>The offering consists of new shares for a maximum amount of €40 million.</p> <p>The offering is divided into two tranches.</p> <p>A first tranche of up to 15% of the offered shares shall be reserved for allocation to retail investors in Belgium, subject to claw back.</p> <p>The balance of the shares shall be reserved for allocation to institutional investors in Belgium and elsewhere in Europe<sup>2</sup>, subject to claw back.</p> <p>The lead managers may over-allot a limited number of shares at the final offering price. The total amount of over-allotted shares shall never exceed 15% of the shares offered in the main offering.</p>
<b>Over-allotment option</b> .....	The lead managers will be granted an option, exercisable as of the listing date until 30 calendar days following the closing date of the offering, at the final offering price, to subscribe to a maximum number of new shares equal to 15% of the shares offered in the main offering. This option consists of warrants granted to the lead managers. The lead managers shall only be entitled to exercise these warrants for the purpose of covering over-allotments, if any.

<sup>2</sup> European Economic Area and Switzerland

<b>Offered shares</b> .....	All offered shares will have the same rights and benefits attached to them as the Company's existing shares. The offered shares will be entitled to share in the profits of the Company as of January 1, 2007 and are therefore entitled to a dividend, if any, for the entire financial year closed on December 31, 2007 and for the following financial years.
<b>Offering period</b> .....	The offering period will begin on March 12, 2007 and will be closed on March 23, 2007. The Company, in consultation with the lead managers, reserves the right to close the offering period at an earlier date and time. Any early closure of the offering period will be announced in the financial press in Belgium. The offering period will in any event be open for at least 6 banking days as of the availability of the prospectus.
<b>Offering price</b> .....	<p>The final offering price will be a single price in Euro that will apply to all investors, whether retail or institutional. The price range within which the final offering price will be determined will be published in the financial press in Belgium on or about March 10, 2007. The Company will determine the final offering price, within the price range, on the basis of the advice of the lead managers following a book-building procedure in which only institutional investors can participate. The final offering price will be determined as soon as possible after the closing of the offering period, which is expected to take place on March 23, 2007, and will most likely be published in the financial press in Belgium on March 24, 2007 or on the first banking day following the determination of the offering price.</p> <p>The final offering price will in no event exceed the upper-end of the price range.</p>
<b>Allocation date</b> .....	The results of the offering and the allocation key for the retail investors will be published in the financial press in Belgium on the allocation date, which is expected to be on March 24, 2007. See section 2.4.5. of chapter 2.
<b>Payment, settlement and delivery</b> .....	The shares must be paid up in full by the investor in Euro upon subscription. It is expected that the shares will be delivered to the subscribers on or about March 29, 2007. All offered shares will be delivered through the book-entry facilities of the Belgian central securities depositories, as well as through Euroclear Bank SA/NV, as operator of the Euroclear System (Euroclear) all in accordance with their normal settlement procedures applicable to equity securities.
<b>Closing date</b> .....	The closing date, <i>i.e.</i> , the date on which the realisation of the offering (including the subscription to the offered shares) will be established by the board of directors of the Company in a notarial deed, is expected to be March 29, 2007, being the third banking day following the allocation date. This date will be published in the financial press in Belgium together with the announcement of the final offering price and the results of the offering.

<b>Lock-up and standstill arrangements .....</b>	<p>All existing shareholders and warrant holders have entered into a lock-up arrangement with the lead managers for a period of 12 months from the first day of trading of the Company's shares. Under the terms of this arrangement, none of these shareholders and warrant holders can transfer the shares or warrants which it held prior to the first listing date or the shares which it subscribed to after the first listing date following the exercise of warrants which it held prior to the first listing date without the prior approval of the lead managers. This arrangement, which will not apply to the lending of shares to the lead managers to cover any over-allotments, is further described in section 2.8.2 of chapter 2 and section 3.5 of chapter 3.</p> <p>In addition, the Company has entered into a standstill arrangement with the lead managers for a period of 12 months from the first day of trading of the Company's shares. This arrangement is further described in section 2.8.2 of chapter 2.</p>	
<b>Use of proceeds .....</b>	<p>The Company intends to use the net proceeds of the offering for research and development, sales and marketing, clinical trials , working capital, capital expenditure, acquisitions if and when they present themselves, and other general corporate purposes.</p>	
<b>Cost of remuneration and intermediaries .....</b>	<p>The aggregate costs of the offering are estimated to be approximately 7.8% of the amount of the offering (including the discretionary fee referred to below, assuming that the over-allotment option is exercised in full).</p> <p>These costs include legal, administrative, audit and other costs (€800,000), remuneration of the CBFA (€15,690), legal publications, cost of advisors, management, underwriting and selling fees (4.6% or €2.1 million, not including a discretionary fee of up to 1.5%) and the initial fees payable to Euronext Brussels (€25,000). The selling fees are to a certain extent divided among all financial intermediaries who register subscriptions and applications in relation to the offering. All these costs will be borne by the Company and will be deducted from the use of proceeds as issuance costs.</p>	
<b>Listing .....</b>	<p>An application has been made for the admission of all shares of the Company to listing on the Eurolist by Euronext Brussels. The Company expects trading to commence on or about March 26, 2007, being the same day as the allocation date, but before the closing date of the offering when the offered shares are delivered to the subscribers. Prior to the delivery of the offered shares these will be traded on an "as-if-and-when-issued" basis. Prior to the listing of the shares, no public market existed for the shares issued by the Company.</p>	
<b>Security codes – shares .....</b>	ISIN:	BE0003864817 on Euronext Brussels
	Security Code:	3864.81 (Belgium)
	Euronext Symbol:	TIG on Euronext Brussels

<b>Timetable</b>	The following dates are all envisaged dates, barring any unforeseen circumstances:
<b>March 10, 2007</b>	Expected publication date of price range
<b>March 12, 2007</b>	Expected start of offering period
<b>March 23, 2007</b>	Expected end of offering period
<b>March 24, 2007</b>	Expected publication date of offering price
<b>March 24, 2007</b>	Expected allocation date
<b>March 26, 2007</b>	Expected listing date (admission to listing and start of trading)
<b>March 29, 2007</b>	Expected closing date (payment, settlement and delivery)

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## SELECTED FINANCIAL INFORMATION

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The tables hereunder outline the selected financial information which is based on the financial statements and should be read in conjunction with the financial statements prepared in accordance with IFRS as at and for each of the financial years ended December 31, 2006, 2005 and 2004 included elsewhere in this prospectus (see chapter 7) and with “*Management’s discussion and analysis of financial condition and results of operations*” (see chapter 6).

Since the Company’s sole subsidiary, TiGenix Inc., has only been incorporated in 2006, the financial statements for each of the financial years ended December 31, 2005 and 2004 are not consolidated financial statements. As required under IFRS, the financial statements for the financial year ended December 31, 2006 are consolidated financial statements although TiGenix Inc. does not yet have any operational activities at this stage.

The (consolidated) financial statements prepared in accordance with IFRS as at and for each of the financial years ended December 31, 2006, 2005 and 2004 were audited by the statutory auditor of the Company who provided an unqualified opinion.

A reconciliation between the financial statements under local Belgian GAAP and IFRS can be found under section 7.1.5.23 of chapter 7.

## INCOME STATEMENT DATA ACCORDING TO IFRS

<i>Thousands of Euro (€)</i>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>Revenues</b>	<b>416</b>	<b>784</b>	<b>567</b>
Research and development expenses	5,765	3,817	3,025
Selling, general and administrative expenses	3,201	1,845	1,338
Other operating income	0	0	0
Other operating expenses	0	0	0
<b>Operating Result (EBIT)</b>	<b>(8,550)</b>	<b>(4,878)</b>	<b>(3,797)</b>
Financial result	304	75	50
<b>Profit / (Loss) before taxes</b>	<b>(8,246)</b>	<b>(4,803)</b>	<b>(3,747)</b>
Income taxes	0	0	0
<b>Net profit / (Loss)</b>	<b>(8,246)</b>	<b>(4,803)</b>	<b>(3,747)</b>

## BALANCE SHEET DATA ACCORDING TO IFRS

<i>Thousands of Euro (€)</i>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>ASSETS</b>			
Total non-current assets	780	440	405
Total current assets	8,299	15,368	3,046
<i>Of which cash and cash equivalents</i>	<i>7,738</i>	<i>14,899</i>	<i>2,796</i>
<b>Total assets</b>	<b>9,079</b>	<b>15,808</b>	<b>3,451</b>
<b>LIABILITIES AND SHAREHOLDERS' EQUITY</b>			
Total equity	7,158	14,707	2,612
Non-current liabilities	399	13	0
Current liabilities	1,522	1,088	839
<b>Total liabilities and shareholders' equity</b>	<b>9,079</b>	<b>15,808</b>	<b>3,451</b>

## CASH FLOW STATEMENT DATA ACCORDING TO IFRS

<i>Thousands of Euro (€)</i>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>Cash and cash equivalents at beginning of period</b>	<b>14,899</b>	<b>2,796</b>	<b>2,271</b>
EBIT	(8,550)	(4,878)	(3,797)
Adjustments	807	334	419
Net cash provided by / (used in) operating activities	(7,743)	(4,544)	(3,378)
Net cash provided by / (used in) investing activities	(225)	(54)	(154)
Net cash provided by / (used in) financing activities	810	16,701	4,057
<b>Net change in cash and cash equivalents</b>	<b>(7,158)</b>	<b>12,103</b>	<b>525</b>
Effect on exchange rate changes	(3)	0	0
<b>Cash and cash equivalents at end of period</b>	<b>7,738</b>	<b>14,899</b>	<b>2,796</b>

## RISK FACTORS

TiGenix' business is subject to several risks including, but not limited to, the following ones:

- at present, none of the TiGenix products have been commercially launched;
- TiGenix products are at varying stages of development and it may never have a product that is commercially successful. Furthermore the market acceptance of TiGenix' products is uncertain;
- regulatory approval of TiGenix' unapproved products as medicinal products may be delayed, not obtained or, in the case of approved products, not maintained. There can also be uncertainty over the reimbursement from third parties for TiGenix' products;
- TiGenix may be unable to compete effectively against new technologies or competitors that could develop products that may be cheaper, more effective or safer than TiGenix' products;
- since its incorporation, the Company has not been profitable and has generated operating losses.

These and other risks related to TiGenix' business and relating to the offering are described in the section "Risk Factors".

## DILUTION

The following table gives an overview of the existing shareholders' structure on a fully-diluted basis immediately prior to the offering and the dilution as a result of the offering, assuming that both the offering and the over-allotment option will be fully subscribed to. The table is to be read together with the notes referred to below and the table and the notes in section 3.7.2 in chapter 3.

	Total shares and warrants before the IPO <sup>(1) (2)</sup>		Total shares and warrants after the IPO including new "personnel" warrants and "existing shareholders" warrants					
	Number	%	Total shares and warrants after the IPO excluding new "personnel" warrants and "existing shareholders" warrants <sup>(3)</sup>					
			Offering price of €5.00		Offering price of €6.50		Offering price of €8.00	
Existing Shareholders	Number	%	Number	%	Number	%	Number	%
Gil Beyen BVBA <sup>(4)</sup> (CEO)	195,000	1.27%	195,000	0.75%	195,000	0.83%	195,000	0.86%
			195,000	0.79%	195,000	0.87%	195,000	0.92%
Axxis V&C BVBA <sup>(4)</sup>	320,000	2.08%	411,748	1.59%	411,748	1.75%	508,083	2.24%
			320,000	1.30%	320,000	1.42%	320,000	1.51%
Prof. Dr. Frank Luyten	515,000	3.35%	606,748	2.34%	606,748	2.57%	703,083	3.10%
			515,000	2.09%	515,000	2.29%	515,000	2.44%
Gemma Frisius-Fonds K.U.Leuven NV	1,025,943	6.67%	1,208,697	4.67%	1,208,697	5.13%	1,400,590	6.18%
			1,025,943	4.17%	1,025,943	4.57%	1,025,943	4.85%
Katholieke Universiteit Leuven <sup>(5)</sup>	295,685	1.92%	348,402	1.35%	348,402	1.48%	403,754	1.78%
			295,685	1.20%	295,685	1.32%	295,685	1.40%
Universiteit Gent	371,498	2.41%	437,703	1.69%	437,703	1.86%	507,218	2.24%
			371,498	1.51%	371,498	1.65%	371,498	1.76%
ING Belgium NV/SA	4,261,452	27.70%	4,261,452	16.47%	4,261,452	18.08%	4,261,452	18.82%
			4,261,452	17.33%	4,261,452	18.97%	4,261,452	20.16%



	Total shares and warrants before the IPO <sup>(1) (2)</sup>		Total shares and warrants after the IPO including new “personnel” warrants and “existing shareholders” warrants					
			Total shares and warrants after the IPO <u>excluding</u> new “personnel” warrants and “existing shareholders” warrants <sup>(3)</sup>					
			Offering price of €5.00		Offering price of €6.50		Offering price of €8.00	
	Number	%	Number	%	Number	%	Number	%
Capricorn Venture Fund II NV	1,572,993	10.22%	1,572,993	6.08%	1,572,993	6.67%	1,572,993	6.95%
			1,572,993	6.40%	1,572,993	7%	1,572,993	7.44%
Fagus NV	2,105,527	13.69%	2,105,527	8.14%	2,105,527	8.93%	2,105,527	9.30%
			2,105,527	8.56%	2,105,527	9.37%	2,105,527	9.96%
Fortis Private Equity Venture Belgium NV	428,571	2.79%	428,571	1.66%	428,571	1.82%	428,571	1.89%
			428,571	1.74%	428,571	1.91%	428,571	2.03%
Auriga Ventures II FCPR	2,440,918	15.87%	2,440,918	9.43%	2,440,918	10.36%	2,440,918	10.78%
			2,440,918	9.93%	2,440,918	10.87%	2,440,918	11.55%
Baekeland Fonds II NV	114,285	0.74%	114,285	0.44%	114,285	0.48%	114,285	0.50%
			114,285	0.46%	114,285	0.51%	114,285	0.54%
BIP Investment Partners SA	142,857	0.93%	142,857	0.55%	142,857	0.61%	142,857	0.63%
			142,857	0.58%	142,857	0.64%	142,857	0.68%
PARTNERS@VENTURE NV	285,714	1.86%	285,714	1.10%	285,714	1.21%	285,714	1.26%
			285,714	1.16%	285,714	1.27%	285,714	1.35%
Technowal SA	71,428	0.46%	71,428	0.28%	71,428	0.30%	71,428	0.32%
			71,428	0.29%	71,428	0.32%	71,428	0.34%
ITX Corporation	200,000	1.30%	200,000	0.77%	200,000	0.85%	200,000	0.88%
			200,000	0.81%	200,000	0.89%	200,000	0.95%
HSS Ventures Inc.	41,071	0.27%	41,071	0.16%	41,071	0.17%	41,071	0.18%
			41,071	0.17%	41,071	0.18%	41,071	0.19%
Other	995,156	6.47%	1,004,049	3.88%	1,004,049	4.24%	1,013,387	4.47%
			995,156	3.85%	995,156	4.39%	995,156	4.39%
<b>Subtotal</b>	<b>15,383,098</b>	<b>100%</b>	<b>15,877,163</b>	<b>61.36%</b>	<b>15,877,163</b>	<b>67.36%</b>	<b>16,395,931</b>	<b>72.40%</b>
			<b>15,383,098</b>	<b>62.58%</b>	<b>15,383,098</b>	<b>68.49%</b>	<b>15,383,098</b>	<b>72.79%</b>
<b>New “personnel” warrants</b>								
New “personnel” warrants <sup>(6)</sup>	-	0.00%	800,000	3.09%	615,384	2.61%	500,000	2.21%
			0	0.00%	0	0.00%	0	0.00%
<b>Subtotal</b>	<b>-</b>	<b>0.00%</b>	<b>800,000</b>	<b>3.09%</b>	<b>615,384</b>	<b>2.61%</b>	<b>500,000</b>	<b>2.21%</b>
			<b>0</b>	<b>0.00%</b>	<b>0</b>	<b>0.00%</b>	<b>0</b>	<b>0.00%</b>



	Total shares and warrants before the IPO <sup>(1) (2)</sup>		Total shares and warrants after the IPO including new “personnel” warrants and “existing shareholders” warrants					
	Number	%	Total shares and warrants after the IPO <u>excluding</u> new “personnel” warrants and “existing shareholders” warrants <sup>(3)</sup>					
			Offering price of €5.00		Offering price of €6.50		Offering price of €8.00	
	Number	%	Number	%	Number	%	Number	%
Free Float								
Offering	-	0.00%	8,000,000	30.91%	6,153,846	26.11%	5,000,000	22.08%
			<i>8,000,000</i>	<i>32.54%</i>	<i>6,153,846</i>	<i>27.40%</i>	<i>5,000,000</i>	<i>23.66%</i>
Over-allotment option	-	0.00%	1,200,000	4.64%	923,076	3.92%	750,000	3.31%
			<i>1,200,000</i>	<i>4.88%</i>	<i>923,076</i>	<i>4.11%</i>	<i>750,000</i>	<i>3.55%</i>
<b>Subtotal</b>	<b>-</b>	<b>0.00%</b>	<b>9,200,000</b>	<b>35.55%</b>	<b>7,076,922</b>	<b>30.03%</b>	<b>5,750,000</b>	<b>25.39%</b>
			<i>9,200,000</i>	<i>37.42%</i>	<i>7,076,922</i>	<i>31.51%</i>	<i>5,750,000</i>	<i>27.21%</i>
<b>Total</b>	<b>15,383,098</b>	<b>100%</b>	<b>25,877,163</b>	<b>100%</b>	<b>23,569,469</b>	<b>100%</b>	<b>22,645,931</b>	<b>100%</b>
			<i>24,583,098</i>	<i>100%</i>	<i>22,460,020</i>	<i>100%</i>	<i>21,133,098</i>	<i>100%</i>

#### Notes

- (1) More tables of the existing securities, can be found in sections 3.7.1 and 3.7.2.
- (2) This column does not include the “existing shareholders” warrants issued by the extraordinary shareholders’ meeting on February 26, 2007 since they were issued subject to the completion of the offering and the listing of the Company’s shares and the number of new warrants depends on the final offering price.
- (3) In this column the numbers in normal text include the “existing shareholders” warrants and the new “personnel” warrants conditionally issued by the extraordinary shareholders’ meeting on February 26, 2007 and the numbers in italics exclude such new warrants.
- (4) Gil Beyen BVBA and Axxis V&C BVBA are controlled by Gil Beyen.
- (5) Including the shares held by Universitaire Ziekenhuizen Leuven.
- (6) These new “personnel” warrants were issued by the extraordinary shareholders’ meeting on February 26, 2007 but have not yet been granted by the Company.

Compared to the fraction of the registered capital and net equity of the Company represented by one share (calculated on a fully diluted basis)<sup>3</sup> as per December 31, 2006, the effect of the offering and the issuance of the new “personnel” warrants, “existing shareholders” warrants and “over-allotment” warrants in the aforementioned hypotheses (calculated on a fully diluted basis)<sup>4</sup> can be summarised as follows:

- **Offering price of €5 per share.** The fraction of the registered capital represented by one share increases by 0.10% and the fraction of the net equity represented by one share increases by 236.73%.

<sup>3</sup> Assuming that (i) all outstanding granted “personnel” warrants are exercised, (ii) for the outstanding granted “personnel” warrants issued on September 15-30, 2003, May 14, 2004 and April 20, 2005, €1 (par value at that time) of the exercise price per warrant is recorded as capital and the excess is recorded as issuance premium, and (iii) for the outstanding granted “personnel” warrants issued on November 3, 2005, €0.997 (par value at that time) of the exercise price per warrant is recorded as capital and the excess is recorded as issuance premium.

<sup>4</sup> Assuming that (i) all outstanding granted “personnel” warrants are exercised (see previous footnote), (ii) where applicable, all “existing shareholders” warrants are exercised at an exercise price of €0.001 per warrant which is recorded as capital, (iii) where applicable, all new “personnel” warrants are granted at an exercise price equal to the final offering price and are fully exercised whereby per warrant €0.997 is recorded as capital and the excess as issuance premium, and (iv) all “over-allotment” warrants are exercised whereby per warrant €0.997 of the exercise price is recorded as capital and the excess as issuance premium.

- **Offering price of €6.50 per share.** The fraction of the registered capital represented by one share decreases by 0.10% and the fraction of the net equity represented by one share increases by 269.73%.
- **Offering price of €8 per share.** The fraction of the registered capital represented by one share decreases by 4.41% and the fraction of the net equity represented by one share increases by 284.79%.

When disregarding the new “personnel” warrants and “existing shareholders” warrants, the effect can be summarised as follows:

- **Offering price of €5 per share.** The fraction of the registered capital represented by one share remains unchanged and the fraction of the net equity represented by one share increases by 231.13%.
- **Offering price of €6.50 per share.** The fraction of the registered capital represented by one share remains unchanged and the fraction of the net equity represented by one share increases by 262.41%.
- **Offering price of €8 per share.** The fraction of the registered capital represented by one share remains unchanged and the fraction of the net equity represented by one share increases by 285.08%.

## RELATED PARTY TRANSACTIONS

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ING Belgium NV/SA holds 4,261,452 shares in the Company and is one of the main shareholders of the Company. ING Belgium NV/SA, corporate finance division, is also one of the lead managers in connection with the offering as described in this prospectus. See also section 4.10 of chapter 4.

In 2003 existing shareholders of the Company concluded a shareholders’ agreement, in which they agreed, as confirmed in a shareholders’ agreement of 2005, to approve, in case of an initial public offering of the shares in the Company meeting certain conditions, an issuance of warrants (herein referred to as the “existing shareholders” warrants) to Axxis V&C BVBA, Prof. Dr. Frank Luyten, Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven), Gemma Frisius-Fonds K.U.Leuven NV, Johan Bellemans, Etienne Schacht and Universiteit Gent, as consideration for the representations and warranties given by some of them and the waiver of their preferential subscription rights with respect to the capital increases in the Company of September 15 and 30, 2003. In accordance with these agreements, the extraordinary shareholders’ meeting of the Company approved on February 26, 2007 the issuance to the aforementioned persons of the following number of “existing shareholders” warrants, subject to completion of the offering and listing of the Company’s shares: (i) 494,065 “existing shareholders” warrants, in case the final offering price is higher than €4.89 per share but lower than €7.84; or (ii) 1,012,833 “existing shareholders” warrants in case the final offering price is higher than €7.83 per share. Subject to the applicable lock-up and standstill arrangements, these “existing shareholders” warrants can be exercised at any time and entitle their holder to acquire one ordinary share in the Company per exercised warrant at an exercise price of €0.01 per warrant or, in case of exercise in blocks of 10 warrants, €0.001 per warrant. See also section 3.5 of chapter 3.

## **ADDITIONAL INFORMATION**

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### **Share Capital**

Prior to the offering and before the exercise of any outstanding warrants, the Company's share capital amounted to €14,115,529.94 represented by 14,157,014 registered common shares without nominal value. The capital is fully paid up.

### **Articles of Association**

The restated articles of association of the Company will be dated February 26, 2007. They will provide amongst others for specific rules relating to the management of the Company, its shareholders' meeting (including rules with respect to the right to attend and to vote at the shareholders' meeting) and the Company's liquidation (see section 3.4 of chapter 3). The entering into force of certain provisions of the Company's articles of association is subject to the completion of the offering of the shares and the admission to listing of the Company's shares (e.g. provisions with respect to the authorised capital).

### **Information available to the public**

Documents disclosed in accordance with applicable laws are available for consultation at the registered office of the Company and/or on the Company's website: [www.tigenix.com](http://www.tigenix.com).



## RISK FACTORS

*Any investment in the offered shares in this prospectus involves substantial risks. Before deciding to purchase shares in the offering, prospective investors should carefully review and consider the following risk factors and the other information contained in this prospectus. The occurrence of one or more of the risks described below may have a material adverse effect on the Company's cash flows, result of operations and financial condition and endanger the Company's ability to continue as a going concern. Moreover, the Company's share price could fall significantly if any of these risks were to materialise, in which case investors could lose all or part of their investment. Any prospective investor should note that the risks discussed below are not the only risks to which the Company is exposed. Additional risks and uncertainties, which are not currently known to TiGenix or which the Company currently believes to be immaterial, could likewise impair its business operations or have an adverse effect on the Company's cash flows, results of operations, financial condition, the Company's ability to continue as a going concern or the price of its shares. The order in which the risks are presented does not necessarily reflect the likelihood of their occurrence or the magnitude of their potential impact on the Company's cash flows, results of operations and financial condition, the Company's ability to continue as a going concern or the price of its shares. This prospectus also contains forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described below and elsewhere in this prospectus. Investors should consider carefully whether an investment in the offered shares is suitable for them in light of the information contained in this prospectus and their personal circumstances.*

### RISKS RELATED TO TIGENIX' BUSINESS

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**TiGenix has a history of operating losses and an accumulated deficit and may never become profitable.**

TiGenix has experienced operating losses since its founding in February 2000. It experienced net losses €3.7 million in 2004, €4.8 million in 2005 and €8.2 million in 2006. As of December 2006, the Company had an accumulated deficit of €21.9 million. These losses have resulted principally from costs incurred in research & development and clinical development and from general and administrative costs associated with the operations. Costs have exceeded revenues, which were generated mainly through grants, but also through revenues from research collaborations and limited product revenues. TiGenix expects to incur further substantial operating losses in the current and future financial years as its research and development activities continue.

There can be no assurance that TiGenix will ever earn significant revenues or achieve profitability, which could impair the Company's ability to sustain operations or obtain any required additional funds and could result in investors' losing all or a part of their investment.

**TiGenix' products are at varying stages of development and it may never have a product that is commercially successful.**

TiGenix has to date no approved product yet. Its lead product, ChondroCelect, is in late-stage clinical development. Whilst the product has demonstrated positive clinical trial results, it will require regulatory review, significant marketing efforts and substantial investment before it can provide the Company with any significant revenues. It cannot be excluded that additional clinical investigation may be required. Due to the inherent risk in the development of medicinal products, it is probable that not all of the product candidates in TiGenix' portfolio will successfully complete development and be launched.

With the exception of ChondroCelect, the Company does not expect to be able to market any of the Company's lead products for a number of years. If the Company is unable to develop, receive approval for, or successfully commercialise one or more of its products, it may be unable to generate significant

revenues. If its development programmes are delayed, the Company may need to raise additional funds or reduce or cease its operations.

**The yearly rate at which TiGenix uses its cash - raised through capital increases - has increased over time and is expected to further increase**

TiGenix has since its inception relied on different capital increases to fund its operations. Over the past six years about €22 million cash has been used in the Company's operating activities such as research, clinical development, manufacturing, pre-marketing and other activities. The yearly rate at which the cash has been used in these activities has increased over time and is expected to further increase over the next 2 to 3 years. In 2006 the net cash used in operating activities amounted to €7.7 million.

**TiGenix may require access to additional funding in the future, and if the Company fails to obtain such funding, the Company may need to delay, scale back or eliminate the development and commercialisation of some of its products or research and development programmes.**

The amount and timing of any expenditures needed to implement the Company's development and commercialisation programmes will depend on numerous factors, some of which are outside TiGenix' control. Additional funds may be necessary due to a number of factors, which could include:

- higher costs and slower progress than expected to develop products or obtain regulatory approvals;
- lower revenues than expected from commercialised products;
- unexpected opportunities to develop additional promising product candidates or to acquire technologies or other businesses;
- costs incurred to file, enforce or protect patents or other intellectual property rights; and
- costs incurred to sustain technological and market developments, scale-up manufacturing and effectively commercialise the Company's products.

The Company is currently not generating sufficient revenues to finance its research, development and commercialisation programmes and other operations, and there can be no assurance that it will do so in the future. If the proceeds of the offering, together with future revenues, are not sufficient to finance the Company's research, development and commercialisation programmes, additional funds would be required. There can be no assurance that additional funds will be available on a timely basis, on favourable terms, or at all, or that such funds, if raised, would be sufficient to enable the Company to continue to implement its business strategy. If TiGenix is unable to raise additional funds through equity or debt financing, it may need to delay, scale back or eliminate expenditures for some of its research, development and commercialisation programmes, or grant rights to develop and market products that it would otherwise prefer to develop and market itself, thereby reducing their ultimate value to the Company. The Company's inability to obtain additional funds necessary to operate its business could materially and adversely affect the market price of the Company's shares and all or part of an investment in shares in the Company could be lost.

**Future changes in the European pharmaceutical legislation could affect the Company's business**

The Company operates in a rapidly changing European and Belgian regulatory environment. On European level, on 16 November 2005, the European Commission has submitted a Proposal for a Regulation on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004. The proposed Regulation, if adopted, will cover all advanced therapies (*i.e.*, gene, cell and tissue-based therapies) with the overall policy objective to improve patient's safe access to these therapies by laying down specific rules concerning their authorisation, supervision and pharmacovigilance. The proposal has passed the vote in the Environment Committee of the European

Parliament on 7 February 2007. According to the procedural file, the plenary vote by the European Parliament is expected to take place in March 2007, whereas a common decision of the governments in the European Council is expected to take place in May 2007. Once adopted, this Regulation may apply to certain of the Company's products. In addition, on 22 December 2005, the European Commission has put forward a Proposal for a Directive to amend the current legislative framework governing medical devices, which may apply to certain products and have an impact on their regulatory classification. The draft Directive on medical devices has been approved by the Environment Committee of the European Parliament on October 2006. According to the procedural file, the plenary vote by the European Parliament is expected to take place in April 2007, whereas a common decision of the governments in the European Council is expected to take place in May 2007. On Belgian level, Directive 2004/23/EC of the European Parliament and of the Council of March 31, 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (the "SANCO-Directive") still needs to be implemented into Belgian law. While the SANCO-Directive foresees that products that are regulated by other legislation (such as the legislation on medicinal products) are not subject to the Directive for the manufacturing, storage and delivery of cells, these products are subject to the Directive for donation, procurement and testing. Consequently, recognition as a tissue establishment or a collaboration between the Company and a tissue establishment may in the future be required for donation, procurement and testing. The deadline for the implementation of the Directive by the Member States was 7 April 2006. At this stage, however, the Directive has not been implemented into Belgian law and discussions regarding the implementation of the rules contained in it are ongoing in the Parliament. The Company cannot predict when such European and Belgian legislation will be enacted, nor can it estimate the potential impact on the Company's business. Furthermore, the Company cannot predict what effect subsequent changes in European or Belgian legislation may have on the Company's business.

**Regulatory approval of TiGenix' unapproved products as medicinal products may be delayed, not obtained or, in the case of approved products, not maintained.**

The clinical evaluation, manufacture and marketing of TiGenix' products and its ongoing research and development activities are subject to regulation by regulatory and governmental authorities in all territories in which TiGenix, or any of its partners or licensees, wishes to test, manufacture or market products. The regulatory approval process is expensive and generally takes many years to complete.

Healthcare products are subject to lengthy and rigorous pre-clinical testing and clinical trials and other extensive, costly and time-consuming procedures mandated by the Food and Drug Administration ("FDA") in the United States and the European Medicine Agency ("EMA") or national regulatory authorities in Europe. Each regulatory authority may impose its own requirements and may refuse to grant, or may require additional data before granting, an approval notwithstanding that regulatory approval may have been granted by other authorities.

Regulatory approval may be delayed, limited or denied for a number of reasons, most of which are beyond TiGenix' control. Such reasons include the product not meeting safety/efficacy requirements or the relevant manufacturing processes or facilities not meeting applicable requirements.

Regulatory authorities, including the FDA and the EMA, may disagree with the Company's interpretations of data from pre-clinical studies and clinical trials. Regulatory authorities also may approve a product for narrower indications than requested or may grant approval subject to the performance of post-marketing studies for a product. There can be no guarantee that such post-approval studies, if required, will corroborate the results of earlier trials. Furthermore, the market use of such products may show different safety and efficacy profiles to those demonstrated in the trials on which marketing approval was based. Such circumstances could lead to the withdrawal or suspension of marketing approval for the product, which could have a material adverse effect on the Company's business, financial condition, operating results or cash flows. In addition, regulatory authorities may not approve the labelling claims that are necessary or desirable for the successful commercialisation of the Company's products.



In addition, a marketed product continues to be subject to strict regulation after approval. Changes in applicable legislation and/or regulatory policies or discovery of problems with the product, production process, site or manufacturer may result in delays in bringing products to the market, the imposition of restrictions on the product's sale or manufacture, including the possible withdrawal of the product from the market, or may otherwise have an adverse effect on TiGenix' business.

The failure to comply with applicable regulatory requirements can, among other things, result in criminal and civil proceedings and lead to imprisonment, fines, injunctions, damages, total or partial suspension of regulatory approvals, refusal to approve pending applications, recalls or seizures of products, operating and production restrictions.

There can be no assurance that regulatory clearance for trials at each stage, and approval for the Company's product candidates still in development, will be forthcoming without delay or at all. If TiGenix fails to obtain or maintain regulatory approval for its products, it will be unable to market and sell such products. Any delay in, or failure to receive or maintain, approval for any of TiGenix' products could prevent it from ever generating meaningful revenues or achieving profitability.

**TiGenix may experience delays in or fail to complete its clinical trials, both of which could affect its financial position and commercial prospects.**

As part of the regulatory approval process, TiGenix must conduct pre-clinical studies and clinical trials for each of its unapproved products to demonstrate safety and efficacy. The number of pre-clinical studies and clinical trials that will be required varies depending on the product, the indication being evaluated, the trial results and the regulations applicable to the particular product. The results of pre-clinical studies and initial clinical trials of TiGenix' unapproved products do not necessarily predict the results of later-stage clinical trials. Unapproved products in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through initial clinical trials. There can be no assurance that the data collected from the pre-clinical studies and clinical trials of the Company's unapproved products will be sufficient to support FDA, EMEA, other regulatory approval, or approval from local ethics committees. In addition, the continuation of a particular study after review by an independent data safety monitoring board or review body does not necessarily indicate that all clinical trials will ultimately be successfully completed.

TiGenix cannot accurately predict when its current clinical trials will be completed, if at all, nor when planned clinical trials will begin or be completed. Successful and timely completion of clinical trials will require TiGenix to recruit a sufficient number of patient candidates, locate or develop manufacturing facilities with regulatory approval sufficient for production of the product to be tested and rely on agreements with clinical research organisations to perform the trials.

The Company's products may produce unexpected side effects or serious adverse events which could interrupt, delay or halt clinical trials of TiGenix' unapproved products and could result in the FDA, the EMEA or other regulatory authorities denying approval of its products for any or all targeted indications. An independent data safety monitoring board, the FDA, the EMEA, other regulatory authorities or TiGenix itself may suspend or terminate clinical trials at any time. There can be no assurances that any of TiGenix' pipeline products will ultimately prove to be safe for human use.

Any delays in completing clinical trials will delay TiGenix' ability to generate meaningful revenue from product sales, and the Company may have insufficient capital resources to support its operations.



**The Company relies or may rely on third parties for certain of its research, clinical trials, technology, manufacturing and sales and marketing.**

The Company has entered into agreements and arrangements with a number of third parties and may enter into additional agreements and arrangements for research, clinical trials, technology, manufacturing and sales and marketing.

The Company relies primarily on third party contract research organisations to conduct its clinical trials. As a result, TiGenix has had and will continue to have less control over the conduct of the clinical trials, the timing and completion of the trials, the required reporting of adverse events and the management of data developed through the trials than would be the case if it relied entirely upon its own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in co-ordinating activities. Outside parties may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct the Company's trials. TiGenix may experience unexpected cost increases that are beyond its control. Problems with the timeliness or quality of the work of a contract research organisation may lead the Company to seek to terminate the relationship and use an alternative service provider. However, making this change may be costly and may delay the Company's trials, and contractual restrictions may make such a change difficult or impossible. Additionally, it may be impossible to find a replacement organisation that can conduct the Company's trials in an acceptable manner and at an acceptable cost.

TiGenix may in the future rely on a number of contract manufacturing organisations to develop and manufacture certain of its products, including for its clinical development programmes. There can be no guarantee that TiGenix will be successful in establishing such manufacturing arrangements on acceptable terms, or at all, or in maintaining those. There is a risk that if one of these organisations were to cease supplying products for TiGenix without warning there would be a delay in, and an increase in the costs of, its product development programmes. There can be no assurance that TiGenix' products, including its currently unapproved products, if approved, can be manufactured in sufficient commercial quantities, in compliance with regulatory requirements and at an acceptable cost.

TiGenix currently has a small marketing and sales force for the pre-launch activities of its products. To the extent that the Company decides to market its own products in the future, significant expenditure and management resources will be needed to develop a marketing and sales capability with appropriate technical expertise and distribution capabilities. TiGenix may attempt to build such a sales and marketing organisation on its own or with the assistance of one or more contract sales organisations or commercial partners. For some market opportunities, the Company may need to enter into co-promotion or other licensing arrangements with larger pharmaceutical or medical device firms in order to increase the commercial success of its products. TiGenix may not be able to establish sales, marketing and distribution capabilities of its own or enter into arrangements with contract sales organisations or larger pharmaceutical or medical device firms in a timely manner or on acceptable terms. Additionally, building marketing and distribution capabilities may be more expensive than TiGenix anticipates, requiring it to divert capital from other intended purposes or preventing it from building its marketing and distribution capabilities to the desired levels.

TiGenix' dependence on third parties may reduce its profit margins and delay or limit its ability to develop and commercialise its products on a timely and competitive basis.

**The Company may not be able to adequately protect its proprietary technology or enforce any related rights thereto, nor can it be certain to be free to operate the same.**

TiGenix' ability to compete effectively with other companies depends, amongst other things, on exploitation of its technology. However, there can be no assurance that competitors have not developed or will not develop substantially equivalent technologies or otherwise gain access to TiGenix' technology. To date, TiGenix' patent applications are progressing through the examination process, and it has been granted 2 patents in the EU. There can be no assurance that further patents will be issued with respect to

TiGenix' applications now pending or which may be applied for in the future. The lack of any such patents may have a material adverse effect on TiGenix' ability to develop and market its proposed products. No assurance can be given that TiGenix will develop products which are patentable or that its current or future patents will be sufficiently broad in their scope to provide commercially meaningful protection against competition from third parties. There can be no assurance as to the ownership, validity or scope of any patents which may be issued to TiGenix or that claims relating to its patents will not be asserted by other parties or that, if challenged, TiGenix' patents will not be revoked. Even if competitors do not successfully challenge TiGenix' patents, there can be no guarantee that they will not be able to design around TiGenix' patents or develop unique technologies or products providing effects similar to TiGenix', which may decrease the Company's future potential revenues.

The commercial success of TiGenix will also depend upon its non-infringement of patents granted to, and other intellectual property rights of, third parties, including any who may have filed applications or who have obtained or may obtain patents relating to products which might inhibit TiGenix' ability to develop or exploit its own products. Additionally, as patent applications, in general, are not published until 18 months after the date of priority applications or, in some cases in the United States, until grant, the Company cannot be certain that it was the first to make, or seek patent protection for, the invention claimed by each of its patents and patent applications. As a result of these factors, to avoid infringing third-party intellectual property rights, TiGenix may need to utilise alternative technology or exploit under licence other parties' intellectual property rights. TiGenix has in the past, and may in the future, license technologies for its development programmes. There can be no assurance that TiGenix will be able to obtain or maintain the right to utilise such technology or, where licences are required, that TiGenix will be able to obtain or maintain any such licence on commercially favourable terms, if at all. This may have a material adverse effect on TiGenix' business, financial condition, operating results and cash flows. In addition there can be no assurance that technologies licensed by TiGenix will not subsequently be found to infringe on third party intellectual property rights.

To the extent that the Company's intellectual property rights are infringed, or the Company is alleged to infringe third-party intellectual property rights, litigation may be necessary to protect the Company's intellectual property rights or to defend the Company against infringement actions, which could result in substantial costs to, and diversion of efforts by, the Company with no guarantee of success. The Company's attempts to obtain patent or other protection for its technologies may also be subject to opposition, in relation to which the Company may need to incur substantial costs to overcome, with no guarantee of success. The Company may also feel it necessary to engage in costly opposition or interference proceedings to prevent third parties obtaining relevant patent or other protection, again with no guarantee of success.

#### **TiGenix in-licenses certain material technologies from third parties.**

TiGenix also in-licenses certain technologies which are material to its business from third parties, including the biodegradable scaffold used in the development of its next generation combination product, ChondroCelect-3D. TiGenix does not own the patents or supplementary protection certificates on the basis of which these licences are granted. These licences may generally be terminated by the licensor in the event of an unremedied breach by TiGenix of its obligations under the licence and in other specified circumstances. If any of the Company's licence agreement is terminated, the further development and commercialisation of some of the development products could be prevented or delayed, reducing its potential revenues. The scope of TiGenix' rights under its licences may be subject to dispute by licensors or third parties. TiGenix generally does not control the filing or the prosecution of the patents to which it holds licences and it is relying upon its licensors to enforce the patents and to prevent and/or to challenge possible infringement by third parties. There can be no assurance that the Company will be able to obtain licences for the technologies that it requires in the future.

**TiGenix' success depends on its key people, and it must continue to attract and retain key employees and consultants.**

In common with many smaller companies, the Company's future success is substantially dependent on a number of key people, including Prof. Dr. Frank Luyten, its scientific founder and medical advisor, Gil Beyen, the controlling shareholder of Axxis V&C BVBA (co-founder of the Company) and Gil Beyen BVBA (Chief Executive Officer of the Company), as well as on its other senior executives and consultants. Competition for qualified employees and personnel in scientific research and biotechnology industries is intense and there are a limited number of persons with knowledge appropriate to, and experience within, such industries. The process of locating such personnel with a combination of skills and attributes required to enable TiGenix to carry out its strategy is often lengthy.

TiGenix' success depends to a significant degree upon its ability to attract and retain qualified management, scientific, technical, marketing and sales personnel and upon the continued contributions of such management and personnel. TiGenix' employees may voluntarily terminate their employment at any time. There is no guarantee that TiGenix will be successful in attracting and retaining qualified executives, scientists and personnel.

The loss of the services of key personnel or the inability to attract additional qualified personnel could have a material adverse effect on the business, financial condition, results of operations and cash flows of TiGenix.

**TiGenix may be unable to compete effectively against new technologies or competitors that could develop products that may be cheaper, more effective or safer than TiGenix' products.**

The biomedical industry is characterised by significant and rapid technological change. Research and discoveries by others may render the Company's products obsolete.

The Company may experience competition for ChondroCelect and its other products currently under development. Competition may come from companies which have greater research, development, marketing, financial and personnel resources than TiGenix, and can, therefore, more quickly adapt to changes in the marketplace. Competitors may precede TiGenix in developing products or may succeed in developing products that are more effective, safe or economically viable than those developed by TiGenix.

Such successes by its competitors or technological changes could render TiGenix' technology and products obsolete and/or otherwise non-competitive. See also section 5.11 of chapter 5.

**TiGenix' manufacturing facilities are subject to regulatory requirements, which may impact on the Company's development and commercialisation of its products.**

The Company's products will need to be manufactured to high standards, in commercial quantities, in compliance with regulatory requirements and at an acceptable cost. The manufacture of such products is subject to regulatory authorisation and to the Good Manufacturing Practice ("GMP") requirements prescribed in the relevant country or territory of manufacture or supply. While TiGenix is currently directing efforts towards ensuring that it meets both European and U.S. requirements, there is a possibility that TiGenix may not meet the EMEA requirements for Europe or the FDA requirements for the United States, which could cause delays and additional expense.

The GMP requirements govern quality control of the manufacturing process and documentation policies and procedures. Compliance by TiGenix and its third-party manufacturers with GMP requires record keeping and quality control to ensure that the product meets applicable specifications and other requirements including audits of vendors, contract laboratories and suppliers. Manufacturing facilities are subject to inspection by regulatory authorities at any time. If an inspection by a regulatory authority

indicates that there are deficiencies, TiGenix or its third-party manufacturers, as appropriate, could be required to take remedial actions, stop production or close the relevant facility, which would disrupt the manufacturing processes and limit the supplies of the Company's products. If they fail to comply with these requirements, TiGenix also may be required to curtail the relevant clinical trials, may not be permitted to sell its products or may be limited as to the countries or territories in which it is permitted to sell them.

TiGenix' European manufacturing facilities, whilst certified for production of ChondroCelect for use in clinical trials, are being prepared for upgrade to the standards required in the EMEA guidelines for commercial supply. To meet the anticipated demand for its products, TiGenix will also need to expand its production capacity. This additional capacity will need to be compliant with the EMEA requirements. Unless and until the facilities comply with these standards, TiGenix may not manufacture for commercial supplies at these facilities. There can be no guarantee that TiGenix' facilities will achieve compliance with these standards. In addition, there can be no guarantee that the regulations or policies applied by the relevant authorities will not change, and any such change may require TiGenix to undertake additional work, which may not be successful in complying with revised standards. There can be no assurance that this upgrade will be successful or that if the facility is certified, the certification will not be suspended because of a failure to maintain compliance or for any other reason.

TiGenix is planning to set up manufacturing facilities in the United States. These facilities will have to comply with the strict regulations of the FDA. There can be no guarantee that TiGenix' facilities will achieve compliance with these standards.

#### **Market acceptance of TiGenix' products is uncertain.**

The success of the Company will depend on the market acceptance of its products and there can be no guarantee that this acceptance will be forthcoming. Notwithstanding the technical merits of a product developed by TiGenix, there can be no assurance that medical practitioners will adopt such products as a standard means of medical practice or that the medical procedures at which TiGenix' products are targeted will maintain market acceptance. Physicians will use TiGenix' products only if they determine, based on experience, clinical data, side effect profiles and other factors, that they are preferable to other products then in use or beneficial in combination with other products. Recommendations and endorsements by influential physicians will be essential for market acceptance of TiGenix' products, and the Company may not be able to obtain these recommendations and endorsements.

Many other factors influence the adoption of new products, including marketing and distribution restrictions, adverse publicity, product pricing and reimbursement by third-party payers, as well as the introduction of competing products. The failure of TiGenix' products to achieve market acceptance would prevent it from ever generating meaningful product revenues.

#### **There may be uncertainty over reimbursement from third parties for newly approved healthcare products.**

TiGenix' ability to commercialise its products may depend, in part, on the extent to which reimbursement for the products will be available from government and health administration authorities, private health insurers, managed care programmes and other third-party payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. In many countries, medicinal products are subject to a regime of reimbursement by government health authorities, private health insurers or other organisations. There is increasing pressure from these organisations to limit healthcare costs by restricting the availability and level of reimbursement. There can be no assurance that adequate public health service or health insurance coverage will be available to enable the Company to obtain or maintain prices for its products sufficient to realise an appropriate return on investment.

In addition, changes to the rules and regulations regarding reimbursement or changes to existing regimes of reimbursement or the introduction of a new regime in any country could impact on whether reimbursement is available at adequate levels or at all. Rules and regulations regarding reimbursement may change frequently, in some cases at short notice. In view of the global cost pressures on healthcare and pharmaceutical markets, further changes should be expected.

**The Company must effectively manage the growth of its operations.**

The Company has in recent years operated in Europe and has more recently expanded its operations through the establishment of its subsidiary, TiGenix Inc., in the United States. The Company's ability to manage its growth effectively will require it to continue to improve its operations, financial and management controls, reporting systems and procedures, and to train, motivate and manage its employees and, as required, to install new management information and control systems. There can be no assurance that the Company will be able to implement improvements to its management information and control systems in an efficient and timely manner or that, if implemented, such improvements will be adequate to support the Company's operations. Any inability of the Company to manage its expansion successfully could have a material adverse effect on its business, results of operations and financial condition.

**If TiGenix faces product liability claims, damages may exceed its insurance.**

TiGenix' business exposes it to potential product liability and professional indemnity risks which are inherent in the research, development, manufacturing, marketing and use of medical treatments. It is impossible to predict the potential adverse effects that the Company's products may have on humans. The Company faces the risk that the use of its products in human clinical trials may result in adverse effects, or that long-term adverse effects may only be identified following clinical trials and approval for commercial sale. In addition, there can be no assurance that physicians and patients will comply with any warnings that identify the known potential adverse effects and any patients who should not receive the Company's products. There can be no assurance that the necessary insurance cover will be available to TiGenix at an acceptable cost or at all, or that, in the event of any claim, the level of insurance carried by TiGenix now or in the future will be adequate or that a product liability or other claim would not materially and adversely affect TiGenix' business. If TiGenix cannot adequately protect against potential liability claims, it may find it difficult or impossible to commercialise its products.

**Exchange rate fluctuations may negatively affect TiGenix' financial condition.**

TiGenix uses the Euro currency for financial reporting purposes. However, the Company may have a significant portion of its operating costs in U.S. Dollar (U.S. subsidiary, U.S. research and development collaborations, U.S. trial collaborations, and U.S. professional services) and expects to have a large share of its future revenues in U.S. Dollar. TiGenix has not engaged in any active hedging techniques nor has it employed any derivative instruments to date. Unfavorable fluctuations in the exchange rate between the Euro and the U.S. Dollar could have a material negative impact on the financial results of the Company.

**The public perception of ethical and social issues surrounding the use of cell-based medicines may limit or discourage the use of TiGenix' products.**

The commercial success of TiGenix' core technologies and any potential products resulting from these technologies will depend in part on market acceptance of these technologies and resulting products. Whilst TiGenix is not involved in embryonic stem cell research, the use of human cells (differentiated cartilage and meniscus cells and adult stem cells) as starting material for the development of its cell-based medicinal products could generate negative public perception for the Company and public



expressions of concern could result in stricter governmental regulation. Any of these factors could delay the successful development of potential products.

## **RISKS RELATED TO THE OFFERING**

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### **Absence of liquid public market.**

Prior to the offering, there has been no public market for the Company's shares and an active public market for the shares may not develop or be sustained after the offering. The final offering price of the offered shares will be determined by the Company in common agreement with the lead managers on the basis of a book-building procedure in which only institutional investors can participate. The final offering price may not be indicative of future market prices, which may fall below the final offering price. Factors that may be relevant in the book-building procedure may include but are not limited to:

- market conditions in effect at the time of the offering;
- the number of shares requested, the size of the orders received, the quality of the investors submitting such orders and the prices at which the orders were made;
- TiGenix' future prospects and its industry's future prospects;
- TiGenix' sales, earnings and other financial and operating information in recent periods; and
- the market prices of securities and financial and operating information of companies engaged in similar activities.

### **Use of proceeds.**

The Company will have significant flexibility and broad discretion to allocate and use the net proceeds of this offering. If the proceeds are not wisely allocated it could harm the Company's ability to carry out its business plan. The Company intends to use the net proceeds of the offering for research and development, sales and marketing, clinical trials, working capital, capital expenditure, acquisitions if and when they present themselves, and other general corporate purposes. The Company's board of directors and management will determine, in their sole discretion and without the need for shareholders' approval, the amounts and timing of the Company's actual expenditures which will depend upon numerous factors, including the status of the Company's product development and commercialisation efforts, if at all, the amount of proceeds actually raised in the offering, and the amount of cash received resulting from partnerships and out-licensing activities. The Company constantly evaluates opportunities to acquire businesses and technologies that it believes are complementary to its business activities. The Company has not determined the amounts it plans to spend on each of its key projects nor the timing of these expenditures.

### **Future dilution.**

The dilution resulting from the exercise of outstanding warrants and from the new warrants issued on February 26, 2007 subject to the completion of the offering and the listing of the shares in the Company on the Eurolist by Euronext Brussels could adversely affect the price of the shares. See also section 3.5 in chapter 3. In addition, the Company may decide to raise capital in the future through public or private convertible debt or equity securities, or rights to acquire these securities, and exclude or limit the preferential subscription rights pertaining to the then outstanding securities. If the Company raises significant amounts of capital by these or other means, it could cause dilution for its holders of securities.

**Future sales of shares of the Company's shareholders could cause the market price of the Company's common stock to drop significantly, even if the business is doing well.**

If shareholders sell substantial amounts of the Company's shares, the market price of the shares may fall. These sales also might make it more difficult for the Company to issue or sell equity or equity-related securities in the future at a time and price that the Company deems appropriate. See also section 2.8.2 of chapter 2 "Lock-up and standstill arrangements".

**The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be highly volatile in the future.**

The following factors, in addition to other risk factors described in this prospectus, may have a significant impact on the market price and volatility of all the shares:

- announcements of technological innovations or new commercial products or collaborations by TiGenix' competitors or TiGenix itself;
- developments concerning proprietary rights, including patents;
- publicity regarding actual or potential results relating to products under development by TiGenix' competitors or TiGenix itself;
- regulatory and reimbursement developments in Europe, the U.S. and other countries;
- litigation; or
- economic, monetary and other external factors.

**Volatility of results.**

The Company's operating results have fluctuated in the past and are likely to do so in the future. These fluctuations could cause the price of its shares to fluctuate or decline significantly. Some of the factors that could cause the Company's operating results to fluctuate include but are not limited to:

- the success rate of its development efforts;
- the Company's ability to manage future clinical trials, given the regulatory environment;
- the timing of approval, if at all, of the Company's product(s) by the appropriate regulatory bodies; and
- the Company's ability to successfully commercialise its product(s).

A large portion of the Company's expenses is relatively fixed and mainly relates to expenses for personnel, trial costs and subcontracting agreements. There is no direct link between the level of its expenses and its revenues. Accordingly, if revenues decline or do not grow as anticipated, the Company may not be able to correspondingly reduce its operating expenses and may suffer losses accordingly.

Due to the possibility of fluctuations in its revenues and expenses, the Company believes that period-to-period comparisons of its operating results are not a good indication of its future performance. The Company's operating results in some periods may not meet the expectations of stock market analysts and investors. In that case, the price of its shares would probably decline.

**Significant shareholders.**

Following the completion of the offering and listing of the Company's shares, the Company will have a number of significant shareholders. For an overview of the Company's significant shareholders before and after completion of the offering, reference is made to section 3.7 of chapter 3.

Currently, the Company is not aware that its existing shareholders have entered into a shareholders' agreement with respect to the exercise of their voting rights in the Company after the completion of the offering. Nevertheless, to the extent that these shareholders were to combine their voting rights, they could have the ability to elect or dismiss directors, and, depending on how broad the Company's other shares are held, approve certain other shareholders' decisions that require more than 50% or 75% of the Company's outstanding votes that are present or represented at shareholders' meetings where such items are submitted to voting by the shareholders. On the other hand, to the extent that these shareholders have insufficient votes to impose certain shareholders' resolutions, they could have the ability to block proposed shareholders' resolutions that require more than 50% or 75% of the Company's outstanding votes that are present or represented at shareholders' meetings where such items are submitted to voting by the shareholders. Any such voting by these significant shareholders may not be in the interest of the Company or the other shareholders of the Company.

**Takeover provisions in the national law may make it difficult for an investor to change management and may also make a takeover difficult.**

Under Belgian law, public takeover bids on all the voting securities issued by the Company are subject to the supervision of the CBFA. If the latter determines that a takeover violates Belgian law, it may lead to suspension of the exercise of the rights attached to any shares that were acquired in connection with the envisaged takeover. Furthermore, in the event that an individual or a company intends to acquire the joint or exclusive control of the Company through one or several transactions and the price of the contemplated transfer includes a control premium, the acquirer must offer to all other shareholders the opportunity to sell their shares at the highest price offered by the acquirer for shares during the 12 months preceding the acquisition of control of the Company. The acquirer must give the other shareholders this opportunity within 30 days after its acquisition of control either (i) in the form of a public takeover bid or (ii) pursuant to an undertaking to maintain the stock price.

The European Directive 2004/25/EC of April 21, 2004 on takeover bids (the "Thirteenth Company Law Directive") provides that if a person acquires a certain percentage – to be determined by each of the EU member states – of the voting rights in a company giving him control of that company and regardless of the price paid, such person will be required to make a bid addressed to all holders of securities in that company at an equitable price. Although the Directive had to be implemented by May 20, 2006, this is not yet the case in Belgium. A draft Belgian Act on public takeover bids (*Wetsontwerp op de openbare overnamebiedingen / Projet de loi relative aux offres publiques d'acquisition*) implementing the Thirteenth Company Law Directive has been submitted to the Belgian Parliament on January 5, 2007. The draft Belgian Act provides that a mandatory bid will be triggered if a person holds more than 30% of the voting securities in the target company. The draft Belgian Act provides that another or an additional threshold percentage of voting securities can be determined by Royal Decree to take into account evolutions on the financial markets or, as the case may be, to take transitional measures. The draft Belgian Act contains a transitional provision granting a exemption from the mandatory bid to persons who individually or acting in concert hold at least 30% of the voting securities on the date the new mandatory bid provision enters into force, provided that the shareholding was duly notified to the CBFA within 120 business days as of the entering into effect of the new mandatory bid provision.

All these measures and provisions may have the effect of substantially discouraging a takeover bid by a third party.

**If securities or industry analysts do not publish research or reports about the Company, or if they change their recommendations regarding the shares adversely, the share price and trading volume could decline.**

The trading market for the shares will be influenced by the research and reports that industry or securities analysts publish about the Company or its industry. If one or more of the analysts who cover the Company, or its industry, downgrade the shares, the market price of the shares would likely decline. If



one or more of these analysts ceases coverage of the Company or fails to regularly publish reports on the Company, the Company could lose visibility in the financial markets, which in turn could cause the market price of the shares or trading volume to decline.

**The Company will incur increased expenses as a result of being a public company.**

As a public company, the Company will incur significant legal, accounting and other expenses that it did not incur as a private company. For example, the Company recently appointed an additional independent director, created additional board committees and adopted additional policies regarding corporate governance. In addition, the Company will incur increased costs associated with investor relations and public company reporting requirements in Belgium, and listing costs.

The Company also expects these new rules and regulations to make it more difficult and expensive for the Company to obtain or maintain director and officer liability insurance, and it may be required to accept low policy limits and coverage or incur substantial costs to obtain adequate coverage.

**As the shares will be listed and traded on the Eurolist by Euronext Brussels on an “as-if-and-when-issued” basis as from the listing date until the envisaged closing date, Euronext Brussels may annul all transactions effected in the shares if the offered shares are not issued on the closing date.**

As of the listing date until the envisaged closing date, the shares will be listed and traded on the Eurolist by Euronext Brussels on an “as-if-and-when-issued” basis. Investors that wish to enter into transactions in the shares prior to the envisaged closing date, whether such transactions are effected on the Eurolist by Euronext Brussels or otherwise, should be aware that the closing date may not take place on March 29, 2007, or not at all, if certain conditions or events are not satisfied or waived or do not occur on or prior to such date. Such conditions include the receipt of officers’ certificates and legal opinions and such events include the suspension of trading on the Eurolist by Euronext Brussels or a material adverse change in TiGenix’ financial condition or business affairs or in the financial markets. Euronext Brussels has indicated that they will annul all transactions effected in the shares if the offered shares are not issued on the envisaged closing date and that they cannot be held liable for any damage arising from the listing and trading on an “as-if-and-when-issued” basis as of the listing date until the envisaged closing date.

**No minimum amount for the offering.**

The Company has the right to proceed with a capital increase in a reduced amount. No minimum number of shares in the offering has been set. The actual number of offered shares will be confirmed in the financial press in Belgium together with the final offering price. Therefore, (i) only a reduced number of shares could be available for trade on the market, which could limit its liquidity and (ii) the Company’s financial means in view of the use of proceeds as described in section 2.2.3 of chapter 2 might be reduced. The Company might therefore reduce its level of investment or have to look for further external funding.



## DISCLAIMERS AND NOTICES

### NO REPRESENTATION

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No dealer, sales person or other person has been authorised to give any information or to make any representation in connection with the offering of the shares and listing that is not contained in this prospectus and, if given or made, such information or representation must not be relied upon as having been authorised or acknowledged by TiGenix or by the lead managers.

Statements made in this prospectus are valid on the date set forth on the cover page of this prospectus. The delivery of this prospectus or the completion of the offering and listing will not imply under any circumstance that there have been no changes in the affairs or financial situation of TiGenix since the date of this prospectus, or that material information contained in this document is correct after the date of this prospectus. In accordance with Belgian law, if a significant new fact occurs between the date of this prospectus and the completion of the offering that could affect investors' assessment of the offered shares, this new fact will need to be mentioned in an addendum to this prospectus. The addendum shall be subject to approval by the Belgian Banking, Finance and Insurance Commission (*Commissie voor het Bank-, Financie- en Assurantiewezen / Commission Bancaire, Financière et des Assurances*) ("CBFA") in the same manner as the prospectus and shall be made public as shall be determined by the CBFA. In the event where an addendum to the prospectus were to be published prior to the closing of the offering, the investors shall have the right to withdraw their subscriptions made prior to the publication of the addendum. Such withdrawal must be done within the time limits set forth in the addendum (which shall not be shorter than two banking days after publication of the addendum).

### DECISION TO INVEST

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In making an investment decision regarding the shares offered herein, potential investors must rely on their own examination of TiGenix and the terms of the offering, including the risks and merits involved as described in the prospectus. Any summary or description set forth in this prospectus of legal provisions, corporate structurings or contractual relationships is for information purposes only and should not be construed as legal or tax advice as to the interpretation or enforceability of such provisions or relationships. In case of any doubt relating to the contents or the meaning of the information contained in this document, prospective investors should consult an authorised or professional person specialised in advice on the acquisition of financial instruments. The shares have not been recommended by any federal or state securities commission or regulatory authority in Belgium or elsewhere.

### CERTAIN RESTRICTIONS ON THE OFFERING AND THE DISTRIBUTION OF THIS PROSPECTUS

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The offering and the distribution of this prospectus may be restricted by law in certain jurisdictions outside Belgium. TiGenix does not represent that this prospectus may be lawfully distributed in jurisdictions outside Belgium or that the shares may be lawfully offered in compliance with any applicable registration or other requirements in jurisdictions outside Belgium, or pursuant to any exemption available thereunder. TiGenix does not assume any responsibility for such distribution or offering. Accordingly, the offered shares may not be offered or sold, directly or indirectly, and neither this prospectus nor any advertising or other offering materials may be distributed or published in any jurisdiction outside Belgium, except in circumstances that will result in compliance with any applicable laws and regulations. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any of the shares of TiGenix to any person in any jurisdiction in which it is unlawful to make such offer or solicitation to such person. Persons

in whose possession this prospectus or any of the shares come, must inform themselves about, and observe, any such restrictions.

It is the responsibility of any person not resident in Belgium who wishes to take part in this offering to ascertain that the legislation applicable in his or her country of residence is complied with, and that all other formalities that may be required are fulfilled, including the payment of all costs and levies.

## **United States**

The offered shares have not been and will not be registered under the Securities Act of the United States. Subject to certain exceptions, the offered shares may not be offered, sold or delivered in the U.S., or to, for the account or benefit of, U.S. persons, except in certain transactions exempt from the registration requirements of the Securities Act. The terms used in this paragraph have the meanings given to them by Regulation S. The offered shares have not been approved or disapproved by the U.S. Securities and Exchange Commission, any state securities commission in the U.S. or any other U.S. regulatory authority, nor have any of the foregoing authorities passed upon or endorsed the merits of the offered shares or the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offence in the U.S.

## **Member States of the European Economic Area**

The shares have not been or will not be offered to the public in any Member State of the European Economic Area (each, a "Member State") other than in Belgium, except that the offer may be made in any Member State under one of the following exemptions set out in the EU Directive 2003/71/EC (the "Prospectus Directive", such expression including any relevant implementing measure in each Member State), assuming such exemptions have been implemented in that Member State:

- (a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (i) an average of at least 250 employees during the last financial year; (ii) a total balance sheet of more than €43,000,000 and (iii) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive); or
- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer in any Member State shall result in a requirement for the publication by TiGenix of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any offered shares in any Member State means the communication in any form and by any means of information on the terms of the offering, the shares to be offered so as to enable an investor to decide to subscribe for any shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State.

Each subscriber for offered shares in the offer located within a member state of the European Economic Area other than Belgium will be deemed to have represented, acknowledged and agreed that:

- (a) it is a "qualified investor" within the meaning of Article 2(1)(e) of the Prospectus Directive; and
- (b) either (i) the offered shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer of resale to, persons in any relevant member state other

than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the lead managers has been given to the offer or resale; or (ii) any acquisition of offered shares by it under the offer on behalf of other persons will be deemed to have been made as a qualified investor because such offered shares are acquired by it on a discretionary basis.

TiGenix, the lead managers and their affiliates, and others will rely upon the truth and accuracy of the foregoing representation, acknowledgement, and agreement. Notwithstanding the above, a person who is not a qualified investor and who has notified the lead managers of such fact in writing may, with the consent of the lead managers, be permitted to subscribe for or purchase offered shares in the offer.

## France

Neither this document nor any other offering material relating to the TiGenix shares has been prepared in the context of a public offer of securities in the Republic of France within the meaning of Article L.411-1 of the French Code monétaire et financier and articles 211-1 et seq. of the General Regulations (*Règlement Général*) of the *Autorité des marchés financiers* (the “AMF”) and has therefore not been and will not be submitted to the clearance procedures of the AMF in the Republic of France.

The shares have not been offered, sold or otherwise transferred and will not be offered, sold or otherwise transferred, directly or indirectly, to the public in the Republic of France. Neither this document nor any other offering material relating to the shares of TiGenix has been or will be (i) released, issued, distributed or caused to be released, issued or distributed to the public in the Republic of France or (ii) used in connection with any offer for subscription or sale of the shares of TiGenix in the Republic of France.

Any offers, sales or other transfers of the shares of TiGenix in the Republic of France will be made in accordance with Article L.411-2 of the French *Code monétaire et financier* only (i) providers of investment services relating to portfolio management for the account of third party (*personnes fournissant le service d’investissement de gestion de portefeuille pour compte de tiers*), and/or (ii) qualified investors (*investisseurs qualifiés*), all as defined in and in accordance with Articles L.411-1, L.411-2 and D.411-1 to D-411-3 of the French *Code monétaire et financier*.

## Switzerland

No offer relating to the new shares has been or shall be made to the public in Switzerland, within the meaning of Article 652a paragraph II of the Swiss Code of Obligations.

## United Kingdom

TiGenix and the lead managers have not authorised any offer of the shares to the public in the United Kingdom within the meaning of the Financial Services and Markets Act 2000 (“FSMA”), such that an approved prospectus would be required to be made available under Section 85 of the FSMA. The offered shares may not be offered or sold to persons in the United Kingdom, except to persons who fall within the definition of “qualified investors” as that term is defined in Section 86(7) of the FSMA or otherwise in circumstances which have not resulted and will not result in an offer to the public in the United Kingdom in respect of which an approved prospectus would be required to be made available under Section 85 of FSMA.

Each lead manager has represented warranted and agreed that:

- (a) It has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of any shares in circumstances in which Section 21(1) of the FSMA does not apply to the issuer; and
- (b) it has complied with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

## **FORWARD-LOOKING INFORMATION**

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This prospectus contains forward-looking statements and estimates made by the Company with respect to the anticipated future performance of TiGenix and the market in which it operates. Certain of these statements, forecasts and estimates can be recognised by the use of words such as, without limitation, “believes”, “anticipates”, “expects”, “intends”, “plans”, “seeks”, “estimates”, “may”, “will” and “continue” and similar expressions. They include all matters that are not historical facts. Such statements, forecasts and estimates are based on various assumptions and assessments of known and unknown risks, uncertainties and other factors, which were deemed reasonable when made but may or may not prove to be correct. Actual events are difficult to predict and may depend upon factors that are beyond the Company's control. Therefore, actual results, the financial condition, performance or achievements of TiGenix, or industry results, may turn out to be materially different from any future results, performance or achievements expressed or implied by such statements, forecasts and estimates. Factors that might cause such a difference include, but are not limited to those discussed in the section “Risk Factors”. Given these uncertainties, no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of the prospectus. TiGenix disclaims any obligation to update any such forward-looking statement, forecast or estimates to reflect any change in the Company's expectations with regard thereto, or any change in events, conditions or circumstances on which any such statement, forecast or estimate is based, except to the extent required by Belgian law.

## **INDUSTRY DATA, MARKET SHARE, RANKING AND OTHER DATA**

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Certain of the information contained in this prospectus is based on the Company's own estimates and assumptions, believed by the Company to be reasonable. Certain information, industry data, market size/share data and other data provided in this prospectus was derived from publications by leading organisations and scientific journals. A bibliography of the sources used is attached to this prospectus as Appendix 2. The information published by such organisations and journals has been accurately reproduced and as far as the Company is aware and able to ascertain, no facts have been omitted which would render the reproduced information inaccurate or misleading. The Company (with respect to information derived from publications by leading organisations) and the lead managers and their respective advisors have not independently verified any of the abovementioned information. Furthermore, market information is subject to change and cannot always be verified with complete certainty due to limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties inherent in any statistical survey of market information. As a result, prospective investors should be aware that market share, ranking and other similar data in this prospectus, and estimates and beliefs based on such data, may not be reliable.

## **ROUNDING OF FINANCIAL AND STATISTICAL INFORMATION**

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Certain financial and statistical information in this prospectus have been subject to rounding adjustments and currency conversion adjustments. Accordingly, the sum of certain data may not be equal to the expressed total.





# 1. GENERAL INFORMATION AND INFORMATION CONCERNING RESPONSIBILITY FOR THE PROSPECTUS AND FOR AUDITING THE ACCOUNTS

## 1.1. RESPONSIBILITY FOR THE CONTENT OF THE PROSPECTUS

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The Company assumes responsibility for the content of this prospectus. The Company declares that, having taken all reasonable care to ensure that such is the case, the information contained in this prospectus is, to the best of its knowledge, in accordance with the facts and contains no omission likely to affect its import.

The lead managers make no representation or warranty, express or implied, as to the accuracy or completeness of the information in this prospectus, and nothing in this prospectus is, or shall be relied upon as, a promise or representation by the lead managers.

This prospectus is intended to provide information to potential investors in the context of and for the sole purpose of evaluating a possible investment in the offered shares. It contains selected and summarised information, does not express any commitment or acknowledgement or waiver and does not create any right expressed or implied towards anyone other than a potential investor. It cannot be used except in connection with the offering. The content of this prospectus is not to be construed as an interpretation of the rights and obligations of TiGenix, of the market practices or of contracts entered into by TiGenix.

## 1.2. RESPONSIBILITY FOR AUDITING THE ACCOUNTS

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BDO ATRIO Bedrijfsrevisoren - BDO ATRIO Réviseurs d'Entreprises CVBA/SCRL, a civil company, having the form of a cooperative company with limited liability (*coöperatieve vennootschap met beperkte aansprakelijkheid / société coopérative à responsabilité limitée*) organised and existing under the laws of Belgium, with registered office at The Corporate Village, Da Vincilaan 9 - Box E.6, Elsinore Building, 1935 Zaventem, Belgium, represented by Luc Annick, has been re-appointed as statutory auditor of TiGenix on February 26, 2007 for a term of 3 years ending immediately after the closing of the shareholders' meeting to be held in 2010 that will have deliberated and resolved on the financial statements for the financial year ended on December 31, 2009. BDO ATRIO Bedrijfsrevisoren - BDO ATRIO Réviseurs d'Entreprises CVBA/SCRL is a member of the Institute of Certified Auditors (*Instituut der Bedrijfsrevisoren / Institut des Réviseurs d'Entreprises*) (membership number B - 00023 - 1986).

The statutory financial statements of the Company as of December 31, 2004, December 31, 2005 and December 31, 2006 and for the financial years then ended were prepared in accordance with generally accepted accounting principles in Belgium or Belgian GAAP. The financial statements of the Company as of December 31, 2004 and December 31, 2005 (no consolidation) and the consolidated financial statements as of December 31, 2006 also have been prepared in accordance with the International Financial Reporting Standards ("IFRS"). All of these financial statements have been audited by BDO ATRIO Bedrijfsrevisoren - BDO ATRIO Réviseurs d'Entreprises CVBA/SCRL, represented by Luc Annick, who delivered unqualified opinions.

## 1.3. APPROVAL AND NOTIFICATION OF THE PROSPECTUS

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On February 27, 2007 the CBFA approved this prospectus written in English for the purposes of the public offering in Belgium and the listing of the Company's shares on the Eurolist by Euronext Brussels in

accordance with Article 23 of the Belgian Act of June 16, 2006 on the public offerings of securities and the admission of securities to trading on a regulated market (*Wet betreffende de openbare aanbiedingen van beleggingsinstrumenten en de toelating van beleggingsinstrumenten tot de verhandeling op een gereguleerde markt / Loi relative aux offres publiques d'instruments de placement et aux admission d'instruments de placement à la négociation sur des marchés réglementés* ). The CBFA's approval does not imply any judgement on the merits or the quality of the offering, the offered shares or the Company.

This prospectus has only been prepared in Dutch and in English. In accordance with Article 31 of the aforementioned Belgian Act of June 16, 2006 the summary has been translated into French. The Company is responsible for verifying the consistency between the Dutch and English versions of the prospectus and between the French, Dutch and English versions of the summary of the prospectus. In connection with the public offering in Belgium, both the English and Dutch version of the prospectus are legally binding. In case of inconsistencies between the different language versions, the English version shall prevail.

The offering and this prospectus have not been submitted for approval to any supervisory body or governmental authority outside Belgium.

## **1.4. AVAILABLE INFORMATION**

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### **1.4.1. Prospectus**

The prospectus is only available in Dutch and in English. The summary of the prospectus is available in French. The prospectus and the summary will be made available to investors at no cost at the registered office of the Company, Technologielaan 3, 3001 Leuven (Heverlee), Belgium. In Belgium, the prospectus and the summary will also be made available to investors at no cost at the counters of ING Belgium NV/SA, Marnixlaan 24, 1000 Brussels, telephone numbers +32 (0)2 464 60 01 (Dutch), +32 (0)2 464 60 02 (French) or +32 (0)2 464 60 03 (English) and Petercam NV/SA, Sint-Goedeleplein 19, 1000 Brussels, telephone number +32 (0)2 229 64 46. Subject to certain conditions, this prospectus and the summary are also available, for information purposes only, on the internet at the following websites: [www.tigenix.com](http://www.tigenix.com), [www.ing.be](http://www.ing.be), [www.petercam.be](http://www.petercam.be) and on the websites of Euronext.

Posting this prospectus and the summary on the internet does not constitute an offer to sell or a solicitation of an offer to buy any of the shares to any person in any jurisdiction in which it is unlawful to make such offer or solicitation to such person. The electronic version may not be copied, made available or printed for distribution. This prospectus is only valid in its original printed version circulated in Belgium in compliance with applicable laws. Other information on the website of the Company or any other website does not form part of the prospectus.

### **1.4.2. Company documents and other information**

The Company must file its (restated and amended) articles of association and all other deeds that are to be published in the annexes to the Belgian Official Gazette with the clerk's office of the Commercial Court of Leuven (Belgium), where they are available to the public. A copy of the most recently restated articles of association and the corporate governance charter is also available on the Company's website after completion of the offering.

In accordance with Belgian law, the Company must also prepare annual audited statutory and consolidated financial statements. The annual statutory and consolidated financial statements and the reports of the board of directors and statutory auditor relating thereto are filed with the Belgian National Bank, where they are available to the public. Furthermore, as a listed company, the Company has to

publish summaries of its annual and semi-annual financial statements. These summaries will generally be made publicly available in the financial press in Belgium in the form of a press release. Copies thereof will also be available on the Company's website.

The Company will also have to disclose price sensitive information, information about its shareholders' structure, and certain other information to the public. In accordance with the Belgian Royal Decree of March 31, 2003 (as amended) relating to the obligations of issuers of financial instruments admitted to trading on a Belgian regulated market (*Koninklijk besluit betreffende de verplichtingen van emittenten van financiële instrumenten die zijn toegelaten tot de verhandeling op een Belgische gereguleerde markt / Arrêté royal relatif aux obligations des émetteurs d'instruments financiers admis aux négociations sur un marché réglementé belge*), such information and documentation will be made available through press releases, the financial press in Belgium, the Company's website (provided the conditions set forth in Article 14 of the Belgian Royal Decree of March 31, 2003 have been complied with), the communication channels of Euronext Brussels or a combination of these media.

The Company's website can be found at [www.tigenix.com](http://www.tigenix.com).



## 2. GENERAL INFORMATION RELATING TO THE OFFERING AND ADMISSION TO LISTING ON THE EUROLIST BY EURONEXT BRUSSELS

### 2.1. INFORMATION RELATED TO THE CAPITAL INCREASE

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At its meeting of February 26, 2007, the extraordinary shareholders' meeting of the Company decided to increase the Company's share capital up to a maximum amount (including issuance premiums) of €40 million (which is an amount that, in the opinion of the Company, should give the Company adequate financial means to execute its business over the coming years, assuming that no extraordinary events occur and that no extraordinary decisions are taken) by way of a contribution in cash through the issuance of new shares. All new shares are offered within the framework of the present offering.

The final offering price will be determined by the Company (acting through a pricing committee) based on the advice of the lead managers and on the basis of a book-building procedure with institutional investors and taking into account various relevant qualitative and quantitative elements. The number of new shares to be issued shall be determined as a quotient, the numerator of which shall be the aggregate amount of the (accepted) subscriptions to the capital increase (with a maximum of €40 million), and the denominator of which shall be the final offering price. The capital increase and the issuance of the new shares are subject to the completion of the offering of the shares and the admission to listing of the Company's shares.

If the capital increase is not fully subscribed to, the board of directors has the right, but not the obligation, to proceed with a capital increase for a reduced amount through the issuance of such number of shares that will have been subscribed to and which will have been accepted by the Company within the framework of the offering.

At the same meeting, the extraordinary shareholders' meeting also decided to issue "over-allotment" warrants to cover the over-allotment option granted to the lead managers and granting the lead managers the right to subscribe to new shares by way of a contribution in cash at the final offering price for a maximum aggregate amount (including issuance premiums) of 15% of the capital increase referred to above. The "over-allotment" warrants are issued exclusively with a view to allowing the lead managers to cover over-allotments, if any. The additional shares to be issued upon exercise of the over-allotment option will have the same issuance price as the new shares to be issued in the offering. Whether or not the capital increase will have been fully subscribed to, the lead managers will be entitled to proceed with over-allotments, if any, with a view to stabilisation after the start of trading. Except for such initial stabilisation, it is currently and in the foreseeable future not the Company's intention to foresee in any liquidity providing or market animating contract.

On February 26, 2007 the extraordinary shareholders' meeting also decided to issue, subject to completion of the offering and listing of the Company's shares, in aggregate 494,065 "existing shareholders" warrants (in case the final offering price is higher than €4.89 per share but lower than €7.84) or 1,012,833 "existing shareholders" warrants (in case the final offering price is higher than €7.83 per share) to Axxis V&C BVBA, Prof. Dr. Frank Luyten, Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven), Gemma Frisius-Fonds K.U.Leuven NV, Johan Bellemans, Etienne Schacht and Universiteit Gent in accordance with a shareholders' agreement initially entered into between existing shareholders in 2003 as confirmed in a shareholders' agreement of 2005, (see also section 3.5 of chapter 3), and (ii) a number of new "personnel" warrants equal to 10% of the number of new shares issued pursuant to the offering (excluding the new shares, if any, issued pursuant to the exercise of the over-allotment option) to be granted to employees, consultants or directors of the Company, as well as to other persons who in the scope of their professional activity have made themselves useful to the Company, including but not limited to the members of the scientific advisory

board and the clinical advisors (see also section 3.5 of chapter 3). The issuance price of the additional shares to be issued upon exercise of the “existing shareholders” warrants referred to under (i) shall be €0.01 per share or, in case of exercise in blocks of 10 warrants, €0.001 per share. The issuance price of the additional shares to be issued upon exercise of the new “personnel” warrants referred to under (ii) shall be equal to the average closing price of the Company’s shares on the Eurolist by Euronext Brussels over the 30 day period preceding the date on which the “personnel” warrants are offered, in accordance with Article 43, §4, 1° of the Belgian Act of March 26, 1999 concerning the Belgian action plan for employment 1998 and concerning various provisions (*Wet betreffende het Belgisch actieplan voor de werkgelegenheid 1998 en houdende diverse bepalingen / Loi relative au plan d'action belge pour l'emploi 1998 et portant des dispositions diverses*).

In connection with the issuance of the above shares, the over-allotment option, and other warrants the existing shareholders and warrant holders individually waived their preferential subscription rights.

For an overview of some of the other resolutions passed at the extraordinary shareholders’ meeting of February 26, 2007, reference is made to section 3.1 of chapter 3.

## 2.2. KEY INFORMATION

### 2.2.1. Working capital statement

As demonstrated from the table below, the Company had net working capital (*i.e.*, trade receivables, deferred charges & accrued income and cash and cash equivalents minus trade payables and other current liabilities) that was largely positive. The Company is confident that the working capital is sufficient for the Company’s present requirements for the coming twelve months.

	Thousands of Euro (€)		
	Years ended December 31,		
	2006	2005	2004
Trade receivable	444	337	237
Deferred charges & accrued income	117	132	13
Cash and cash equivalents	7,738	14,899	2,796
<b>Total</b>	<b>8,299</b>	<b>15,368</b>	<b>3,046</b>
Trade payables	749	775	540
Other current liabilities	768	308	299
<b>Total</b>	<b>1,517</b>	<b>1,083</b>	<b>839</b>
<b>Net Working Capital</b>	<b>6,782</b>	<b>14,285</b>	<b>2,207</b>

### 2.2.2. Capitalisation and indebtedness

The following table sets forth the Company’s capitalisation as per December 31, 2006 under IFRS. This table should be read in conjunction with the Company’s audited statements in IFRS (see chapter 7), including the notes thereto and with “*Management discussion and analysis of financial condition and results of operations*” (see chapter 6).

Thousands of Euro (€)	Years ended December 31,		
	2006	2005	2004
Share capital	13,044	12,645	8,259
Share premium	15,335	15,312	3,014
Accumulated losses, including loss of the year	(21,911)	(13,665)	(8,862)
Share-based compensation	693	416	201
Translation adjustments	(3)	0	0
<b>Total Equity</b>	<b>7,158</b>	<b>14,707</b>	<b>2,612</b>
Subordinated loan	391	0	0
Short and long term portion on leases	13	18	0
<b>Total Financial Debt</b>	<b>404</b>	<b>18</b>	<b>0</b>
<b>Gearing ratio (Financial Debt/Equity)</b>	<b>5.6%</b>	<b>0.1%</b>	<b>0.0%</b>
Cash and cash equivalents	7,738	14,899	2,796

The Company had several capital increases, bringing the registered capital at €14,115k (from which the aggregate issuance cost in the amount of €1,071k is to be deducted under IFRS) at the date of this offering. In 2006, the Company entered into a subordinated loan agreement with the Institute for the Promotion of Innovation by Science and Technology (*Instituut voor de aanmoediging van Innovatie door Wetenschap en Technologie in Vlaanderen*, or "IWT") bringing the gearing ratio to 5.6%.

On December 31, 2006, the Company had cash and cash equivalents amounting to a total of €7,738k.

### 2.2.3. Background of the offering and use of proceeds

The principal purposes of the offering are to support the Company's growth, to increase the Company's capitalisation and financial flexibility, to provide a public market for the Company's shares and to facilitate access to public equity capital markets.

If the offering is fully subscribed, the net proceeds from the issue of the offered shares are estimated to be €37.4 million, which will be allocated to the Company. If the over-allotment option granted to the lead managers is exercised in full, the net proceeds from the issue of the additional shares is estimated to be €5.7 million, which will be allocated to the Company. For further information on the costs and expenses of the offering, see section 2.9.

The Company intends to use the net proceeds of the offering (*i.e.*, after commissions and offering expenses payable by the Company have been deducted) for research and development, clinical trials, sales and marketing, working capital, capital expenditure, acquisitions if and when they present themselves, and other general corporate purposes.

More specifically, the Company intends to use the net proceeds of the offering as follows:

- to pre-market and to launch its lead product ChondoCelect;
- to put in place the necessary production capacity in Europe and the United States;
- to design and start clinical trials for the next generation ChondroCelect product (ChondroCelect 3D);
- to increase R&D efforts for developing MeniscoCelect, a product for meniscal repair;
- to increase R&D spending for advancing the Company's research programmes;
- to ensure active intellectual property management.

The Company also constantly evaluates opportunities to acquire businesses and technologies that it believes may be complementary to its business activities.



The amounts and timing of the Company's actual expenditures will depend upon numerous factors, including the status of the Company's product development and commercialisation efforts, the amount of proceeds actually raised in the offering, the amount of cash received resulting from grants, etc. The Company has not determined the amounts it plans to spend on any of the areas listed above or the timing of these expenditures. Overall, the Company currently estimates to spend (i) approximately 40-50 % of the net proceeds on the activities related to the launch of its lead product, ChondroCelect, and (ii) approximately 50-60% on the development of its next generation and pipeline products. The Company's management will have significant flexibility to allocate the net proceeds from the offering.

The Company intends to hold the proceeds it receives in connection with the offering at banks and in short-term, interest-bearing, investment grade securities, including governmental obligations and other money market instruments, until the Company will use them.

## **2.3. INTEREST OF NATURAL AND LEGAL PERSONS INVOLVED IN THE OFFERING**

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ING Belgium NV/SA holds 4,261,452 shares in the Company, representing 30.1% of all the issued and outstanding shares in the Company prior to closing (see also section 3.7.1 of chapter 3). ING Belgium NV/SA, corporate finance division, is one of the lead managers. The shares held by ING Belgium NV/SA will, as of closing, be subject to the lock-up arrangement, as further discussed in section 2.8. ING Belgium NV/SA will not be a member of the pricing committee.

In 2003 existing shareholders of the Company concluded a shareholders' agreement, in which they agreed, as confirmed in a shareholders' agreement of 2005, to approve, in case of an initial public offering of the shares in the Company meeting certain conditions, an issuance of warrants (herein referred to as the "existing shareholders" warrants) to Axxis V&C BVBA, Prof. Dr. Frank Luyten, Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven), Gemma Frisius-Fonds K.U.Leuven NV, Johan Bellemans, Etienne Schacht and Universiteit Gent, as consideration for the representations and warranties given by some of them and the waiver of their preferential subscription rights with respect to the capital increases in the Company of September 15 and 30, 2003. In accordance with these agreements, the extraordinary shareholders' meeting of the Company approved on February 26, 2007 the issuance to the aforementioned persons of in aggregate (i) 494,065 "existing shareholders" warrants, in case the final offering price is higher than €4.89 per share but lower than €7.84, or (ii) 1,012,833 "existing shareholders" warrants in case the final offering price is higher than €7.83 per share. Subject to the applicable lock-up and standstill arrangements, these "existing shareholders" warrants can be exercised at any time and entitle their holder to acquire one ordinary share in the Company per exercised warrant at an exercise price of €0.01 per warrant or, in case of exercise in blocks of 10 warrants, €0.001 per warrant. See also section 3.5 of chapter 3.

## **2.4. TERMS AND CONDITIONS OF THE OFFERING**

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### **2.4.1. Conditions and nature of the offering**

The offering consists of new shares, coupons No. 1 and following attached, for a maximum amount of up to €40 million. The new offered shares will not benefit from the right to reduced withholding tax, known as "*Verminderde Voorheffing / Précompte Réduit*" or "VVPR".

The offering can be increased with an additional number of new shares for a maximum amount up to 15% of the shares issued in the main offering, subject to exercise of the over-allotment option that will be granted to the lead managers to cover over-allotments, if any. See also section 2.7 below. The shares subject to the over-allotment option will not benefit from the VVPR status either. In the event where not all

offered shares are subscribed to, the board of directors has the right, but not the obligation, to proceed with the closing of the offering for the amount of subscriptions received.

The offering is subject to (i) the board of directors concluding that the quantity and quality of the subscription received is such that the offering can be closed in the interest of the Company, and (ii) the Company and the lead managers reaching a final agreement on the terms of the underwriting agreement.

The offering is organised as a public offering to retail investors in Belgium and a private placement with institutional investors in Belgium and elsewhere in Europe<sup>5</sup>.

The offering is divided into two tranches:

- a first tranche of up to 15% of the offered shares (excluding the shares covered by the over-allotment option granted to the lead managers) is reserved for allocation to retail investors in Belgium, subject to claw back;
- the balance of the shares (including the shares subject to the over-allotment option granted to the lead managers) shall be reserved for allocation to institutional investors in Belgium and elsewhere in Europe<sup>6</sup>, subject to claw back.

For the purpose of the offering, a retail investor shall mean (a) an individual person resident in Belgium, or (b) the legal entities in Belgium that apply for shares in an amount of €50,000 or less.

The existing shareholders shall have no priority or preference in the subscription to or allocation of the shares.

No special tranche will be reserved for the personnel of TiGenix.

#### **2.4.2. Offering price**

The final offering price will be a single price in Euro that will apply to all investors whether retail or institutional.

The final offering price will be determined within a price range determined by the board of directors of the Company upon advice of the lead managers. The price range will a.o. be based on the outcome of a two weeks pre-marketing by analysts of the syndicate members. Pre-marketing is the process that is undertaken by the lead managers of an IPO, in order to assess institutional investor appetite for the company going public and to evaluate a proper valuation/price range for the company's shares offered to the public. The pre-marketing process starts with the publication of an institutional research report, which is marketed to institutional investors by the lead managers' institutional sales force. The applicable price range will be published in the financial press in Belgium on or about March 10, 2007. As major shareholder of the Company and lead manager of the transaction, ING Belgium NV/SA will not take the lead role in the final pricing of the offering. The final offering price will be determined by the Company based on the advice of the lead managers and on the basis of a book-building procedure during the offering period, in which only institutional investors can participate, and taking into account various relevant qualitative and quantitative elements, including but not limited to the number of shares requested, the size of the orders received, the quality of the investors submitting such orders and the prices at which the orders were made, as well as the market conditions at that time. Piper Jaffray Ltd. will take the lead in formulating this advice, with the support of ING Belgium NV/SA as joint-lead manager.

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<sup>5</sup> European Economic Area and Switzerland.

<sup>6</sup> European Economic Area and Switzerland.

The applicable price range will be published as an addendum to the prospectus in the Belgian financial press on or about March 10, 2007. The final offering price will be determined as soon as possible after closing of the offering period, which is expected to take place on March 23, 2007 and will be published on the Saturday or first banking day following its determination, which is expected to be on March 24, 2007. The final offering price will in no event exceed the upper-end of the initial price range. The aforementioned dates are subject to early closing of the offering period.

#### **2.4.3. Offering period**

The offering period will begin on March 12, 2007 and will be closed on March 23, 2007, unless it is closed earlier as may be decided by the Company, in consultation with the lead managers. Any early closure of the offering period will be announced in the financial press in Belgium. The offering period will in any event be open for at least six banking days as of the availability of the prospectus. The offering period for retail and institutional investors will be the same.

In principle, prospective investors can submit their applications during the offering period, unless this period is closed prematurely.

Taking into account the fact that the offering period may be closed earlier, investors are urged to submit their applications as promptly as possible.

#### **2.4.4. Subscription procedure**

##### **General**

Subscriptions can be submitted to the syndicate members at no cost to the investor. Subscriptions are not binding upon the Company as long as they are not accepted, in accordance with the allocation rules described below in section 2.4.5.

Only one application form per investor will be accepted. If the lead managers determine, or have reason to believe, that a single investor has submitted several orders, through one or more syndicate members, they may disregard such orders. There is no minimum or maximum amount on the number of shares that can be subscribed to on one order.

Investors wishing to subscribe through intermediaries other than the syndicate members should request details of the costs which these intermediaries may charge and which they will have to pay themselves.

To be valid, subscriptions and applications must be submitted at the latest at 4.00 p.m. (Central European Time, GMT+1) on the final day of the offering period.

##### **Retail Investors**

Retail investors must indicate in their orders the number of offered shares they commit to subscribe to. Retail investors can only subscribe to the offered shares at the final offering price as explained in section 2.4.2.

In Belgium, orders by retail investors can be submitted, at no cost, at the counters of the syndicate members.

Retail investors are invited to introduce their orders as soon as possible with the syndicate members in Belgium. Only in the event where an addendum to the prospectus were to be published prior to the closing of the offering, the investors shall have the right to withdraw their subscriptions made prior to the publication of the addendum. Such withdrawal must be done within the time limits set forth in the addendum (which shall not be shorter than two banking days after publication of the addendum).

### **Institutional Investors**

Institutional investors must indicate in their orders the number of offered shares they commit to subscribe to, and the prices (within the price range) at which they are making such orders.

Institutional investors only can participate in the book-building procedure during the offering period, which runs from March 12, 2007 to March 23, 2007, unless it is closed prematurely. During the book-building period, institutional investors will have to indicate how many shares they wish to obtain and at what price (within the price range).

Institutional investors are invited to introduce their orders as soon as possible with the syndicate members. Only in the event where an addendum to the prospectus were to be published prior to the closing of the offering, the investors shall have the right to withdraw their subscriptions made prior to the publication of the addendum. Such withdrawal must be done within the time limits set forth in the addendum (which shall not be shorter than two banking days after publication of the addendum).

### **2.4.5. Allocation of the shares**

#### **General**

The exact number of offered shares allotted to respectively the retail investors and the institutional investors will be determined at the end of the book-building and offering period by the lead managers in consultation with the Company and will depend on the quantitative and qualitative analysis of the order book.

The shares will be allocated amongst retail and institutional investors in a balanced way, taking into account the 15% retail tranche and the 85% institutional tranche described under section 2.4.1 above, without prejudice to clawback as described below. In case of over-subscription, the allocation to retail and institutional investors will be made on the basis of an allocation key. In the event that the offered shares are oversubscribed, preferential treatment may be given to applications submitted at the branches of the syndicate members rather than through other financial intermediaries.

The allocation key will be determined at the end of the book-building period. Without prejudice to a potential preferential treatment given to orders submitted at the counters of the syndicate members, all retail investors will be subject to the same allocation key that will take into account such elements as the number of shares subscribed to. The allocation of shares amongst institutional investors will take into account other elements such as the nature of the investor concerned.

The results of the offering and the allocation key for the retail investors will be published in the financial press in Belgium on the allocation date, which is expected to be on March 24, 2007.

## Clawback

It is expected that up to 15% of the offered shares effectively allocated (excluding the shares covered by the over-allotment option granted to the lead managers) will be allocated to retail investors in Belgium. However, (i) the proportion of offered shares allocated to retail investors may be increased and possibly substantially, if applications received from them exceed 15% of the offered shares effectively allocated or, conversely, (ii) such proportion may be reduced, but not below 10% (to the extent that 10% of the retail tranche has been subscribed for) if the relative demand from the institutional investors at the offering price significantly exceeds that of the retail investors.

### 2.4.6. Payment, settlement and delivery of the shares

The shares must be paid up in full in Euro upon subscription, together with any applicable stock exchange tax. For further information about applicable taxes, see section 2.12.3, *"Tax on stock exchange transactions"* and section 2.12.4, *"Tax on the physical delivery of bearer securities"*.

The payment date is set at three banking days after the allocation date and is expected on March 29, 2007, unless the offering period closes earlier.

It is expected that the shares will be delivered to the investors on or about March 29, 2007.

All offered shares will be delivered in book-entry form, represented by one or more global certificates that will have been filed with the book-entry facilities of the Belgian central securities depositories ("CIK"), as well as through Euroclear Bank SA/NV, as operator of the Euroclear System ("Euroclear"), all in accordance with their normal settlement procedures applicable to equity securities.

As described in section 2.4.7 below, the shares will upon closing of the offering not be delivered in physical form but will be available in book-entry form only.

### 2.4.7. Form of the shares

All offered shares will have the same rights and benefits attached to them as the Company's other shares. For a further description of the Company's shares and the rights and benefits attached thereto, see section 3.4.2, *"Description of rights and benefits attached to the shares"*, in chapter 3, *"General information about the Company and its share capital"*.

As described in section 2.4.6 above, all shares will be delivered in book-entry form, represented by one or more global certificates that will have been filed with the CIK for safekeeping on behalf of those persons entitled to the shares.

Upon delivery of the shares, the shares will therefore be bearer securities in book-entry form. The shares cannot yet be delivered as bearer securities in physical form. The physical certificates will be available as soon as possible and in any case within three months of the listing date. They will be available in the form of physical certificates representing, 1, 10 or 100 shares or any other denomination, which the Company may be able to print, with coupons No.1 and following attached. Until they are delivered in physical form, a global certificate will represent the bearer shares and only book-entry transactions will be possible.

Shareholders requesting physical delivery of bearer shares should take into account delivery costs amounting to €12.50 (+VAT) for delivery in Belgium at the counters of ING Belgium NV/SA, and to €20.00 (+VAT) at the counters of Petercam NV/SA. In addition, any direct or indirect costs for printing the bearer shares shall be charged to the shareholders requesting physical delivery *pro rata* to the number of shares they requested be delivered physically. Shareholders are requested to enquire about any additional costs

which financial institutions that are not accompanying institutions or selling agents may charge and which shareholders will have to bear themselves. In addition, a tax on the physical delivery of bearer shares equal to 0.6% of the purchase price will be due. See also section 2.12.4 below.

For shareholders who opt for registered shares, the shares will be recorded in the Company's shareholder register. Holders of registered shares may request that their registered shares be converted into bearer shares and vice versa at any time. Any costs incurred by the conversion of registered shares into bearer securities will be borne by the shareholder. All shares for which the physical delivery in bearer form has been requested by December 31, 2007 at the latest, can remain in bearer form until January 1, 2013 at the latest, at which time they will be converted into dematerialised shares or registered shares, at the choice of the owner.

In accordance with the Belgian Act of December 14, 2005 on the abolition of bearer securities (*Wet houdende afschaffing van de effecten aan toonder / Loi portant suppression des titres au porteur*), all securities held on securities accounts for which the physical delivery in bearer form has not been requested prior to January 1, 2008, will automatically be converted in dematerialised securities as from January 1, 2008. Bearer securities that are put on a securities account after December 31, 2007 are also automatically converted in dematerialised securities as from the moment that they are put on the securities account.

All of the offered shares will be fully paid upon their delivery, and freely transferable.

#### **2.4.8. Dividends**

##### **Entitlement to dividends**

The offered shares will be entitled to a share in the profits as of January 1, 2007 and are therefore entitled to dividends, if and when declared, for the financial year closed on December 31, 2007 and the following financial years. For further information on the declaration and payment of dividends, see also section 2.12.1, "Dividends".

##### **Dividend policy**

The Company has never declared or paid any dividends on its shares. Following this offering, the Company's dividend policy will be determined and may change from time to time by determination of the Company's board of directors. Any declaration of dividends will be based upon the Company's earnings, financial condition, capital requirements and other factors considered important by the board of directors. Belgian law and the Company's articles of association do not require the Company to declare dividends. Currently, the board of directors expects to retain all earnings, if any, generated by the Company's operations for the development and growth of its business and does not anticipate paying any dividends to the shareholders in the near future.

## **2.5. LISTING AND FIRST TRADING**

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An application has been made for the admission of all shares of the Company to listing on the Eurolist by Euronext Brussels, including the shares subject to the over-allotment option granted to the lead managers, as well as the shares to be issued upon exercise of the outstanding warrants of the Company. The shares are expected to be listed under international code number ISIN BE0003864817 and symbol TIG on the Eurolist by Euronext Brussels.



The Company expects trading to commence on or about March 26, 2007, being the first banking day following the allocation date, but at the latest on the closing date of the offering when the offered shares are delivered to the investors. See also the underwriting agreement, referred to in section 2.6.

Prior to the closing date and delivery of the shares to the investors, the shares will be listed and traded on an “as-if-and-when-issued” basis. Investors that wish to enter into transactions in shares of the Company prior to the closing date of the offering, whether such transactions are effected on the Eurolist by Euronext Brussels or otherwise, should be aware that the closing date of the offering may not take place on March 29, 2007 or not at all, in the event where certain conditions or events referred to in the underwriting agreement are not satisfied or waived or do not occur on or prior to such date. Such conditions include the receipt of officers’ certificates and legal opinions and such events include the suspension of trading on the Eurolist by Euronext Brussels or a material adverse change in the Company’s financial condition or business affairs or in the financial markets. Euronext Brussels has indicated that they will annul all transactions effected on it if the shares offered hereby are not delivered on the closing date of the offering and that they cannot be held liable for any damage arising from the listing and trading on an “as-if-and-when-issued” basis as of the listing date until the envisaged closing date.

Prior to the listing of the shares, no public market existed for the offered shares.

## 2.6. UNDERWRITING AGREEMENT

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Subject to the right of the parties involved in the underwriting agreement not to sign such an agreement, the Company and the lead managers are expected to enter into an underwriting agreement no later than at the determination of the final offering price, which is expected to take place on March 23, 2007. The conclusion of this agreement may depend on various factors including, but not limited to, the market circumstances and the result of the book-building procedure.

In the underwriting agreement, the Company is expected to make certain representations and warranties and to agree to indemnify the lead managers against certain liabilities.

Subject to the terms and conditions of the underwriting agreement, the syndicate members will, severally but not jointly, agree to subscribe in their own name but for the account of the retail and institutional investors to the following percentages of the offered shares in the main offering with a view to immediately distributing these shares to the investors concerned:

- ING Belgium NV/SA      40%
- Piper Jaffray Ltd.      40%
- Petercam NV/SA      20%

The syndicate members will distribute the shares to investors, subject to prior issue, when, as and if delivered to and accepted by them, subject to the satisfaction or waiver of the conditions that are expected to be contained in the underwriting agreement, such as the receipt by the syndicate members of officer’s certificates and legal opinions.

The underwriting agreement is also expected to provide that, upon the occurrence of certain events, such as the suspension of trading on the Eurolist by Euronext Brussels or a material adverse change in the Company’s financial condition or business affairs or in the financial markets, or other *force majeure* events, the syndicate members will have, on certain conditions and after consultation with the Company, the right to withdraw from the offering before the delivery of the shares. In such event, the investors will be informed by publication in the Belgian financial press that no offered shares can be delivered and that their acceptances are cancelled.



## **2.7. OVER-ALLOTMENT AND STABILISATION**

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In connection with the offering, the lead managers may as of the listing date until 30 calendar days after the closing date (the “stabilisation period”) over-allot or effect transactions that stabilise or maintain the market price of the shares at levels above those, which might otherwise prevail in the open market. For this purpose, Piper Jaffray Ltd. will act as stabilisation agent for the lead managers. This possibility will exist whether or not the offering is fully subscribed to. Such transactions, if any, may be effected on the Eurolist by Euronext Brussels on the over-the-counter market or otherwise. There is no assurance that such stabilisation will be undertaken and, if it is, it may be discontinued at any time and will in any event be discontinued 30 calendar days after the closing date. The stabilisation will be performed in accordance with the applicable laws and regulations (including European Regulation 2273/2003).

If the lead managers create a short position in the shares in connection with the offering, they may reduce that short position by purchasing shares in the open market. Purchases of shares to stabilise the trading price or to reduce a short position may cause the price of the Company’s shares to be higher than it might be in the absence of such purchases. Neither the Company nor the lead managers makes any representation or prediction as to the direction or the magnitude of any effect that the transactions described above may have on the price of the shares.

Within a week of the end of the stabilisation period, the following information will be published on the website of the Company in accordance with article 8, §3 of the Belgian Royal Decree of March 5, 2006 regarding market abuse (*Koninklijk besluit betreffende marktmisbruik / Arrêté royal relatif aux abus de marché*): (i) whether or not stabilisation was undertaken, (ii) the date at which stabilisation started, (iii) the date at which stabilisation last occurred and (iv) the price range within which stabilisation was carried out for each of the dates during which stabilisation transactions were carried out.

The lead managers may also elect to reduce any short position by exercising all or part of the over-allotment option. This over-allotment option will be exercisable as of the listing date until 30 days after the closing date.

The over-allotment option will apply to an aggregate number of shares, at the final offering price, of up to 15% of the shares offered in the main offering.

In order to cover any over-allotment prior to the exercise of the over-allotment option, it is expected that the lead managers will enter into a stock lending agreement with one or more existing shareholders.

## **2.8. INTENTIONS OF THE SHAREHOLDERS**

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### **2.8.1. Existing shareholders**

To the extent known to the Company, the existing shareholders or members of the Company’s management, supervisory, or administrative bodies do not intend to subscribe to the offered shares in the offering.

### **2.8.2. Lock-up and standstill arrangements**

The number of shares available for sale in the public market following the admission to listing of the Company’s shares will be limited by several transfer restrictions, which are summarised hereafter.

All existing shareholders and warrant holders have entered into a lock-up agreement with the lead managers whereby they agree not to transfer any of their shares or warrants in the Company for a period

starting on the listing date and ending 12 months from the listing date. This lock-up undertaking will not apply to the lending of shares to the lead managers to cover any over-allotments.

The above lock-up will apply only to shares and warrants (including the “existing shareholders” warrants) held by the relevant existing shareholders and warrant holders on the date of completion of the offering and to shares acquired by the relevant warrant holders following the exercise of the aforementioned warrants.

The lock-up undertaking will not apply to (i) any transfer of shares or warrants to the legal successor of the holder of such shares or warrants pursuant to the merger, liquidation or de-merger of such holder, provided that the legal successor agrees to similar lock-up obligations in favour of the lead managers, (ii) any transfer of such shares or warrants that has been approved by the lead managers.

For a period of 12 months after the listing date, the Company shall not issue, without the prior authorisation of the lead managers, any new shares or other securities, including options, warrants convertible securities or other rights to subscribe to any new shares or other securities, or otherwise transfer or dispose of or enter into any swap or any other transaction (including any derivative transaction) or commitment with like effect, of whatever kind, which directly or indirectly leads to a total or partial issue of new shares or securities irrespective whether these are or are not listed on a stock exchange or a regulated market.

The above standstill commitment shall not apply to (i) the issuance of warrants of the Company and the grant thereof to employees, consultants and directors of the Company or its subsidiaries, and other persons who in the scope of their professional activity made themselves useful to the Company or its subsidiaries, in the framework of a stock option plan set up as an incentive for the future growth and development of the Company or its subsidiaries, provided that the total amount of outstanding warrants, including the warrants existing and outstanding at the date hereof, shall not, at any given time during the standstill period, exceed 15% of the total amount of all outstanding securities (on a fully diluted basis) of the Company, and (ii) the issuance of new shares or other securities by the Company with a view to fund the acquisition, whether by means of the transfer of shares and/or assets (and liabilities), a merger, consolidation, contribution, or other business combination, of a company, a business or technology in the field of biotechnology and/or which subject matter is similar, closely related or complementary with the activities of the Company at such point in time.

The restrictions and lock-up undertaking referred to in the previous paragraph will not apply to the issue of new shares pursuant to the exercise of the warrant issued to the lead managers to cover over-allotments.

### **2.8.3. Shareholders’ intentions at and after the offering**

To the best knowledge of the Company, all existing shareholders’ agreements, other than the abovementioned lock-up and standstill arrangements, shall terminate with effect on the listing date. The Company is not aware that new shareholders’ agreements have been entered into or that any of the existing shareholders or members of its management, supervisory or administrative bodies have the intention to subscribe for the offered shares.

## **2.9. COSTS AND REMUNERATION OF INTERMEDIARIES**

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The costs of the offering borne in the current financial year (including the discretionary fee referred to below) are estimated to be approximately 7.8% of the amount of the offering. These costs include legal, audit, consulting and administrative costs, costs of legal publications and the printing of the prospectus and other costs (€800,000) the remuneration of the CBFA (€15,690.00), initial fees payable to Euronext

Brussels (€25,000) as well as the management, underwriting and selling fees for the lead managers (estimated at €1.8 million or €2.1 million depending on whether or not the over-allotment option is exercised, not including a discretionary fee of up to 1.50% of the total amount raised by the Company in the offering). The latter are to a certain extent divided among all financial intermediaries who register subscriptions and applications in relation to the offering described in this prospectus.

## **2.10. FINANCIAL SERVICE**

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The financial service for the shares of the Company is provided in Belgium by ING Belgium NV/SA free of charge for the shareholders. Should the Company alter its policy in this matter, this will be announced in the Belgian financial press.

## **2.11. LEGISLATION AND COMPETENT COURTS**

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The offering is subject to Belgian law. The courts and tribunals of Brussels have sole jurisdiction should any dispute arise in relation to the offering.

## **2.12. BELGIAN TAXATION**

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The following is a summary of certain Belgian tax consequences of the acquisition, ownership and disposal of shares in the Company. It is based on the tax laws and administrative interpretations applicable in Belgium as presently in effect and is subject to changes in Belgian law, including changes that could have a retroactive effect. The following summary does not take into account or discuss the tax laws of any country other than Belgium, nor does it take into account the individual circumstances of each investor. Prospective investors should consult their own advisers as to the Belgian and foreign tax consequences of the acquisition, ownership and disposal of the shares.

For the purpose of this summary, a Belgian resident is an individual subject to Belgian personal income tax (*i.e.*, an individual who has his domicile in Belgium or has the seat of his wealth in Belgium, or a person assimilated to a Belgian resident), a company subject to Belgian corporate income tax (*i.e.*, a company that has its registered office, its main establishment, its administrative seat or its seat of management in Belgium) or a legal entity subject to the Belgian tax on legal entities (*i.e.*, a legal entity other than a corporation subject to the corporate income tax, that has its registered office, its main establishment, its administrative seat or its seat of management in Belgium). A Belgian non-resident is a person that is not a Belgian resident.

### **2.12.1. Dividends**

For Belgian income tax purposes, the gross amount of all distributions made by the Company to its shareholders is generally taxed as a dividend, except for the repayment of paid-up capital carried out in accordance with the Belgian Company Code to the extent that the capital qualifies as “fiscal” capital. The gross amount paid by the Company to redeem its shares and the gross amount of distributions made by the Company to its shareholders as a result of the Company’s complete or partial liquidation is also generally taxed as a dividend, insofar as the payment exceeds the fully paid-up fiscal capital of the Company. In general, a 10% Belgian withholding tax is levied on such redemption and liquidation distributions. For redemptions, the basis on which the 10% tax will be levied and the circumstances of the

levy will depend on the final destination of the shares thus redeemed (e.g. cancellation, sale,...). No withholding tax will be due for redemptions carried out on the central market of Euronext or any other similar stock exchange market.

In general, a Belgian withholding tax of 25% is levied on dividends. Under certain circumstances, the 25% withholding tax rate is reduced to 15%. Belgian domestic tax law, however, provides for an exemption from Belgian withholding tax in certain cases.

European Union resident companies that qualify under the EU Parent-Subsidiary Directive of 23 July 1990 (90/435/EEC) are exempt from withholding tax if they own at least a 15% interest in the capital of the Company for an uninterrupted period of at least one year (or, alternatively, if they undertake to hold such interest for at least one year and certain other conditions are satisfied).

Moreover, no withholding tax will be due on dividend payments by the Company provided that the (i) the beneficiary is a company limited by shares located in a country having a double tax treaty with Belgium and is subject to the common system of corporate tax in its country of residence, (ii) the beneficiary holds at least 15% of the share capital of the Belgian company, (iii) the shares are held (or will be held) during an uninterrupted period of 1 year, and (iv) the double tax treaty concerned contains an exchange of information clause.

Belgium has concluded tax treaties with more than 80 countries, reducing the dividend withholding tax rate to 15%, 10% or 5% for resident of those countries, depending on conditions, among others, related to the size of the shareholding and certain identification formalities.

The existing shares of the Company and the shares that will be issued by the Company upon the exercise of previously issued warrants will not benefit from the 15% withholding tax. The offered shares will not benefit from the 15% withholding tax since the Company has decided not to issue VVPR shares. The new shares that will be issued upon exercise by the lead managers of the over-allotment option or upon exercise of the new “personnel” and “existing shareholders” warrants will also not benefit from the 15% withholding tax.

If the dividend is paid through a Belgian financial institution, such institution must withhold the above-mentioned tax, if applicable.

For private investors who are Belgian residents and for legal entities subject to the Belgian tax on legal entities, the Belgian withholding tax generally constitutes the final tax on their dividend income. The tax base is the amount of the dividend paid. If a private investor elects to report the dividend income in his tax return, he will then be taxed at the separate rate of 25% or, if applicable, at the reduced rate of 15%, to be increased with the municipal surcharge or at the applicable progressive personal income tax taking into account the taxpayer's other declared income, whichever is lower. If progressive income tax rates apply, the payable income tax is also increased by the municipal surcharge. The reporting of a dividend income that has been subject to Belgian withholding tax is generally only more favourable in case the overall income of the taxpayer does not exceed the applicable tax-free minimum for that income year.

For Belgian resident companies and for companies with their tax residence outside Belgium holding the shares of the Company through a permanent establishment in Belgium, the gross dividend income, including the withholding tax, must be added to their taxable income, which is taxed at the income tax rate of 33.99%. Under certain circumstances lower tax rates may apply. If such a company holds, at the time of the dividend distribution, a shareholding of at least 10% in the capital of the Company or a share participation with an acquisition value of at least €1,200,000, then 95% of the gross dividend received may be deducted from the taxable amount (“dividend received deduction”), provided that the shareholding in the Company qualifies as a “fixed financial asset” according to Belgian GAAP, the shareholding has or will be held during an uninterrupted period of at least one year and that the shares are held in full legal ownership.

The minimum participation requirement does not apply to dividends received by Belgian credit institutions, insurance companies and stock exchange companies. Additionally, the minimum participation, legal ownership, accounting qualification and minimum holding period requirements do not apply to dividends received by Belgian qualifying collective investment companies.

Belgian resident companies and companies with their tax residence outside Belgium holding the shares of the Company through a permanent establishment in Belgium are, under certain conditions, entitled to credit the Belgian withholding tax on dividends against their corporate income tax liability and to claim the reimbursement of the Belgian withholding tax that exceeds this liability.

A non-resident shareholder, who does not hold the shares of the Company through a permanent establishment in Belgium, will not be subject to any Belgian income tax other than the withholding tax on dividends, which normally constitutes the final Belgian income tax. Belgian tax law provides for certain exemptions from withholding tax on Belgian source dividends distributed to non-resident investors. In the event there is no exemption applicable under Belgian domestic tax law, the Belgian dividend withholding tax can potentially be reduced for investors who are non-residents pursuant to the treaty for the avoidance of double taxation concluded between the State of Belgium and the State of residence of the non-resident shareholder of the Company, if any.

#### **2.12.2. Capital gains and losses**

Private investors who are Belgian residents are in principle not subject to Belgian income tax on capital gains realised upon the disposal of the shares, unless the capital gain is the result of speculation or cannot be characterised as resulting from the normal management of a private estate. In such an event, the capital gain is taxable at 33%, to be increased with communal surcharges.

The capital gains realised upon the sale of shares belonging, during the five years before the transfer of the shares, to an important shareholding of 25% or more (taking into account the shares held by certain relatives) are taxable at 16.5%, to be increased with communal surcharges, in case the shares are sold to a non-EU corporation.

Legal entities subject to the Belgian tax on legal entities are in principle not subject to Belgian income tax on capital gains realised upon the disposal of the shares.

Belgian resident companies and companies with a tax residence outside Belgium holding shares through a permanent establishment in Belgium are generally not subject to Belgian income tax on capital gains realised upon the disposal of the shares.

Conversely, capital losses realised upon the disposal of the shares are generally not tax deductible under Belgian tax law.

A non-resident shareholder who does not hold the shares through a permanent establishment in Belgium will generally not be subject to Belgian income tax on capital gains realised upon the disposal of the shares.

#### **2.12.3. Tax on stock exchange transactions**

The purchase and the sale and any other acquisition or transfer for consideration in Belgium, through a “professional intermediary”, of existing shares (secondary market) is subject to the tax on stock exchange transactions, generally in the amount of 0.17% of the purchase price, capped at €500 per transaction and

per party. Upon the issuance of new shares (primary market), no tax on stock exchange transactions is due.

In any event, no tax on stock exchange transactions is payable by (i) professional intermediaries described in Articles 2, 9° and 10° of the Belgian Act of 2 August 2002 on the supervision of the financial sector and financial services (*Wet betreffende het toezicht op de financiële sector en de financiële diensten / Loi relative à la surveillance du secteur financier et aux services financiers*), acting for their own account; (ii) insurance companies described in Article 2, §1 of the the Belgian Act of July 9, 1975 on the supervision of insurance companies (*Wet betreffende de controle der verzekeringsondernemingen / Loi relative au contrôle des entreprises d'assurances*) acting for their own account, (iii) pension funds described in Article 2, 1° of the Act of 27 October 2006 (*Wet betreffende het toezicht op de instellingen voor bedrijfspensioenvoorzieningen / Loi relative au contrôle des institutions de retraite professionnelle*) on the supervision of pension funds acting for their own account; (iv) collective investment institutions acting for their own account or (v) non-residents acting for their own account. The existing (borrowed) shares that are used for purposes of over-allocation, if any, will be allocated on a priority basis to investors that are exempt from the tax on stock exchange transactions.

#### **2.12.4. Tax on the physical delivery of bearer securities**

The physical delivery of bearer shares acquired on the secondary market for consideration through a “professional intermediary” in Belgium is generally subject to the Belgian tax on the physical delivery of bearer securities. The tax payable is equal to 0.6% of the purchase price. The tax is also due upon the physical delivery of shares in Belgium pursuant to the withdrawal of the shares from “open custody” or as a result of the conversion of registered shares into bearer shares.

In accordance with the Belgian Act of December 14, 2005 on the abolition of bearer shares (*Wet houdende afschaffing van de effecten aan toonder / Loi portant suppression des titres au porteur*), all bearer shares held on securities accounts for which the physical delivery in bearer form has not been requested prior to January 1, 2008, will automatically be converted in dematerialised shares as from January 1, 2008. Bearer shares that are put on a securities account after December 31, 2007 are also automatically converted in dematerialised shares as from the moment that they are put on the securities account.

No tax on the physical delivery of bearer securities is due upon the issuance of new shares.



### 3. GENERAL INFORMATION ABOUT THE COMPANY AND ITS SHARE CAPITAL

#### 3.1. GENERAL

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TiGenix was incorporated on February 21, 2000 for an unlimited duration. The Company has the legal form of a limited liability company (*naamloze vennootschap - NV / société anonyme - SA*) organised and existing under the laws of Belgium. Pursuant to the Belgian Company Code, the liability of the shareholders is limited to the amount of their respective committed contribution to the capital of the Company. The Company's registered office is located at Technologielaan 3, 3001 Leuven (Heverlee), Belgium. The Company is registered with the register of legal entities (*rechtspersonenregister – RPR / registre des personnes morales - RPM*) (Leuven) under company number 0471.340.123. The Company can be reached by phone at the number +32 (0)16 39 60 60.

This chapter 3 summarises the corporate purpose, share capital and corporate structure of the Company and the material rights of its shareholders under Belgian law and the Company's articles of association. It is based on the Company's articles of association that have been amended by the extraordinary shareholders' meeting of February 26, 2007 and that will become effective upon completion of the offering and listing of the Company's shares.

At its meeting of February 26, 2007, the extraordinary shareholders' meeting of the Company passed amongst other things the following resolutions:

- the decision to cancel the existing classes of shares and to convert all shares into common shares, the decision to amend the terms and conditions of the existing "personnel" warrants of the Company to take into account the cancellation of the classes of shares;
- the decision to increase the Company's share capital within the framework of the proposed offering and listing, to issue "existing shareholders" warrants to certain existing shareholders subject to certain conditions, to create new "personnel" warrants, and to create the over-allotment option (see also section 2.1 of chapter 2);
- the confirmation that the existing shares and the shares to be issued upon exercise of outstanding "personnel" warrants do not have any VVPR right;
- the decision to equalise the par value of all shares;
- the decision to amend and restate the articles of association in view of the capital increase and the proposed listing of the Company, including, amongst other things, the decision to grant the board of directors the authority to increase the Company's share capital within the framework of the authorised capital.

The aforementioned resolutions of the extraordinary shareholders' meeting of February 26, 2007, including the cancellation of the existing classes of shares and related amendments of the terms and conditions of the warrants, and the amendment and restatement of the Company's articles of association, are subject to the completion of the offering and listing of the Company's shares on the Eurolist by Euronext Brussels.

The description hereafter is only a summary and does not purport to give a complete overview of the articles of association, nor of all relevant provisions of Belgian law. Neither should it be considered as legal advice regarding these matters. The description below assumes that the changes to the Company's articles of association, which were approved on February 26, 2007 subject to the condition precedent of the closing of the offering and the listing of the shares on the Eurolist by Euronext Brussels, have become effective.



## 3.2. CORPORATE PURPOSE

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The corporate purpose of the Company is set forth in article 3 of its articles of association and reads as follows:

*“The company has as its corporate purpose engaging in activities in the field of research and development regarding biological compounds and biomaterials for its own account and for the account of third parties, as well as the industrialisation and commercialisation of the results hereof.*

*It may engage in all possible commercial, industrial, movable and immovable, transactions, which are, directly or indirectly related to its corporate purpose or which are likely to enhance it. It may, amongst others, cooperate with, participate in, in any way whatsoever, directly or indirectly, take a stake in each enterprise the corporate purpose of which is similar, analogous or related to its own purpose.*

*It may mortgage its real estate and may pledge all its other assets, including its entire business, and it may guarantee a bill for all loans, credits and other undertakings, on its own behalf as well as on behalf of third parties, provided that the company itself has an interest thereto.”*

## 3.3. GROUP STRUCTURE

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TiGenix' main business is conducted through the Company itself. Because its core commercial markets are based in the United States and in Europe, TiGenix has a presence in both locations today. On February 7, 2006 the Company incorporated a wholly-owned U.S. subsidiary, TiGenix Inc. The Company is currently looking to recruit personnel to start the active operations (regulatory and sales & marketing) at the subsidiary.

The physical presence at the heart of the two largest markets allows TiGenix (i) to increase its visibility and (ii) to prepare the commercialisation of ChondroCelect into these markets.

## 3.4. SHARE CAPITAL AND SHARES

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### 3.4.1. Share capital and shares

On the date of this prospectus, the Company's registered capital amounts to €14,115,529.94, represented by 14,157,014 registered common shares without nominal value. The capital is fully paid up.

The table below provides an overview of the history of the Company's share capital since its incorporation in 2000. The overview should be read together with the notes set out below the table.

Date	Transaction	Number and class of shares issued	Issue price per share (€) (incl. issuance premium)	Capital increase (€)	Share capital after transaction	Aggregate number of shares after capital increase
INCORPORATION						
February 21, 2000	Incorporation <sup>(1)</sup>	85,800 Class A 50,000 Class B 14,200 Class C	€1.00	€150,000.00	€150,000.00	150,000
PHASE I CAPITAL ROUND						
March 13, 2000	Capital increase in cash <sup>(2)</sup>	364,200 Class A 60,800 Class C	€1.00	€425,000.00	€575,000.00	575,000
March 22, 2001	Capital increase in cash <sup>(3)</sup>	150,000 Class A 40,000 Class B 100,000 Class C 30,000 Class D	€1.25	€320,000.00	€895,000.00	895,000
PHASE II CAPITAL ROUND - EXERCISE OF WARRANTS						
September 15, 2003	Capital increase in cash <sup>(4)</sup>	4,049,383 Class E	€1.00	€4,049,383.00	€4,944,383.00	4,944,383
September 15, 2003	Capital increase in kind <sup>(5)</sup>	290,896 Class A 394,106 Class C	€1.55	€685,002.00	€5,629,385.00	5,629,385
September 15, 2003	Conversion of 200,000 profit certificates (incorporation of issuance premiums) <sup>(6)</sup>	175,000 Class B 25,000 Class C	€1.00	€200,000.00	€5,829,385.00	5,829,385
September 30, 2003	Capital increase in cash <sup>(7)</sup>	1,518,519 Class E	€1.00	€1,518,519.00	€7,347,904.00	7,347,904
May 14, 2004	Capital increase in cash <sup>(8)</sup>	1,358,024 Class E	€3.00	€1,358,024.00	€8,705,928.00	8,705,928
April 20, 2005	Capital increase in cash <sup>(9)</sup>	452,680 Class E	€3.00	€452,680.00	€9,158,608.00	9,158,608
August 23, 2005	Capital increase in cash pursuant to the exercise of 3 "adjustment" warrants <sup>(10)</sup>	11,762 Class A 15,935 Class C	exercise price of €0.01 per warrant	€0.03	€9,158,608.03	9,186,305

Date	Transaction	Number and class of shares issued	Issue price per share (€) (incl. issuance premium)	Capital increase (€)	Share capital after transaction	Aggregate number of shares after capital increase
November 3, 2005	Capital increase in cash pursuant to the exercise of 22,500 "personnel" warrants <sup>(11)</sup>	22,500 Class D	exercise price of €1.25 per warrant	€22,432.50	€9,181,040.53	9,208,805
PHASE III CAPITAL ROUND - EXERCISE OF WARRANTS						
November 3, 2005	Capital increase in cash <sup>(12)</sup>	114,285 Class A 57,142 Class C 4,374,282 Class E	€3.50	€4,532,071.91	€13,713,112.44	13,754,514
April 20, 2006	Capital increase in cash pursuant to the exercise of 27,500 "personnel" warrants <sup>(13)</sup>	27,500 Class D	exercise price of €1.25 per warrant	€27,417.50	€13,740,529.94	13,782,014
October 31, 2006	Capital increase in cash pursuant to the exercise of 375,000 warrants <sup>(14)</sup>	375,000 Class B	exercise price of €1.00 per warrant	€375,000.00	€14,115,529.94	14,157,014

#### Notes

- (1) The shares were subscribed to by Gemma Frisius-Fonds K.U.Leuven NV (85,800 A), Katholieke Universiteit Leuven (14,200 C), Axxis V&C BVBA (25,000 B) and Prof. Dr. Frank Luyten (25,000 B). At the time of incorporation, also 200,000 profit certificates were issued to Katholieke Universiteit Leuven (25,000 C), Axxis V&C BVBA (87,500 B) and Prof. Dr. Frank Luyten (87,500 B). These profit certificates were converted into 200,000 shares on September 15, 2003.
- (2) The shares were subscribed to by Gemma Frisius-Fonds K.U.Leuven NV (364,200 A) and Katholieke Universiteit Leuven (60,800 C).
- (3) The shares were subscribed to by Gemma Frisius-Fonds K.U.Leuven NV (150,000 A), Axxis V&C BVBA (20,000 B) and Prof. Dr. Frank Luyten (20,000 B), Katholieke Universiteit Leuven (more precisely, its division Universitaire Ziekenhuizen Leuven) (100,000 C), Johan Bellemans (20,000 D) and Etienne Schacht (10,000 D).
- (4) The shares were subscribed to by ING Belgium NV/SA (1,771,605 E), Capricorn Venture Fund II NV (1,012,346 E) and Fagus NV (1,265,432 E).
- (5) The shares were subscribed to by Gemma Frisius-Fonds K.U.Leuven NV (290,896 A), Katholieke Universiteit Leuven (64,506 C) and Universiteit Gent (329,600 C).
- (6) The profit certificates were issued on February 21, 2000 and were converted on September 15, 2003 by Katholieke Universiteit Leuven (25,000 C), Axxis V&C BVBA (87,500 B) and Prof. Dr. Frank Luyten (87,500 B).
- (7) The shares were subscribed to by Auriga Ventures II FCPR (1,518,519 E).
- (8) The shares were subscribed to by ING Belgium NV/SA (432,099 E), Capricorn Venture Fund II NV (246,913 E), Fagus NV (308,642 E) and Auriga Ventures II FCPR (370,370 E).
- (9) The shares were subscribed to by ING Belgium NV/SA (144,034 E), Capricorn Venture Fund II NV (82,306 E), Fagus NV (102,882 E) and Auriga Ventures II FCPR (123,458 E).
- (10) The "adjustment" warrants were issued on September 15, 2003 to and exercised in 2005 by Gemma Frisius-Fonds K.U.Leuven NV (11,762 A), Katholieke Universiteit Leuven (2,608 C) and Universiteit Gent (13,327 C). The "adjustment" warrants were used as an instrument to adjust the subscription price paid by the warrant holders for new shares issued in September 2003 compared to the average subscription price paid by other investors who also committed in September 2003 to contribute a fixed amount but in three instalments at variable subscription prices.
- (11) The "personnel" warrants were issued on March 22, 2001 and exercised in 2005 by Karel Fol (12,500 D) and Koen Huygens (10,000 D). Subsequently, 9,000 of these shares were sold by Karel Fol (5,000 D) and Koen Huygens (4,000 D) to Gemma Frisius-Fonds K.U.Leuven NV and were re-allocated to Class A.

- (12) The shares were subscribed to by Gemma Frisius-Fonds K.U.Leuven NV (114,285 A), Katholieke Universiteit Leuven (28,571 C), Universiteit Gent (28,571 C), ING Belgium NV/SA (2,714,285 E), Capricorn Venture Fund II NV (231,428 E), Fagus NV (428,571 E), Auriga Ventures II FCPR (428,571 E, ), Fortis Private Equity Venture Belgium NV (428,571 E), Baekeland Fonds II NV (114,285 E) and HSS Ventures Inc. (28,571 E). Subsequently, ING Belgium NV/SA sold a number of its new shares to ITX Corporation (200,000 E), Partners@Venture NV (285,714 E), Ferdinand Verdonck and Margriet Van Houtte (28,572 E), Kris Vansanten (36,000 E), Werner Vanlembegen (36,000 E), BGL Investment Partners SA (142,857 E) and Technowal SA (71,428 E).
- (13) The “personnel” warrants were issued on March 22, 2001 and exercised in 2006 by Nancy Veulemans (3,750 D), Jenny Peeters (1,250 D), Johan Vanlauwe (2,500 D) and Etienne Schacht (20,000 D).
- (14) The warrants were issued on March 13, 2000 and exercised in 2006 by Axxis V&C BVBA (187,500 B) and Prof. Dr. Frank Luyten (187,500 B).

The issue price of €3.50 per share at the occasion of the capital increase of November 3, 2005 was the result of at arm’s length negotiations with existing shareholders and, at that time, third parties between August and October 2005, resulting in a final agreement in October 2005. Elements that, in the opinion of TiGenix, could be considered to have changed since then include, amongst others (i) the fact that the clinical trial results are available and demonstrate that the primary endpoints of the study have been achieved as described in section 5.6 of chapter 5 and (ii) the entering into by the Company of a strategic partnership with Fidia Advanced Biopolymers (“FAB”) to be in a position to develop the next generation product as described in section 5.6.1.3 of chapter 5.

On February 26, 2007, the Company’s extraordinary shareholders’ meeting also decided to authorise the capital increase required for the purpose of the present offering, to create the over-allotment option, the “existing shareholders” warrants and the new “personnel” warrants. See also section 2.1 “*Information related to the capital increase*” of chapter 2 and section 3.5 “*Warrants*” of chapter 3.

Upon completion of the offering and listing, all existing shareholders’ agreements will terminate automatically, other than the specific lock-up and standstill arrangements described in section 2.8.2 of chapter 2, and all existing shares will be converted into common shares with the same rights and benefits and the same fractional value as the offered shares.

### 3.4.2. Description of rights and benefits attached to shares

#### Voting rights

Each shareholder of the Company is entitled to one vote per share.

Voting rights can be suspended in relation to shares:

- which were not fully paid up, notwithstanding the request thereto of the board of directors of the Company;
- to which more than one person is entitled, except in the event a single representative is appointed for the exercise of the voting right;
- which entitle their holder to voting rights above the threshold of 3%, 5%, or any multiple of 5% of the total number of voting rights attached to the outstanding financial instruments of the Company on the date of the relevant general shareholders’ meeting, except in the event where the relevant shareholder has notified the Company and the CBFA at least 20 days prior to the date of the general shareholders’ meeting on which he or she wishes to vote (see also below under section 3.8) of its shareholding reaching or exceeding the thresholds above; and
- of which the voting right was suspended by a competent court or the CBFA.

Generally, the shareholders’ meeting has sole authority with respect to:

- the approval of the annual accounts of the Company;
- the appointment and resignation of directors and the statutory auditor of the Company;

- the granting of discharge of liability to the directors and the statutory auditor;
- the determination of the remuneration of the directors and of the statutory auditor for the exercise of their mandate;
- the distribution of profits;
- the filing of a claim for liability against directors;
- the decisions relating to the dissolution, merger and certain other re-organisations of the Company; and
- the approval of amendments to the articles of association.

## **Right to attend and vote at shareholders' meetings**

### **Annual shareholders' meeting**

The annual shareholders' meeting is held at the registered office of the Company or at the place determined in the notice convening the shareholders' meeting. The meeting is held every year on April 20 at 10 a.m. If this date is a Saturday, Sunday or a legal holiday, the meeting is held at the next business day. In 2007, however, the annual shareholders' meeting has been held on February 26, 2007. At the annual shareholders' meeting, the board of directors submits the audited statutory and consolidated financial statements and the reports of the board of directors and of the statutory auditor with respect thereto to the shareholders. The shareholders' meeting then decides on the approval of the statutory financial statements, the proposed allocation of the Company's profit or loss, the discharge from liability of the directors and the statutory auditor, and, when applicable, the (re-)appointment or resignation of the statutory auditor and/or of all or certain directors.

### **Special and extraordinary shareholders' meetings**

The board of directors or the statutory auditor can, at any given time when the interest of the Company so requires, convene a special or extraordinary shareholders' meeting. Such shareholders' meeting must also be convened every time one or more shareholders holding at least 20% of the Company's share capital so demand. Shareholders that do not hold at least 20% of the Company's share capital do not have the right to have the shareholders' meeting convened.

### **Notices convening the shareholders' meeting**

The notice of the shareholders' meeting must state the place, date and hour of the meeting and shall include an agenda indicating the items to be discussed as well as any motions for resolutions.

The notice must be published in the Belgian Official Gazette (*Belgisch Staatsblad / Moniteur belge*) at least 24 days prior to the shareholders' meeting or the registration date (if specified in the convening notices). The notice must also be published in a national newspaper 24 days prior to the date of the shareholders' meeting or the registration date (if specified in the convening notices), except if the meeting concerned is an annual shareholders' meeting held at the municipality, place, day and hour mentioned in the articles of association of the Company and whose agenda is limited to the examination of the annual accounts, the annual report of the board of directors, the annual report of the statutory auditor and the vote on the discharge of the directors and the statutory auditor. The annual accounts, the annual report of the board of directors and the annual report of the statutory auditor must be made available to the public at least 15 days prior to the date of the annual shareholders' meeting.

Convening notices must be sent 15 days prior to the shareholders' meeting to the holders of registered shares, holders of registered bonds, holders of registered warrants, holders of registered certificates issued with the cooperation of the Company and to the directors and statutory auditor of the Company. This communication is made by ordinary letter unless the addressees have individually and expressly accepted in writing to receive the notice by another form of communication, without having to give evidence of the fulfilment of such formality.

When all the shares, bonds, warrants and certificates issued with the co-operation of the Company are registered, the communication may be limited to the sending of the notices by registered letter unless the addressees have individually and expressly accepted in writing to receive the notice by another form of communication.

### **Formalities to attend the shareholders' meeting**

All holders of shares, warrants, bonds (if any) issued by the Company and all holders of certificates issued with the co-operation of the Company (if any) can attend shareholders' meetings. Only shareholders, however, can vote at shareholders' meetings.

In order to attend the shareholders' meeting, holders of bearer instruments in book-entry form must deposit a certificate issued by a recognised account holder with the clearing agency for the financial instruments concerned or the clearing agency itself, confirming the number of financial instruments that have been registered in the name of the holder concerned and stating that these financial instruments are blocked until after the date of the general meeting. The certificate must be deposited at the Company's registered office or any other place indicated in the notice convening the shareholders' meeting at the latest three business days prior to the meeting. Holders of bearer instruments in physical form must deposit their financial instruments at the Company's registered office or any other place indicated in the notice convening the shareholders' meeting within the same term. Holders of registered instruments must be registered in the relevant register book and, where applicable, can be requested to inform the board of directors at the latest three business days prior to the shareholders' meeting whether and with how many shares they will attend the shareholders' meeting.

### **Registration date**

The articles of association also allow the board of directors to specify a registration date in the notice convening the shareholders' meeting. If the board of directors decides to set a registration date in the notice, only shareholders who have shares at 24:00 hours (Central European Time, GMT+1) on the registration date may participate and vote with such shares at the shareholders' meeting, regardless of the number of shares that they hold on the actual date of the shareholders' meeting. The specified registration date can be no earlier than 15 calendar days, and no later than five business days, before the date of the shareholders' meeting.

### **Power of attorney**

Each shareholder has the right to attend a shareholders' meeting and to vote at the shareholders' meeting in person or through a proxy holder. The proxy holder does not need to be a shareholder. The board of directors can request the participants to the meeting to use a model of power of attorney (with voting instructions), which must be deposited at the Company's registered office at least three business days prior to the meeting.



## Quorum and majorities

In general, there is no quorum requirement for a shareholders' meeting and decisions are generally passed with a simple majority of the votes of the shares present and represented. Capital increases not decided by the board of directors within the framework of the authorised capital, decisions with respect to the Company's dissolution, mergers, de-mergers and certain other reorganisations of the Company, amendments to the articles of association (other than an amendment of the corporate purpose), and certain other matters referred to in the Belgian Company Code do not only require the presence or representation of at least 50% of the share capital of the Company but also the approval of at least 75% of the votes cast. An amendment of the Company's corporate purpose, requires the approval of at least 80% of the votes cast at a shareholders' meeting, which in principle can only validly pass such resolution if at least 50% of the share capital of the Company and at least 50% of the profit certificates, if any, are present or represented. In the event where the required quorum is not present or represented at the first meeting, a second meeting needs to be convened through a new notice. The second shareholders' meeting can validly deliberate and decide regardless of the number of shares present or represented.

## Dividends

All shares participate in the same manner in the Company's profits (if any). The offered shares carry the right to receive dividends (if any) payable with respect to the entire financial year started on January 1, 2007 and each subsequent year. Pursuant to the Belgian Company Code, the shareholders can in principle decide on the distribution of profits with a simple majority vote at the occasion of the annual general shareholders' meeting, based on the most recent audited annual accounts, prepared in accordance with the generally accepted accounting principles in Belgium and based on a (non-binding) proposal of the Company's board of directors. The Company's articles of association also authorise the board of directors to declare interim dividends subject to the terms and conditions of the Belgian Company Code.

Dividends can only be distributed if following the declaration and issuance of the dividends the amount of the Company's net assets on the date of the closing of the last financial year as follows from the annual accounts (*i.e.*, the amount of the assets as shown in the balance sheet, decreased with provisions and liabilities, all as prepared in accordance with Belgian accounting rules), decreased with the non-amortised costs of incorporation and extension and the non-amortised costs for research and development, does not fall below the amount of the paid-up capital (or, if higher, the called capital), increased with the amount of non-distributable reserves. In addition, prior to distributing dividends, 5% of the net profits must be allotted to a legal reserve, until the legal reserve amounts to 10% of the share capital.

In relation to bearer shares, the Belgian Act of July 24, 1921, provides that, in the event the payment of dividends on bearer shares has not been claimed by the legal holder thereof, the Company has the right to deposit those dividends with the *Deposito en Consignatiekas / Caisse de Dépôts et Consignations*. The right to demand the distribution of dividends so deposited expires after thirty years, at which time the related dividends become the property of the Belgian State. With regard to registered shares, the right to payment of dividends expires five years after the board of directors declared the dividend payable.

## Rights regarding liquidation

The Company can only be dissolved by a shareholders' resolution passed with a majority of at least 75% of the votes cast at an extraordinary general shareholders' meeting where at least 50% of the share capital is present or represented.



If as a result of losses incurred the ratio of the Company's statutory net-assets (determined in accordance with Belgian legal and accounting rules) to share capital is less than 50%, the board of directors must convene a special shareholders' meeting within two months as of the date the board of directors discovered or should have discovered this undercapitalisation. At this shareholders' meeting the board of directors needs to propose either the dissolution of the Company or the continuation of the Company, in which case the board of directors must propose measures to redress the Company's financial situation. Shareholders representing at least 75% of the votes validly cast at this meeting have the right to dissolve the Company, provided that at least 50% of the Company's share capital is present or represented at the meeting. If as a result of losses incurred the ratio of the Company's net assets to share capital is less than 25%, the same procedure must be followed, it being understood, however, that in that event shareholders representing 25% of the votes cast at the meeting can decide to dissolve the Company. If the amount of the Company's net assets has dropped below €61,500 (the minimum amount of share capital of a public limited liability company), each interested party is entitled to request the competent court to dissolve the Company. The court can order the dissolution of the Company or grant a grace period within which the Company is to remedy the situation.

In the event the Company is dissolved, the assets or the proceeds of the sale of the remaining assets, after payment of all debts, costs of liquidation and taxes, must be distributed on an equal basis to the shareholders, taking into account possible preferential rights with regard to the liquidation of shares having such rights, if any. Upon completion of the offering and listing, none of the shares will have any preferred liquidation rights.

## **Changes to the share capital**

### **Changes to the share capital decided by the shareholders**

The shareholders' meeting can at any given time decide to increase or decrease the share capital of the Company. Such resolution must satisfy the quorum and majority requirements that apply to an amendment of the articles of association, as described above under section 3.4.2.

### **Capital increases by the board of directors**

Subject to the same quorum and majority requirements, the shareholders' meeting can authorise the board of directors, within certain limits, to increase the Company's share capital without any further approval of the shareholders. This is the so-called authorised capital. This authorisation needs to be limited in time (*i.e.*, it can only be granted for a renewable period of maximum five years), and in scope (*i.e.*, the authorised capital may not exceed the amount of the registered capital at the time of the authorisation). On February 26, 2007, the shareholders' meeting authorised the board of directors to increase the share capital of the Company within the framework of the authorised capital. These authorisation and powers are further discussed in section 3.4.5 below.

### **Preferential subscription right**

In the event of a capital increase in cash with issue of new shares, or in the event of an issue of convertible bonds or warrants, the shareholders have a preferential right to subscribe to the new shares, convertible bonds or warrants, pro rata of the part of the share capital represented by the shares that they already have. The shareholders' meeting can decide to limit or cancel this preferential subscription right, subject to special reporting requirements. Such decision needs to satisfy the same quorum and majority requirements as the decision to increase the Company's share capital.

The shareholders can also decide to authorise the board of directors to limit or cancel the preferential subscription right within the framework of the authorised capital, subject to the terms and conditions set forth in the Belgian Company Code. See also under section 3.4.5 below.

Normally, the authorisation of the board of directors to increase the share capital of the Company through contributions in cash with cancellation or limitation of the preferential right of the existing shareholders is suspended as of the notification to the Company by the CBFA of a public takeover bid on the financial instruments of the Company. The shareholders' meeting can, however, authorise the board of directors to increase the share capital by issuing shares in an amount of not more than 10% of the existing shares of the Company at the time of such a public takeover bid. Such authorisation has not been granted to the board of directors of the Company.

### **3.4.3. Form and transferability of the shares**

The shares of the Company can take the form of bearer shares, registered shares or dematerialised shares. The shares being offered will take the form of bearer shares.

Until their physical delivery, bearer shares will be represented by one or more global certificates and only book-entry settlement will be possible.

Belgian Company law and the Company's articles of association entitle shareholders to request, upon written request and at their expense, the physical delivery of their bearer shares. Such request would imply that an individualised physical bearer certificate be delivered to the shareholder concerned. A special tax on the physical delivery of bearer shares would be imposed. See also section 2.12.4 in chapter 2. As soon as legally authorised and possible in practice, the shares may be converted into dematerialised shares in accordance with the relevant provisions in the Company's articles of association.

In accordance with the Belgian Act of December 14, 2005 on the abolition of bearer securities (*Wet houdende afschaffing van de effecten aan toonder / Loi portant suppression des titres au porteur*), all bearer securities held on securities accounts for which the physical delivery in bearer form has not been requested prior to January 1, 2008, will automatically be converted in dematerialised securities as from January 1, 2008. Bearer securities that are put on a securities account after December 31, 2007 are also automatically converted in dematerialised securities as from the moment that they are put on the securities account.

All of the Company's shares, including the offered shares upon delivery, are fully paid up and freely transferable, subject, however, to the lock-up arrangements further described in section 2.8.2 in chapter 2.

### **3.4.4. Purchase and sale of own shares**

In accordance with the Company's articles of association and the Belgian Company Code, the Company can only purchase and sell its own shares by virtue of a special shareholders' resolution approved by at least 80% of the votes validly cast at a general shareholders' meeting where at least 50% of the share capital and at least 50% of the profit certificates, if any, are present or represented. The prior approval by the shareholders is not required if the Company purchases the shares to offer them to the Company's personnel.

In accordance with the Belgian Company Code, an offer to purchase shares must be made to all shareholders under the same conditions. This does not apply to the acquisition of shares via a regulated market or the acquisition of shares that has been unanimously decided by the shareholders at a meeting

where all shareholders were present or represented. Shares can only be acquired with funds that would otherwise be available for distribution as a dividend to the shareholders. The total amount of shares held by the Company can at no time be more than 10% of its share capital. At the date of this prospectus, the board of directors of the Company did not have any authorisation from the shareholders' meeting to redeem shares. The articles of association, however, authorise the board of directors to purchase own shares in case of imminent serious harm to the Company in accordance with article 620, §1, al. 3 of the Belgian Company Code. The latter authorisation is valid for a period of three years as from the date of publication in the annexes to the Belgian Official Gazette of the amendment to the articles of association inserting this authorisation.

### **3.4.5. Authorised capital**

On February 26, 2007, the extraordinary shareholders' meeting authorised the board of directors to increase the Company's share capital in one or more transactions with a maximum amount that cannot exceed the amount of the Company's share capital upon completion of the offering and listing of the Company's shares (excluding issuance premiums, if any).

If the capital is increased within the limits of the authorised capital, the board of directors will be authorised to request payment of an issuance premium. This issuance premium will be booked on a non-available account, which may only be decreased or disposed of by a resolution of a shareholders' meeting taken in accordance with the provisions governing an amendment of the articles of incorporation.

This board of directors' authorisation will be valid for capital increases subscribed for in cash or in kind, or made by capitalisation of reserves and issuance premiums, with or without issuing new shares. The board of directors is authorised to issue convertible bonds, warrants, a combination thereof or other securities within the limits of the authorised capital.

The board of directors is authorised, within the limits of the authorised capital, to restrict or exclude the preferential subscription rights granted by law to the holders of existing shares if in doing so it is acting in the best interests of the Company and in accordance with article 596 and following of the Belgian Company Code. The board of directors is authorised to limit or cancel the preferential subscription rights in favour of one or more persons, even if such limitation or cancellation is in favour of persons who are not members of the personnel of the Company or its subsidiaries.

The powers of the board of directors within the framework of the authorised capital will be effective upon the closing of the offering and listing of the Company's shares, and will be valid for a period of five years as of the publication thereof in the annexes to the Belgian Official Gazette.

## **3.5. WARRANTS**

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The Company has created a number of warrants. This section provides an overview of the outstanding warrants at the date of this prospectus, including the warrants created at the extraordinary shareholders' meeting of February 26, 2007 subject to completion of the offering but excluding the over-allotment option. For a further description of the main terms and conditions of the warrants reference is made to section 7.1.5.19 of chapter 7.

Upon proposal of the board of directors, the extraordinary shareholders' meeting of the Company approved the issuance of in aggregate 1,419,930 "personnel" warrants on September 15, 2003 (632,439), September 30, 2003 (151,851), May 14, 2004 (135,802), April 20, 2005 (45,268) and November 3, 2005 (454,570), subject to the warrants being granted to and accepted by the beneficiaries. Of these warrants (i), (ii) 154,883 warrants have not and will not be granted (for lack of exercise window), and (ii) 38,963

have lapsed due to their beneficiaries leaving the Company, bringing the total of outstanding “personnel” warrants at 1,226,084. The warrants are granted to employees, consultants or directors of the Company, as well as to other persons who in the scope of their professional activity have made themselves useful to the Company, including but not limited to the members of the scientific advisory board and the clinical advisors. The warrants have been granted free of charge. Subject to the cancellation of the various classes of shares approved conditionally by the extraordinary shareholders’ meeting of February 26, 2007, each warrant entitles its holder to subscribe to one common share (instead of shares of class B or D shares) of the Company at a subscription price equal to the subscription price paid at the occasion of the most recent capital increase preceding or following shortly after the granting of the warrants. The warrants have a term of 5 years. Upon expiration of the 5 year term, the warrants become null and void. The warrants vest in cumulative tranches of 25% per year, *i.e.*, 25% as of the first anniversary date of their granting, 50% as of the second anniversary date of their granting, 75% as of the third anniversary date of their granting, 100% as of the fourth anniversary date of their granting, unless the board of directors of the Company approved a deviation from this vesting scheme when granting the warrants. The warrants (i) can only be exercised by the warrant holder if they have effectively vested, and (ii) can only be exercised as of the fourth calendar year following the year in which the board of directors of the Company granted the warrants to the warrant holder. However, the terms and conditions of the warrants provide that in case of an initial public offering, the warrants can also be exercised immediately prior to the admission of all or part of the shares in the Company to the listing of a regulated market, such as Euronext Brussels.

On February 26, 2007 the extraordinary shareholders’ meeting, upon proposal of the board of directors, also decided to issue a number of new “personnel” warrants equal to 10% of the number of new shares issued pursuant to the offering (excluding the new shares, if any, issued pursuant to the exercise of the over-allotment option). These new “personnel” warrants were issued subject to the completion of the offering and the listing of the Company’s shares and subject to the warrants being granted to and accepted by the beneficiaries. They can be granted by the board of directors of the Company to employees, consultants or directors of the Company or its subsidiaries, as well as to other persons who in the scope of their professional activity have made themselves useful to the Company or its subsidiaries, including but not limited to the members of the scientific advisory board and the clinical advisors. However, the Company intends to grant the new “personnel” warrants mainly to its employees or to employees of its subsidiaries. They will be granted, to the board of directors’ choice, free of charge or against payment of a price equal to the market value of the warrants. The new “personnel” warrants that have not been granted by the board of directors within 6 months following the closing date of the offering can no longer be granted and shall automatically become null and void. Each warrant granted while the Company’s shares are listed or traded on a stock exchange entitles its holder to subscribe to one common share in the Company at a subscription price equal to the average closing price of the Company’s shares on the Eurolist by Euronext Brussels over the 30 day period preceding the date on which the “personnel” warrants are offered. Upon exercise, the portion of the exercise price up to the par value of the existing shares needs to be recorded as capital. The portion of the exercise price exceeding the par value of the existing shares needs to be recorded on a separate account unavailable for distribution called “Issuance premiums”. The warrants have a term of 10 years calculated as from February 26, 2007. Upon expiration of the 10 year term, the warrants become null and void. The warrants vest in cumulative tranches of 25% per year, *i.e.*, 25% as of the first anniversary date of their granting, 50% as of the second anniversary date of their granting, 75% as of the third anniversary date of their granting, 100% as of the fourth anniversary date of their granting, unless the board of directors of the Company approved a deviation from this vesting scheme. Except in case of a public squeeze-out bid on the securities in the Company, the warrants are not transferable *inter vivos* once they have been granted to a beneficiary. The warrants (i) can only be exercised by the warrant holder if they have effectively vested, and (ii) can only be exercised as of the fourth calendar year following the year in which the board of directors of the Company granted the warrants to the warrant holder. In the event of a change of control over the Company, the board of directors has the power to shorten the exercise periods of the warrants provided that it shall offer the warrant holder a term of at least 1 month in which the warrant holder can exercise its warrants. Such reduction of the exercise periods shall be accompanied by the right of the warrant holders to exercise immediately all of their warrants that have not yet expired (including warrants that have not yet vested effectively). The board of directors may modify all terms and conditions

of the new “personnel” warrants to the extent that the express consent of the shareholders’ meeting of the Company is not legally required.

Upon proposal of the board of directors and pursuant to shareholders’ agreements entered into in 2003 and 2005, the extraordinary shareholders’ meeting of the Company of February 26, 2007 approved, subject to the completion of the offering and the listing of the Company’s shares, the issuance of in aggregate 494,065 warrants (in case the final offering price is higher than €4.89 per share but lower than €7.84) or 1,012,833 warrants (in case the final offering price is higher than €7.83 per share) to Axxis V&C BVBA, Prof. Dr. Frank Luyten, Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven), Gemma Frisius-Fonds K.U.Leuven NV, Johan Bellemans, Etienne Schacht and Universiteit Gent (referred to in this prospectus as the “existing shareholders” warrants). The “existing shareholders” warrants have been granted as consideration for the representations and warranties given by some of the warrant holders and the waiver of their preferential subscription rights with respect to the capital increases in the Company of September 15 and 30, 2003. Each “existing shareholders” warrant entitles its holder to subscribe to one common share of the Company at a subscription price equal to €0.01 per share or, in case of exercise in blocks of 10 warrants, €0.001 per share. The warrants have a term of 5 years. Upon expiration of the 5 year term, the warrants become null and void.

The table below gives an overview (as at February 26, 2007) of the outstanding “personnel” warrants and “existing shareholders” warrants described above. The table should be read together with the notes referred to below.

Issue date	Term	Number of warrants issued <sup>(1)</sup>	Number of warrants granted	Exercise price (€)	Number of warrants no longer exercisable	Number of warrants outstanding	Exercise periods vested warrants <sup>(2) (3)</sup>
September 15, 2003	From September 15, 2003 to September 14, 2008	632,439	632,439	€1.00 (October 20, 2003 grant)  €3.00 (March 12, 2004, May 14, 2004 and December 13, 2004 grants)	18,186 <sup>(4)</sup>	614,253	From March 16 to 31, and from September 15 to 30
September 30, 2003	From September 30, 2003 to September 29, 2008	151,851	151,851	€3.00 (September 6, 2004 and December 13, 2004 grants)	3,750 <sup>(5)</sup>	148,101	From March 16 to 31, and from September 15 to 30.
May 14, 2004	From May 14, 2004 to May 13, 2009	135,802	133,684	€3.00 (May 14, 2004 and May 23, 2005 grants)  €3.50 (December 9, 2005 grant)	19,145 <sup>(6)</sup>	116,657	From March 16 to 31, and from September 15 to 30. <sup>(7)</sup>

Issue date	Term	Number of warrants issued <sup>(1)</sup>	Number of warrants granted	Exercise price (€)	Number of warrants no longer exercisable	Number of warrants outstanding	Exercise periods vested warrants <sup>(2) (3)</sup>
April 20, 2005	From April 20, 2005 to April 19, 2010	45,268	45,268	€3.00 (May 23, 2005 grant)  €3.50 (February 6, 2006 grant)	/	45,268	From March 1 to 31, and from September 1 to 30.
November 3, 2005	From November 3, 2005 to November 2, 2010	454,570	301,805	€3.50 (February 6, 2006, March 24, 2006, May 2, 2006, July 3, 2006 and August 24, 2006 grants)	152,765 <sup>(8)</sup>	301,805	From March 1 to 31, and from September 1 to 30.
February 26, 2007 <sup>(9)</sup>	From February 26, 2007 to February 25, 2017	10% of the offered shares <sup>(10)</sup>	None	Average closing price <sup>(11)</sup>	/	10% of the offered shares <sup>(10)</sup>	From May 1 to 31, and from November 1 to 30.
February 26, 2007 <sup>(12)</sup>	From February 26, 2007 to February 25, 2012	494,065 <sup>(13)</sup> or 1,012,833 <sup>(14)</sup>	All	€0.01 or, in case of exercise in blocks of 10 warrants, €0.001	/	494,065 <sup>(13)</sup> or 1,012,833 <sup>(14)</sup>	At any time.

#### Notes

- (1) Issuance under the condition precedent of the "personnel" warrants being granted and accepted.
- (2) In principle, the "personnel" warrants can only be exercised as of the fourth calendar year following the grant of the warrants. However, deviating from the aforementioned principle and in addition to the regular exercise periods, the terms and conditions of the "personnel" warrants provide that in case of an initial public offering, the warrants can also be exercised at the time of a trade sale or immediately prior to the admission of all or part of the shares in the Company to the listing of a regulated market, such as Euronext Brussels.
- (3) The Company has approved deviations from the normal vesting scheme of the "personnel" warrants (i.e., 25% of the granted "personnel" warrants vest on each anniversary of the grant date) in negotiations with certain beneficiaries of the warrants or to allow the warrant holders to have at least one exercise window after 100% of their warrants have vested.
- (4) 18,186 warrants have lapsed due to their beneficiaries leaving the Company.
- (5) 3,750 warrants have lapsed due to their beneficiary leaving the Company.
- (6) 2,118 warrants have not and will not be granted (for lack of exercise window prior to the expiry of the warrants) and 17,027 warrants have lapsed due to their beneficiaries leaving the Company.
- (7) In deviation of the normal exercise windows, the vested warrants granted to HSS Ventures Inc. can be exercised during the following exercise windows: March 16-31, 2007 ; September 15-30, 2007 ; March 16-31, 2008 ; September 15-30, 2008; March 16-30, 2009.
- (8) 152,765 warrants have not and will not be granted (for lack of exercise window prior to the expiry of the warrants).
- (9) Issued subject to the completion of the offering and the listing of the Company's shares and subject to these new "personnel" warrants being granted to and accepted by the beneficiaries.
- (10) The number of new "personnel" warrants shall be equal to 10% of the number of new shares issued pursuant to the offering (excluding the new shares, if any, issued pursuant to the exercise of the over-allotment option).
- (11) Average closing price of the Company's shares on the Eurolist by Euronext Brussels over the 30 day period preceding the date on which the warrants are granted.



- (12) Issued by the extraordinary shareholders' meeting on February 26, 2007, subject to the completion of the offering and the listing of the Company's shares. This issuance of warrants results from the shareholders agreement between the existing shareholders of the Company of 2003, in which the existing shareholders agree, as confirmed in a shareholders' agreement of 2005, to approve, in case of an initial public offering of the shares in the Company, an issuance of "existing shareholders" warrants to Axxis V&C BVBA, Prof. Dr. Frank Luyten, Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven), Gemma Frisius-Fonds K.U.Leuven NV, Johan Bellemans, Etienne Schacht and Universiteit Gent, as consideration for the representations and warranties given by some of them and the waiver of their preferential subscription rights with respect to the capital increases in the Company of September 15 and 30, 2003.
- (13) In case the final offering price is higher than €4.89 per share but lower than €7.84.
- (14) In case the final offering price is higher than €7.83 per share.

On February 26, 2007, the total number of all outstanding warrants that have already been granted represent approximately 7.97% of the total number of all outstanding shares (on a fully diluted basis, but excluding the "existing shareholders" warrants that have been issued and granted conditionally and the new "personnel" warrants that have been issued conditionally but have not yet been granted).

Except for certain warrant holders holding a very limited number of the total number of the Company's securities at the time of the offering, all warrant holders have entered into a lock-up agreement with the lead managers whereby they agree not to transfer any of their warrants in the Company for a period starting on the listing date and ending 12 months from the listing date. This arrangement is further described in section 2.8.2 of chapter 2.

### 3.6. OUTSTANDING FINANCIAL INSTRUMENTS

The table below provides an overview of the issued and outstanding voting financial instruments, whether or not representing the Company's share capital, issued by the Company prior to the offering and listing of the Company's shares. The overview must also be read together with the notes referred to below.

Prior to IPO <sup>(1)</sup>	Number	%
<b>A Shares</b>	14,157,014	92.03%
<b>B Shares to be issued upon the exercise of warrants that are exercisable<sup>(2)</sup></b>	402,011	2.61%
<b>C Total (A)+(B)</b>	14,559,025	94.64%
<b>D Shares to be issued upon the exercise of warrants that are not yet exercisable<sup>(2)</sup></b>	824,073	5.36%
<b>E. Total (B)+(D)</b>	1,226,084	7.97%
<b>F. Total (A)+(B)+(D)</b>	15,383,098	100.00%

#### Notes

- (1) This overview does not include the "existing shareholders" and new "personnel" warrants issued by the extraordinary shareholders' meeting on February 26, 2007 since they were issued subject to the completion of the offering and the listing of the Company's shares and the number of new warrants depends on the final offering price and the number of shares issued pursuant to the offering.
- (2) As at March 16, 2007.



### 3.7. SHAREHOLDERS

#### 3.7.1. Shareholders prior to the completion of the offering and listing

The table below provides an overview of the shareholders of the Company prior to the completion of the offering and listing of the Company's shares. The overview must be read together with the notes referred to below.

	Shares		Warrants		Total shares and warrants	
	Number	%	Number	%	Number	%
<b>A. Executive management<sup>(2)</sup>:</b>						
Gil Beyen BVBA <sup>(3)</sup> (CEO)	0	0%	195,000	15.90%	195,000	1.27%
Other members of the executive management.	9,750	0.07%	418,750	34.15%	428,500	2.78%
<b>Subtotal</b>	<b>9,750</b>	<b>0.07%</b>	<b>613,750</b>	<b>50.06%</b>	<b>623,500</b>	<b>4.05%</b>
<b>B. Independent directors<sup>(4)</sup>:</b>						
Marie-Hélène Plais	0	0%	60,000	4.89%	60,000	0.39%
Sven Andréasson	0	0%	60,000	4.89%	60,000	0.39%
<b>Subtotal</b>	<b>0</b>	<b>0%</b>	<b>120,000</b>	<b>9.79%</b>	<b>120,000</b>	<b>0.78%</b>
<b>C. Founding shareholders:</b>						
Axxis V&C BVBA <sup>(3)</sup>	320,000	2.26%	0 <sup>(1)</sup>	0%	320,000 <sup>(1)</sup>	2.08%
Prof. Dr. Frank Luyten	320,000	2.26%	195,000 <sup>(1)</sup>	15.90%	515,000 <sup>(1)</sup>	3.35%
<b>Subtotal</b>	<b>640,000</b>	<b>4.52%</b>	<b>195,000<sup>(1)</sup></b>	<b>15.90%</b>	<b>835,000<sup>(1)</sup></b>	<b>5.43%</b>
<b>D. Institutional shareholders:</b>						
Gemma Frisius- Fonds K.U.L.euven NV <sup>(5)</sup>	1,025,943	7.25%	0 <sup>(1)</sup>	0%	1,025,943 <sup>(1)</sup>	6.67%
Katholieke Universiteit Leuven <sup>(6)</sup>	295,685	2.09%	0 <sup>(1)</sup>	0%	295,685 <sup>(1)</sup>	1.92%
Universiteit Gent	371,498	2.62%	0 <sup>(1)</sup>	0%	371,498 <sup>(1)</sup>	2.41%
ING Belgium NV/SA <sup>(7)</sup>	4,261,452	30.10%	0	0%	4,261,452	27.70%
Capricorn Venture Fund II NV <sup>(8)</sup>	1,572,993	11.11%	0	0%	1,572,993	10.22%

	Shares		Warrants		Total shares and warrants	
	Number	%	Number	%	Number	%
Fagus NV <sup>(9)</sup>	2,105,527	14.87%	0	0%	2,105,527	13.69%
Fortis Private Equity Venture Belgium NV	428,571	3.03%	0	0%	428,571	2.79%
Auriga Ventures II FCPR <sup>(10)</sup>	2,440,918	17.24%	0	0%	2,440,918	15.87%
Baekeland Fonds II NV	114,285	0.81%	0	0%	114,285	0.74%
BIP Investment Partners SA	142,857	1.01%	0	0%	142,857	0.93%
PARTNERS@V ENTURE NV	285,714	2.02%	0	0%	285,714	1.86%
Technowal SA	71,428	0.50%	0	0%	71,428	0.46%
ITX Corporation	200,000	1.41%	0	0%	200,000	1.30%
HSS Ventures Inc.	28,571	0.20%	12,500	1.02%	41,071	0.27%
<b>Subtotal</b>	<b>13,345,442</b>	<b>94.27%</b>	<b>12,500<sup>(1)</sup></b>	<b>1.02%</b>	<b>13,357,942<sup>(1)</sup></b>	<b>86.83%</b>
<b>E. Others:</b>						
Consultants <sup>(11)</sup>	52,500	0.37%	130,371 <sup>(1)</sup>	10.63%	182,871 <sup>(1)</sup>	1.19%
Personnel	7,500	0.05%	91,512	7.46%	99,012	0.64%
Other <sup>(12)</sup>	101,822	0.72%	62,951	5.13%	164,773	1.07%
<b>Subtotal</b>	<b>161,822</b>	<b>1.14%</b>	<b>284,834<sup>(1)</sup></b>	<b>23.23%</b>	<b>446,656<sup>(1)</sup></b>	<b>2.90%</b>
<b>Total (A)+(B)+(C)+(D)</b>	<b>13,995,192</b>	<b>98.86%</b>	<b>941,250<sup>(1)</sup></b>	<b>76.77%</b>	<b>14,936,442<sup>(1)</sup></b>	<b>97.10%</b>
<b>Total (A)+(B)+(C)+(D)+(E)</b>	<b>14,157,014</b>	<b>100.00%</b>	<b>1,226,084<sup>(1)</sup></b>	<b>100.00%</b>	<b>15,383,098<sup>(1)</sup></b>	<b>100.00%</b>

## Notes

- (1) This overview does not include the “existing shareholders” and new “personnel” warrants issued by the extraordinary shareholders’ meeting on February 26, 2007 since they were issued subject to the completion of the offering and the listing of the Company’s shares and the number of new warrants depends on the final offering price and the number of shares that are issued pursuant the offering. These new warrants are included in the overview in section 3.7.2.
- (2) See also under section 4.4. of chapter 4.
- (3) Gil Beyen BVBA and Axxis V&C BVBA are controlled by Gil Beyen
- (4) See also under 4.2.3. of chapter 4.
- (5) Gemma Frisius-Fonds K.U.Leuven NV is the seed capital fund of the Katholieke Universiteit Leuven. It is a joint venture of the Katholieke Universiteit Leuven (20%), Fortis Private Equity Belgium NV (40%) and KBC Private Equity NV (40%).
- (6) Includes the shares held by Universitaire Ziekenhuizen Leuven.
- (7) ING Belgium NV/SA is with its division ING Corporate Investments an active venture capitalist in the Belgian and French markets, with an extended focus on South West Europe.
- (8) Capricorn Venture Fund II NV is a venture capital fund managed by Capricorn Venture Partners NV. Capricorn Venture Partners NV is a Leuven (Belgium) based, independent manager of venture capital funds that focus on innovative European companies with technology as competitive advantage.

- (9) *Fagus NV is an early-stage venture capital fund managed by Fortis Private Equity Belgium NV. Fagus NV is a joint venture between Fortis Private Equity Belgium NV (55%) and the European Investment Fund (45%).*
- (10) *Auriga Partners SA is a Paris-based independent venture capital firm, managing several early-stage funds specializing in Information Technology and Life Sciences.*
- (11) *“Consultants” includes (i) the persons providing services to TiGenix on the basis of a consultancy agreement and who are not a member of the executive management, and (ii) other external scientific and clinical advisors.*
- (12) *“Other” includes (i) former TiGenix personnel, and (ii) small shareholders or warrant holders of TiGenix who are not employees or consultants of TiGenix.*

While the Corporate Governance Code recommends that TiGenix discloses the number of shares and warrants held by each individual member of the executive management, TiGenix takes the view that such disclosure is not recommended in the given circumstances for reasons of privacy and because the human resources policy of a company such as TiGenix does not warrant that each key executive has full access to the remuneration package of his or her colleagues.

### 3.7.2. Shareholders after completion of the offering and listing

The table below provides an overview of the shareholders of the Company after the completion of the offering and listing of the Company's shares.

The number of outstanding shares and warrants after the completion of the offering and listing assumes that the offering of €40 million has been fully subscribed, and that the over-allotment option has been fully exercised.

As the final offering price is not yet known, the overview contains a simulation for the following hypotheses:

- The hypothesis that the new shares are issued at €5.00 per share: in that event, 8,000,000 new shares are issued in the offering (assuming that the offering is fully subscribed), and 1,200,000 new shares are issued upon exercise of the over-allotment option (assuming that the over-allotment option is fully exercised).
- The hypothesis that the new shares are issued at €6.50 per share: in that event, 6,153,846 new shares are issued in the offering (assuming that the offering is fully subscribed), and 923,076 new shares are issued upon exercise of the over-allotment option (assuming that the over-allotment option is fully exercised).
- The hypothesis that the new shares are issued at €8.00 per share: in that event, 5,000,000 new shares are issued in the offering (assuming that the offering is fully subscribed), and 750,000 new shares are issued upon exercise of the over-allotment option (assuming that the over-allotment option is fully exercised).

The simulation is merely for information purposes only. The hypothetical offering prices are no indication and do not express an expectation as to the final offering price of the offered shares. Prospective investors should note that the final offering price could be different from the hypothetical prices set out in the overview below. If the final offering price is higher, fewer new shares will be issued, assuming that the offering is fully subscribed and the over-allotment option is fully exercised. If the final offering price is lower, more new shares will be issued, assuming that offering is fully subscribed and the over-allotment option is fully exercised.

Furthermore, prospective investors should note that it is possible that the offering is not fully subscribed to or that the over-allotment option is not fully exercised. If the offering is not fully subscribed, fewer new shares will be issued (unless the offering is cancelled).

The overview must be read together with the notes referred to below.

Total shares and warrants before the IPO <sup>(1)</sup>			Total shares and warrants after the IPO including new “personnel” warrants and “existing shareholders” warrants					
			Total shares and warrants after the IPO <u>excluding</u> new “personnel” warrants and “existing shareholders” warrants <sup>(2)</sup>					
			Offering price of €5.00		Offering price of €6.50		Offering price of €8.00	
	Number	%	Number	%	Number	%	Number	%
A. Executive management <sup>(3)</sup> :								
Gil Beyen BVBA <sup>(4)</sup> (CEO)	195,000	1.27%	195,000	0.75%	195,000	0.83%	195,000	0.86%
			195,000	0.79%	195,000	0.87%	195,000	0.92%
Other members of the executive management	428,500	2.78%	428,500	1.66%	428,500	1.82%	428,500	1.89%
			428,500	1.74%	428,500	1.91%	428,500	2.03%
Subtotal	623,500	4.05%	623,500	2.41%	623,500	2.65%	623,500	2.75%
			623,500	2.54%	623,500	2.78%	623,500	2.95%
B. Independent directors <sup>(5)</sup> :								
Marie-Hélène Plais	60,000	0.39%	60,000	0.23%	60,000	0.25%	60,000	0.26%
			60,000	0.24%	60,000	0.27%	60,000	0.28%
Sven Andréasson	60,000	0.39%	60,000	0.23%	60,000	0.25%	60,000	0.26%
			60,000	0.24%	60,000	0.27%	60,000	0.28%
Subtotal	120,000	0.78%	120,000	0.46%	120,000	0.51%	120,000	0.53%
			120,000	0.49%	120,000	0.53%	120,000	0.57%
C. Founding shareholders:								
Axxis V&C BVBA <sup>(4)</sup>	320,000	2.08%	411,748	1.59%	411,748	1.75%	508,083	2.24%
			320,000	1.30%	320,000	1.42%	320,000	1.51%
Prof. Dr. Frank Luyten	515,000	3.35%	606,748	2.34%	606,748	2.57%	703,083	3.10%
			515,000	2.09%	515,000	2.29%	515,000	2.44%
Subtotal	835,000	5.43%	1,018,496	3.93%	1,018,496	4.32%	1,211,166	5.35%
			835,000	3.40%	835,000	3.72%	835,000	3.95%
D. Institutional shareholders:								
Gemma Frisius-Fonds K.U.L.euven NV	1,025,943	6.67%	1,208,697	4.67%	1,208,697	5.13%	1,400,590	6.18%
			1,025,943	4.17%	1,025,943	4.57%	1,025,943	4.85%
Katholieke Universiteit Leuven <sup>(6)</sup>	295,685	1.92%	348,402	1.35%	348,402	1.48%	403,754	1.78%
			295,685	1.20%	295,685	1.32%	295,685	1.40%
Universiteit Gent	371,498	2.41%	437,703	1.69%	437,703	1.86%	507,218	2.24%
			371,498	1.51%	371,498	1.65%	371,498	1.76%

	Total shares and warrants before the IPO <sup>(1)</sup>		Total shares and warrants after the IPO <u>including</u> new “personnel” warrants and “existing shareholders” warrants					
	Number	%	Total shares and warrants after the IPO <u>excluding</u> new “personnel” warrants and “existing shareholders” warrants <sup>(2)</sup>					
			Offering price of €5.00		Offering price of €6.50		Offering price of €8.00	
			Number	%	Number	%	Number	%
ING Belgium NV/SA	4,261,452	27.70%	4,261,452	16.47%	4,261,452	18.08%	4,261,452	18.82%
			4,261,452	17.33%	4,261,452	18.97%	4,261,452	20.16%
Capricorn Venture Fund II NV	1,572,993	10.22%	1,572,993	6.08%	1,572,993	6.67%	1,572,993	6.95%
			1,572,993	6.40%	1,572,993	7%	1,572,993	7.44%
Fagus NV	2,105,527	13.69%	2,105,527	8.14%	2,105,527	8.93%	2,105,527	9.30%
			2,105,527	8.56%	2,105,527	9.37%	2,105,527	9.96%
Fortis Private Equity Venture Belgium NV	428,571	2.79%	428,571	1.66%	428,571	1.82%	428,571	1.89%
			428,571	1.74%	428,571	1.91%	428,571	2.03%
Auriga Ventures II FCPR	2,440,918	15.87%	2,440,918	9.43%	2,440,918	10.36%	2,440,918	10.78%
			2,440,918	9.93%	2,440,918	10.87%	2,440,918	11.55%
Baekeland Fonds II NV	114,285	0.74%	114,285	0.44%	114,285	0.48%	114,285	0.50%
			114,285	0.46%	114,285	0.51%	114,285	0.54%
BIP Investment Partners SA	142,857	0.93%	142,857	0.55%	142,857	0.61%	142,857	0.63%
			142,857	0.58%	142,857	0.64%	142,857	0.68%
PARTNERS @VENTURE NV	285,714	1.86%	285,714	1.10%	285,714	1.21%	285,714	1.26%
			285,714	1.16%	285,714	1.27%	285,714	1.35%
Technowal SA	71,428	0.46%	71,428	0.28%	71,428	0.30%	71,428	0.32%
			71,428	0.29%	71,428	0.32%	71,428	0.34%
ITX Corporation	200,000	1.30%	200,000	0.77%	200,000	0.85%	200,000	0.88%
			200,000	0.81%	200,000	0.89%	200,000	0.95%
HSS Ventures Inc.	41,071	0.27%	41,071	0.16%	41,071	0.17%	41,071	0.18%
			41,071	0.17%	41,071	0.18%	41,071	0.19%
<b>Subtotal</b>	<b>13,357,942</b>	<b>86.83%</b>	<b>13,659,618</b>	<b>52.79%</b>	<b>13,659,618</b>	<b>57.95%</b>	<b>13,976,378</b>	<b>61.72%</b>
			<b>13,357,942</b>	<b>54.34%</b>	<b>13,357,942</b>	<b>59.47%</b>	<b>13,357,942</b>	<b>63.21%</b>

	Total shares and warrants before the IPO <sup>(1)</sup>		Total shares and warrants after the IPO <u>including</u> new “personnel” warrants and “existing shareholders” warrants					
	Number	%	Total shares and warrants after the IPO <u>excluding</u> new “personnel” warrants and “existing shareholders” warrants <sup>(2)</sup>					
			Offering price of €5.00		Offering price of €6.50		Offering price of €8.00	
			Number	%	Number	%	Number	%
<b>E. Others:</b>								
Consultants <sup>(7)</sup>	182,871	1.19%	191,764	0.74%	191,764	0.81%	201,102	0.89%
			<i>182,871</i>	<i>0.74%</i>	<i>182,871</i>	<i>0.81%</i>	<i>182,871</i>	<i>0.86%</i>
Personnel <sup>(8)</sup>	99,012	0.64%	99,012	0.38%	99,012	0.42%	99,012	0.44%
			<i>99,012</i>	<i>0.40%</i>	<i>99,012</i>	<i>0.44%</i>	<i>99,012</i>	<i>0.47%</i>
Other	164,773	1.07%	164,773	0.64%	164,773	0.70%	164,773	0.73%
			<i>164,773</i>	<i>0.67%</i>	<i>164,773</i>	<i>0.73%</i>	<i>164,773</i>	<i>0.78%</i>
<b>Subtotal</b>	<b>446,656</b>	<b>2.90%</b>	<b>455,549</b>	<b>1.77%</b>	<b>455,549</b>	<b>1.93%</b>	<b>464,887</b>	<b>2.05%</b>
			<i>446,656</i>	<i>1.82%</i>	<i>446,656</i>	<i>1.99%</i>	<i>446,656</i>	<i>2.11%</i>
<b>F. New “personnel” warrants:</b>								
New “Personnel” Warrants	-	0.00%	800,000	3.09%	615,384	2.61%	500,000	2.21%
			<i>0</i>	<i>0.00%</i>	<i>0</i>	<i>0.00%</i>	<i>0</i>	<i>0.00%</i>
<b>Subtotal</b>	<b>-</b>	<b>0.00%</b>	<b>800,000</b>	<b>3.09%</b>	<b>615,384</b>	<b>2.61%</b>	<b>500,000</b>	<b>2.21%</b>
			<i>0</i>	<i>0.00%</i>	<i>0</i>	<i>0.00%</i>	<i>0</i>	<i>0.00%</i>
<b>G. Free float:</b>								
Offering	-	0.00%	8,000,000	30.91%	6,153,846	26.11%	5,000,000	22.08%
			<i>8,000,000</i>	<i>32.54%</i>	<i>6,153,846</i>	<i>27.40%</i>	<i>5,000,000</i>	<i>23.66%</i>
Over-allotment option	-	0.00%	1,200,000	4.64%	923,076	3.92%	750,000	3.31%
			<i>1,200,000</i>	<i>4.88%</i>	<i>923,076</i>	<i>4.11%</i>	<i>750,000</i>	<i>3.55%</i>
<b>Subtotal</b>	<b>-</b>	<b>0.00%</b>	<b>9,200,000</b>	<b>35.55%</b>	<b>7,076,922</b>	<b>30.03%</b>	<b>5,750,000</b>	<b>25.39%</b>
			<i>9,200,000</i>	<i>37.42%</i>	<i>7,076,922</i>	<i>31.51%</i>	<i>5,750,000</i>	<i>27.21%</i>
<b>Total</b>	<b>15,383,098</b>	<b>100%</b>	<b>25,877,163</b>	<b>100%</b>	<b>23,569,469</b>	<b>100%</b>	<b>22,645,931</b>	<b>100%</b>
			<i>24,583,098</i>	<i>100%</i>	<i>22,460,020</i>	<i>100%</i>	<i>21,133,098</i>	<i>100%</i>

#### Notes

- (1) This column does not include the “existing shareholders” warrants issued by the extraordinary shareholders’ meeting on February 26, 2007 since they were issued subject to the completion of the offering and listing of the Company’s shares and the number of new warrants depends on the final offering price.
- (2) In this column the numbers in normal text include the “existing shareholders” warrants and the new “personnel” warrants conditionally issued by the extraordinary shareholders’ meeting on February 26, 2007 and the numbers in italics exclude such new warrants.
- (3) See also under section 4.4 of chapter 4.
- (4) Gil Beyen BVBA and Axxis V&C BVBA are controlled by Gil Beyen.
- (5) See also under section 4.2.3 of chapter 4.
- (6) Includes the shares held by Universitaire Ziekenhuizen Leuven.
- (7) “Consultants” includes (i) the persons providing services to TiGenix on the basis of a consultancy agreement and who are not a member of the executive management, and (ii) other external scientific and clinical advisors.
- (8) “Other” includes (i) former TiGenix personnel, and (ii) small shareholders or warrant holders of TiGenix who are not employees or consultants of TiGenix.

Compared to the fraction of the registered capital and net equity of the Company represented by one share (calculated on a fully diluted basis)<sup>7</sup> as per December 31, 2006, the effect of the offering and the issuance of the new “personnel” warrants, “existing shareholders” warrants and “over-allotment” warrants in the aforementioned hypotheses (calculated on a fully diluted basis)<sup>8</sup> can be summarised as follows:

- **Offering price of €5 per share.** The fraction of the registered capital represented by one share increases by 0.10% and the fraction of the net equity represented by one share increases by 236.73%.
- **Offering price of €6.50 per share.** The fraction of the registered capital represented by one share decreases by 0.10% and the fraction of the net equity represented by one share increases by 269.73%.
- **Offering price of €8 per share.** The fraction of the registered capital represented by one share decreases by 4.41% and the fraction of the net equity represented by one share increases by 284.79%.

When disregarding the new “personnel” warrants and “existing shareholders” warrants, the effect can be summarised as follows:

- **Offering price of €5 per share.** The fraction of the registered capital represented by one share remains unchanged and the fraction of the net equity represented by one share increases by 231.13%.
- **Offering price of €6.50 per share.** The fraction of the registered capital represented by one share remains unchanged and the fraction of the net equity represented by one share increases by 262.41%.
- **Offering price of €8 per share.** The fraction of the registered capital represented by one share remains unchanged and the fraction of the net equity represented by one share increases by 285.08%.

### 3.8. NOTIFICATION OF IMPORTANT PARTICIPATIONS

Belgian law, in conjunction with article 8 of the Company’s articles of association, imposes disclosure requirements on any individual or entity acquiring or transferring voting securities or securities which give a right to voting securities, as soon as, following such acquisitions or transfer, the total number of voting rights directly or indirectly held by such individual or entity, alone or in concert with others, increases above or falls below a threshold of 3%, 5%, or any multiple of 5%, of the total number of voting rights attached to the Company’s securities. Pursuant to article 5 of the Act of 2 March 1989 on the disclosure of important participations in listed companies and on the regulations in relation to public takeover offers (*Wet op de openbaarmaking van belangrijke deelnemingen in ter beurze genoteerde vennootschappen*

<sup>7</sup> Assuming that (i) all outstanding granted “personnel” warrants are exercised, (ii) for the outstanding granted “personnel” warrants issued on September 15-30, 2003, May 14, 2004 and April 20, 2005, €1 (par value at that time) of the exercise price per warrant is recorded as capital and the excess is recorded as issuance premium, and (iii) for the outstanding granted “personnel” warrants issued on November 3, 2005, €0.997 (par value at that time) of the exercise price per warrant is recorded as capital and the excess is recorded as issuance premium.

<sup>8</sup> Assuming that (i) all outstanding granted “personnel” warrants are exercised (see previous footnote), (ii) where applicable, all “existing shareholders” warrants are exercised at an exercise price of €0.001 per warrant which is recorded as capital, (iii) where applicable, all new “personnel” warrants are granted at an exercise price equal to the final offering price and are fully exercised whereby per warrant €0.997 is recorded as capital and the excess as issuance premium, and (iv) all “over-allotment” warrants are exercised whereby per warrant €0.997 of the exercise price is recorded as capital and the excess as issuance premium.



*en tot reglementering van de openbare overnameaanbiedingen / Loi relative à la publicité des participations importantes dans les sociétés cotées en bourse et réglementant les offres publiques d'acquisition*), the Company has exercised its right to reduce the disclosure threshold provided by the abovementioned Act to 3%. A shareholder whose shareholding increases above or falls below any such thresholds must, each time, disclose this fact to the CBFA and to the Company. The documents pursuant to which the transaction was effected must be submitted to the CBFA. When the participation of a shareholder reaches 20%, the notification must indicate in which strategy the acquisition or transfer concerned fits, as well as the number of securities acquired during a period of twelve months before the notification and in which manner such securities were acquired. Such notification is also required if an individual or an entity acquires or transfers control (either direct or indirect, either *de iure* or *de facto*) on a company that possesses 3% of the voting rights of the Company.

The forms to make the aforementioned notifications, as well as further explanations can be found on the website of the CBFA ([www.cbfa.be](http://www.cbfa.be)).

The Company is required to publicly disclose any notifications received regarding increases or decreases in a shareholder's ownership of the Company's securities on the next business day, and must mention these notifications in the notes to its annual accounts. Euronext Brussels will publish details of the notifications. Violation of the disclosure requirements may result in the suspension of voting rights, a court order to sell the securities to a third party and/or criminal liability. The CBFA may also impose administrative sanctions.

### **3.9. PUBLIC TAKEOVER BIDS**

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Public takeover bids on the Company's shares and other voting securities (such as warrants or convertible bonds, if any) are subject to the supervision by the CBFA. Public takeover bids must be made for all of the Company's voting securities, as well as for all other securities that entitle the holders thereof to the subscription to, the acquisition of or the conversion in voting securities. Prior to making a bid, a bidder must issue and disseminate a prospectus, which must be approved by the CBFA. The bidder must also obtain approval of the relevant competition authorities, where such approval is legally required for the acquisition of the Company.

In the event that a natural person or legal entity, alone or in concert with others, intends to acquire a controlling interest through one or several transactions relating to the Company's securities, he must notify the CBFA of the contemplated transaction at least five business days before the completion of the transaction. The acquisition of a controlling interest is currently defined as an acquisition of voting securities or rights to acquire voting securities giving the purchaser the legal or *de facto* ability to decisively influence the appointment of a majority of the members of the Company's board of directors or the orientation of the Company's policy. Under Belgian law, the acquisition of a controlling interest over a listed company is not determined by reference to a particular threshold percentage of share ownership, but is instead based on the application of a qualitative definition of control to the specific facts and circumstances of each situation.

If the acquirer of a controlling interest pays a premium over the market value of the securities, it must make a public takeover bid or issue a standing order (*koershandhaving / maintien de cours*) for all of the Company's remaining voting securities (or rights to acquire voting securities). The consideration offered to the remaining security holders must equal the highest price paid to the seller or sellers of the controlling interest during the preceding twelve months.

If the acquirer of a controlling interest pays a price higher than the market price at the moment of the acquisition, the acquirer must offer all other shareholders the opportunity to sell their securities at the same price (if the controlling interest is acquired through a single acquisition of securities) or at the highest price offered by the acquirer for the Company's securities during the twelve months preceding the

acquisition of the controlling interest (if the controlling interest is acquired through several acquisitions of securities). The acquirer must give the other holders of securities this opportunity within 30 business days after the acquisition of the controlling interest either in the form of a public takeover bid, or, under certain conditions, pursuant to an undertaking to support the stock price (*koershandhaving / maintien de cours*) on the stock exchange where the Company's shares will then be listed.

Belgium is required to implement the Thirteenth Company Law Directive (European Directive 2004/25/EC of April 21, 2004), which may afford minority investors greater protection than that is currently available. Although the Directive had to be implemented by May 20, 2006, this is not yet the case in Belgium. A draft Belgian Act on public takeover bids (*Wetsontwerp op de openbare overnamebiedingen / Projet de loi relative aux offres publiques d'acquisition*) implementing the Thirteenth Company Law Directive has been submitted to the Belgian Parliament on January 5, 2007. The draft Belgian Act provides that a mandatory bid will be triggered if a person, as a result of its own acquisition or the acquisition by persons acting in concert with him or by persons acting for their account, directly or indirectly holds more than 30% of the voting securities in a company having its registered office in Belgium and of which at least part of the voting securities are being traded on a regulated market or on a multilateral trading facility designated by Royal Decree. The draft Belgian Act provides that another or an additional threshold percentage of voting securities can be determined by Royal Decree to take into account evolutions on the financial markets or, as the case may be, to take transitional measures. The mere fact of exceeding the relevant threshold will give rise to a mandatory bid, irrespective of whether or not the price paid in the relevant transaction exceeds the current market price. The draft Belgian Act contains a transitional provision granting a exemption from the mandatory bid to persons who individually or acting in concert hold at least 30% of the voting securities on the date the new mandatory bid provision enters into force (date to be determined by Royal Decree after adoption of the draft Act), provided that the shareholding was duly notified to the CBFA within 120 business days as of the entering into effect of the new mandatory bid provision.

There are several provisions of Belgian company law and certain other provisions of Belgian law, such as the obligation to disclose important shareholdings (see under section 3.8) and merger control, that may apply to the Company and which may make an unfriendly tender offer, merger, change in management or other change in control, more difficult. These provisions could discourage potential takeover attempts that other shareholders may consider to be in their best interest and could adversely affect the market price of the Company's shares. These provisions may also have the effect of depriving the shareholders of the opportunity to sell their shares at a premium.

Normally, the authorisation of the board of directors to increase the share capital of the Company through contributions in cash with cancellation or limitation of the preferential right of the existing shareholders is suspended as of the notification to the Company by the CBFA of a public takeover bid on the securities of the Company. The general shareholders' meeting can, however, authorise the board of directors to increase the share capital by issuing shares in an amount of not more than 10% of the existing shares of the Company at the time of such a public takeover bid. Such authorisation has not been granted to the board of directors of the Company.

### 3.10. SQUEEZE-OUT

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Pursuant to Article 513 of the Belgian Company Code, or the regulations promulgated thereunder, a person, acting alone or in concert, who owns 95% of the securities conferring voting power in a public company, can acquire the totality of the securities conferring voting rights in that company following a squeeze-out offer. The shares that are not voluntarily tendered in response to such offer are deemed to be automatically transferred to the bidder at the end of the procedure. At the end of the offer, the company is no longer deemed a public company, unless bonds issued by the company are still spread among the public. The consideration for the securities must be in cash and must represent the fair value as to safeguard the interests of the transferring shareholders.

A simplified squeeze-out procedure is applicable (Belgian Act of March 2, 1989), if following a voluntary public takeover in cash and provided that the bidder has reserved the right to do so in the prospectus, the bidder owns at least 95% of the target securities and in the event where the bidder was already a controlling shareholder prior to the bid and has acquired 66% of the securities it did not hold before the launch of the offer. In that case, the bidder may reopen its offer at the same conditions for 15 days as from the date of publication of the results of the offer in order to launch a squeeze-out offer on the remaining securities.



## 4. CORPORATE GOVERNANCE

### 4.1. GENERAL PROVISIONS

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This chapter 4 summarises the rules and principles by which the corporate governance of the Company has been organised pursuant to Belgian Company law, the Company's articles of association and the Company's corporate governance charter. It is based on the Company's articles of association that have been amended by the extraordinary shareholders' meeting of February 26, 2007 and on the Company's corporate governance charter, both of which will become effective upon completion of the offering and listing of the Company's shares.

The Company's corporate governance charter has been adopted in accordance with the recommendations set out in the Belgian Code on Corporate Governance (the "Code") that has been issued on December 9, 2004 by the Belgian Corporate Governance Committee. Corporate governance has been defined in the Code as a set of rules and behaviours according to which companies are managed and controlled. The Code is based on a "comply or explain" system: Belgian listed companies should follow the Code, but can deviate from its provisions and guidelines (though not the principles) provided they disclose the justifications for such deviation.

The Company's board of directors intends to comply with the Belgian Code for Corporate Governance, but believes that certain deviations from its provisions are justified in view of the Company's particular situation. These deviations include, but are not limited to, the following:

- Article 6.1. of the Code: as there is only one executive director (the Chief Executive Officer, or "CEO") and there is no management committee (*directiecomité / comité de direction*), the Company has not drafted specific terms of reference of the executive management, except for the terms of reference of the CEO.
- Article 7.4. of the Code: only the independent directors shall receive a fixed remuneration in consideration of their membership of the board of directors and their attendance at the meetings of committees of which they are members. They will not receive any performance related remuneration, nor will any option or warrants be granted to them in their capacity as director. However, upon advice of the nomination and remuneration committee, the board of directors may propose to the shareholders' meeting to deviate from the latter principle in case in the board's reasonable opinion the granting of options or warrants would be necessary to attract independent directors with the most relevant experience and expertise.
- Article 8.9. of the Code: only shareholders who individually or collectively represent at least 20% of the total issued share capital may submit proposals to the board for the agenda of any shareholders' meeting. This percentage is in line with Article 532 of the Belgian Company Code (relating to the convening of a shareholders' meeting) but deviates from the 5% threshold provided by the Code.

The board of directors of the Company will review its corporate governance charter from time to time and make such changes as it deems necessary and appropriate. The charter will be made available on the Company's website ([www.tigenix.com](http://www.tigenix.com)) and can be obtained free of charge at the registered office of the Company after completion of the offering and listing. In its annual report for the financial year ended December 31, 2007, to be published in 2008, the board of directors will also devote a specific chapter to corporate governance, describing the Company's corporate governance practices during that year and including explanations, if applicable, on any deviations from the Code, in accordance with the requirement to "comply or explain".

## **4.2. BOARD OF DIRECTORS**

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### **4.2.1. General provisions**

The board of directors of the Company has the broadest powers to manage and represent the Company, except to the extent provided otherwise by applicable law or the Company's articles of association. The board of directors acts as a collegiate body but can delegate its competencies for special and specific matters to an authorised representative, even if this person is not a shareholder or a director.

Pursuant to the Company's articles of association, the board of directors of the Company is to be composed of at least 3 directors and a maximum of nine (9) members. At least half of the directors shall be non-executive directors upon completion of the offering and the listing of the shares.

The directors of the Company are appointed by the general shareholders' meeting. However, in accordance with the Belgian Company Code, if the mandate of a director becomes vacant due to his death or resignation, the remaining directors have the right to appoint temporarily a new director to fill the vacancy until the first general shareholders' meeting after the mandate became vacant. The new director completes the term of the director whose mandate became vacant. The corporate governance charter provides that directors can be appointed for a maximum (renewable) term of four years.

A meeting of the board of directors is validly constituted if there is a quorum, consisting of at least half of the members present in person or represented at the meeting. If this quorum is not present, a new board meeting may be convened to deliberate and decide on the matters on the agenda of the board meeting for which a quorum was not present. In any event, the board of directors may only validly proceed if at least two directors are present. Meetings of the board of directors are convened by the chairman of the board or by at least two directors whenever the interests of the Company so require. In principle, the board will meet at least six (6) times per year.

The chairman of the board of directors has a casting vote on matters submitted to the board of directors.

### **4.2.2. Chairman**

The Company's corporate governance charter provides that the board of directors appoints a chairman amongst the independent directors. The CEO cannot be the chairman.

To ensure the continuity in the period immediately following the closing of the offering, the current chairman Koenraad Debackere, who is a non-executive but not an independent director, will stay on as chairman of the board in deviation of the above paragraph. It is, however, the Company's intention to appoint an independent director as chairman of the board within a period of six months following the closing of the offering.

The chairman of the board of directors is responsible for the leadership of the board of directors. The chairman takes the necessary measures to develop a climate of trust within the board of directors, contributing to open discussion, constructive dissent and support for the decisions of the board of directors. The chairman promotes effective interaction between the board and the executive management. The chairman establishes a close relationship with the CEO, providing support and advice, while fully respecting the executive responsibilities of the CEO.

The chairman has additional specific tasks. These are further described in the terms of reference of the board of directors as set out in the Company's corporate governance charter.

#### 4.2.3. Independent directors

As to independent directors, a director can only be considered an independent director if he or she meets at least the criteria set out in Article 524 of the Belgian Company Code, which can be summarised as follows:

- (a) During a term of two years prior to his or her election he or she has not exercised the mandate or function of director, manager, executive committee member, day-to-day manager or executive in the Company or an affiliate of the Company. This criterion does not apply to the re-election of an independent director.
- (b) He or she does not own any corporate rights that represent 10% or more of the share capital, the corporate funds or of a category of shares of the Company.

If he or she has corporate rights which represent less than 10%, then:

- (i) such rights, taken together with rights in the same Company held by companies over which he or she has control, may not represent 10% or more of the share capital, the corporate funds or of a category of shares of the Company; or
  - (ii) the disposal of these shares, or the exercise of the rights attached thereto may not be subject to agreements or unilateral commitments entered into by him or her.
- (c) He or she is not the spouse of, is not the unmarried legal partner of, or is not a relative (via birth or marriage) up to the second degree of a person who (i) is a director, manager, executive committee member, day-to-day manager or executive in the Company or an affiliate of the Company, or (ii) has a financial interest as set out under (b) above.
- (d) He or she does not have a relationship with the Company that is of a nature to prejudice his or her independency.

In considering a director's independence, also the criteria set out in the Company's corporate governance charter will be taken into account. The board of directors will disclose in its annual report which directors it considers independent directors.

Upon closing of the offering, the independent directors of the Company will be Marie-Hélène Plais, Sven Andréasson and Willy Duron.



#### 4.2.4. Composition of the board of directors

Upon completion of the offering and listing of the Company's shares, the board of directors will consist of nine (9) members.

Name	Age	Position	Term <sup>(1)</sup>	Professional Address
Koenraad Debackere <sup>(2)</sup>	45	Chairman (non-executive)	2011	Naamsestraat, 3000 Leuven
Gil Beyen BVBA <sup>(3)</sup> , represented by Gil Beyen	45	CEO (executive)	2011	Boetsenberg 20, 3053 Haasrode, Belgium
Prof. Dr. Frank P. Luyten <sup>(2)</sup>	52	Director (non-executive)	2011	Herestraat 45, 3000 Leuven
Capricorn Venture Partners NV/SA <sup>(3)</sup> , represented by Claude Stoufs	56	Director (non-executive)	2011	Lei 19/1, 3000 Leuven, Belgium
Fortis Private Equity Belgium NV/SA <sup>(3)</sup> , represented by Raf Moons	37	Director (non-executive)	2011	Warandeborg 3, 1000 Brussels, Belgium
ING Belgium NV/SA <sup>(3)</sup> , represented by Alain Parthoens	47	Director (non-executive)	2011	Marnixlaan 24, 1000 Brussels, Belgium
Sven Andréasson <sup>(2)</sup>	54	Independent director	2011	Scheelevägen 22, SE-220 07 Lund, Sweden
Marie-Hélène Plais <sup>(4)</sup>	57	Independent director	2011	48, avenue du Président Wilson, 75116 Paris, France
Willy Duron <sup>(5)</sup>	62	Independent director	2011	Oude Pastorijstraat 2, 3050 Oud- Heverlee, Belgium

#### Notes

- (1) The term of the mandates of the directors will expire immediately after the annual shareholders' meeting held in the year set forth next to the director's name.
- (2) First appointed upon incorporation on February 21, 2000. Appointment renewed on September 15, 2003 and on February 26, 2007.
- (3) First appointed by the shareholders' meeting on September 15, 2003 (Gil Beyen BVBA was already appointed on a provisional basis by the board of directors on June 30, 2003). Appointment renewed on February 26, 2007.
- (4) First appointed by the shareholders' meeting on May 14, 2004. Appointment renewed on February 26, 2007.
- (5) First appointed by the shareholders' meeting on February 26, 2007.

The following paragraphs contain brief biographies of each of the directors or in case of legal entities being director, their permanent representatives, with an indication of other mandates as member of administrative, management or supervisory bodies in other companies during the previous five years (with the exception of the subsidiaries of the Company):

#### **Koenraad Debackere, PhD:** Chairman of the Board

Dr. Koenraad Debackere is full professor in Technology and Innovation Management at the Katholieke Universiteit Leuven and visiting professor at various European business schools. Prof. Debackere is Managing Director of K.U.Leuven Research & Development and Chairman of the Gemma Frisius-Fonds K.U.Leuven NV, the Venture Fund of the Katholieke Universiteit Leuven. In February 2005 Dr. Debackere became General Manager of the Katholieke Universiteit Leuven. He also serve(d)s on the board of

4AZA Bioscience NV, 4AZA Holding NV, AlgoNomics NV, Better3Fruit NV, Eyetronics NV, ISW Limits NV, IPCOS NV, IriDM NV, Living Stone Co-operatie CVBA, MetaLogic NV, MEAC NV, PharmaDM NV, Bico NV, QMedit NV, RNA-TEC NV, Synes NV, Leuven Innovatie VZW, Gemma Frisius-Fonds II NV, Leuven.Inc VZW, DCRF (Désiré Collen Research Foundation) VZW, eMedit NV, IWT, Netherlands Genomics Initiative, Hoover Stichting VZW, Stichting Amici Almae Matris VZW, Werf en Vlasnatie NV, Aquacare Belgium NV, Aquacare International NV, KBC Verzekeringen NV, Groep Joos NV, Vlerick Leuven Gent Management School NV.

**Prof. Dr. Frank P. Luyten:** Scientific founder and medical advisor of the Company

Frank Luyten is since 1997 Professor at the Faculty of Medicine of the Katholieke Universiteit Leuven (KUL). He is Chairman of the Department of Musculoskeletal Sciences and the Division of Rheumatology, and Director of the Laboratory for Skeletal Development and Joint Disorders at the same university. Frank Luyten has extensive experience in the field of cell and developmental biology of skeletal tissue with a specific focus on joint disorders. He holds a Medical Degree (1980) and PhD (1986) from the Universiteit Gent and obtained his board certification in Rheumatology in 1986. From 1986 until 1992 he was a visiting scientist at the National Institutes of Health, Bethesda, Maryland, U.S.A. From 1992 until 1997 he headed the Developmental Biology Unit of the Craniofacial and Skeletal Diseases Branch at the National Institute of Dental and Craniofacial Research in Bethesda, MD, U.S.A. He serve(d)s as Scientific and Medical advisor for institutions and companies including INSERM, Wellcome Foundation UK, Galapagos, Genera, Astra Zeneca and Pfizer.

**Gil Beyen:** permanent representative of Gil Beyen BVBA, Chief Executive Officer of the Company

Gil Beyen holds an MSc in Bioengineering from the Katholieke Universiteit Leuven (Belgium) in 1984 and obtained an MBA from the University of Chicago (U.S.) in 1990. Before founding TiGenix, he worked as a management consultant at Arthur D. Little (ADL) in Brussels, where he was a Partner, responsible for their Healthcare and Biotechnology Practice. In this function, he has assisted a broad range of companies in the biomedical and biotech industries through different stages of their growth. Before his MBA, he worked three years as a research engineer in environmental biotechnology. Gil Beyen is a manager of AxxisV&C BVBA, as well as member of the board of Eclosion SA and FlandersBio VZW, and commissioner (regeringscommissaris) for the Flemish government on the board of the Flemish Institute of Biotechnology (VIB).

**Sven Andréasson:** Independent Director

Sven Andréasson has been President & CEO and a Board Member of Active Biotech AB since 1999. He has longstanding experience in the international pharmaceuticals industry, including time spent as President and Vice President of mainly Swedish, French and German companies within the Pharmacia Corporation. Sven Andréasson has a MSc in Business Administration and Finance from the Stockholm School of Economics. He is chairman of Operations Leadership Oil AB. During the last five years he has resigned from the boards of Dial N' Smile AB and SwedenBIO AB.

**Marie-Hélène Plais:** Independent Director

Marie-Hélène Plais, MD, is an independent board member of TiGenix since May 2004. Previously, she has been president of Sofamor-Danek International, a spinal company, where she also held positions as Medical Director, President International, and EVP New Business Development. She graduated as Medical Doctor from the University René Descartes, Paris and she holds a degree in Human Genetics. She is also member of the board of directors of the Yves Cotrel Spinal Foundation in Paris, Vitalitec SA in France, Biospace SA and Spine Medica Corp. During the last five years she has resigned from the boards of Spinext SA and Conceptus Inc.

**Claude Stoufs:** permanent representative of Capricorn Venture Partners NV

Claude Stoufs is a senior investment manager at Capricorn Venture Partners NV. Previously, he was responsible for M&A activities in Europe at FMC Corp. and prior to this post he was responsible for European business development and M&A at Occidental Petroleum. Prior to joining Occidental Petroleum in 1985, he held several management positions with Akzo / Fabelta and Patscentre / PA Technology. He holds a Master of Science degree in chemistry and is a graduate in Business Administration and International Commerce from the Université Libre de Bruxelles. Claude Stoufs serves or has served at the

board of directors of BioAlliance, Elbion / 4AZA Bioscience NV, and UroGene. He is also a member of the board of directors of FlandersBio VZW/ASBL, the (Belgian) Flemish Biotech and Life Sciences Network foundation.

**Raf Moons:** permanent representative of Fortis Private Equity Belgium NV

Raf Moons is a senior investment manager at Fortis Private Equity and is actively involved in managing university-linked seed capital funds. Prior to joining Fortis Private Equity in November 1999, he served as industrial advisor at the business development group of IMEC and as a scientific researcher at the K.U.Leuven. He holds a PhD in physics and an MBA, both from the Katholieke Universiteit Leuven. He served as a member of the board of directors of 4AZA Bioscience NV, Luciad NV, Toxi-Test NV, RNA-Tec NV and AnaXis NV. He is member of the board of directors of the following companies, either in his personal capacity or as the permanent representative of Fortis Private Equity Belgium NV: AlgoNomics NV, OMP NV, XenICs NV, METALogic NV, AIC NV, Baekeland-Fonds NV, Baekeland Fonds II NV, Brussels I3 Fund NV, ISW Limits NV, MEAC NV, BRTM NV, Ultragenda NV, Fortis Private Equity Management NV, Fortis Private Equity Arkimedes NV, Fagus NV, PharmaDM NV, Qmedit NV, Gemidis NV, Velleman International NV and Velleman Components NV.

**Alain Parthoens:** permanent representative of ING Belgium NV/SA

Alain Parthoens is an Investment Director at ING Belgium NV/SA, where he specialises in the biotechnology sector. Prior to joining ING in 2001, he led the pharmaceutical practice of the Applied Decision Group of PricewaterhouseCoopers in London and before that he held several management positions in the food and life sciences sector. Alain Parthoens holds an MSc in agronomy and speciality biochemistry from the Université Catholique de Louvain, an MSc in human and computer sciences from the Université Libre de Bruxelles and a management degree from the Solvay Business School (CEPAC). He is member of the Board of Directors of UnibioScreen SA, Maize Technologies International NV, OncoMethylome Sciences SA, Biotechnological Enzymatic Catalyse SA and Belgium Venturing Association and served on the board of CropdDesign NV, Tibotec-Virco NV (now Tibotec-Virco Comm.VA) and Devgen NV either in his personal capacity or as the permanent representative of ING Belgium NV/SA.

**Willy Duron:** Independent Director

Willy Duron, is an independent board member of TiGenix NV since February 2007. Mr Duron has been CEO (*Voorzitter van het Directiecomité*) of KBC Groep NV. He started his career at ABB verzekeringen in 1970 where he became a member of the executive committee in 1984. Willy Duron holds a MSc degree in Mathematics (*Licentiaat Wiskunde*) from the University of Gent and a MSc degree in Actuarial Sciences (*Licentiaat in Actuariële Wetenschappen*) from the Katholieke Universiteit Leuven. He is also member of the board of directors of Ravago NV, Vanbreda Risk & Benefits NV, Universitaire Ziekenhuizen Leuven, Katholieke Universiteit Leuven, Universitair Centrum St Jozef Kortenberg, W&K and Amonis, and has served on the board of directors of KBC Groep NV, KBC Bankerzekeringsholding NV and KBC Asset Management NV, Synes NV, Argosz, CSOB, Warta, FBD, Secura and ADD.

***Litigation statement concerning the directors or their permanent representatives***

At the date of this prospectus, none of the directors or, in case of corporate entities being director, none of their permanent representatives, of the Company has, for at least the previous five years:

- any convictions in relation to fraudulent offences;
- held an executive function in the form of a senior manager or a member of the administrative, management or supervisory bodies of any company at the time of or preceding any bankruptcy, receivership or liquidation; or has been subject to any official public incrimination and/or sanction by any statutory or regulatory authority (including any designated professional body); or,
- has ever been disqualified by a court from acting as member of the administrative, management or supervisory bodies of any company or from acting in the management or conduct of affairs of any company.

### **4.3. COMMITTEES OF BOARD OF DIRECTORS**

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#### **4.3.1. General**

The board of directors can set up specialised committees to analyse specific issues and advise the board of directors on those issues. The committees are advisory bodies only and the decision-making remains within the collegial responsibility of the board of directors. The board of directors determines the terms of reference of each committee with respect to the organization, procedures, policies and activities of the committee.

#### **4.3.2. Audit committee**

The board of directors has appointed an audit committee. The committee must be composed of at least three members. The committee must be composed exclusively of non-executive directors. To the extent possible, a majority of its members should be independent directors. The composition of the committee may deviate from the above if, in the reasonable opinion of the board of directors, a different composition can bring more relevant experience and expertise to the committee. The committee appoints a chairman amongst its members. The chairman of the board of directors should not chair the committee.

The role of the audit committee is to supervise financial reporting and the observance of administrative, legal and fiscal procedures and the follow-up of financial and operational audits and advises on the choice and remuneration of the statutory auditor. The committee should report regularly to the board of directors on the exercise of its functions. It should inform the board of directors about all areas in which action or improvement is necessary in the opinion of the audit committee. The audit committee should produce recommendations concerning the necessary steps that need to be taken. The audit review and the reporting on that review should cover the Company and its subsidiaries as a whole.

The committee has specific tasks, which include the Company's financial reporting, internal controls and risk management, and the internal and external audit process. These are further described in the terms of reference of the audit committee, as set out in the Company's corporate governance charter. In principle, the committee will meet at least five (5) times per year.

The members of the committee shall at all times have full and free access to the Chief Financial Officer ("CFO") and to any other employee to whom they may require access in order to carry out their responsibilities.

On completion of the offering and listing of the Company's shares, the following directors shall be member of the audit committee: Willy Duron, Sven Andréasson and ING Belgium NV/SA, represented by Alain Parthoens.

#### **4.3.3. Nomination and remuneration committee**

The board of directors has appointed a nomination and remuneration committee. The committee must be composed of at least three members, including the CEO. The other members of the committee must be non-executive directors. To the extent possible, a majority of its members shall be independent directors. The composition of the committee may deviate from the above if, in the reasonable opinion of the board of directors, a different composition can bring more relevant experience and expertise to the committee. The committee is chaired by the chairman of the board of directors or by another non-executive director appointed by the committee.

The role of the nomination and remuneration committee is:

- to make recommendations to the board of directors with regard to the (re-)election of directors, and
- to make proposals to the board on the remuneration policy for directors, and the remuneration policy for executive management.

The committee has specific tasks. These are further described in the terms of reference of the nomination and remuneration committee as set out in the Company's corporate governance charter. In principle, the committee will meet at least two (2) times per year.

On completion of the offering and listing of the Company's shares, the following directors shall be member of the nomination and remuneration committee: Sven Andréasson, Marie-Hélène Plais and Capricorn Venture Partners NV/SA, represented by Claude Stoufs.

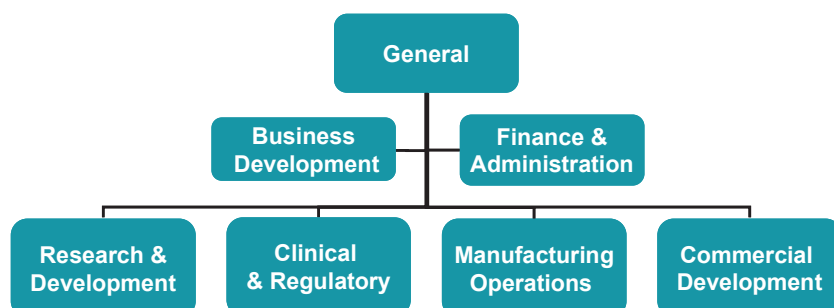
## **4.4. EXECUTIVE MANAGEMENT**

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### **4.4.1. General provisions**

The board of directors has appointed the executive management of the Company. The terms of reference of the executive management have been determined by the board of directors in close consultation with the CEO.

The structure and organisation of TiGenix is illustrated below:



### **4.4.2. Chief executive officer**

The CEO is appointed, and can be removed, by the board of directors of the Company.

The CEO is charged by the board of directors with the day-to-day management of the Company and is therefore also managing director of the Company. In this function, the CEO has the following general responsibilities:

- he is responsible vis-à-vis the board of directors for the management of the Company and the implementation of the decisions of the board of directors;
- he heads and oversees the management team and reports to the board of directors on their activities; and

- he is responsible for the development of proposals for the board of directors relating to strategy, business opportunities, operations and human resources, and such other matters that are to be dealt with at the level of the board of directors.

The CEO has certain specific tasks. These are further described in the terms of reference of the CEO, as set out in the Company's corporate governance charter.

#### 4.4.3. Other members of the executive management

The other members of the executive management are appointed and removed by the board of directors or by the CEO in close consultation with the board of directors of the Company. They report to the CEO.

#### 4.4.4. Composition of the executive management

Since January 1, 2007 the executive management consists and upon completion of the offering and listing of the Company's shares, the executive management will consist of seven (7) members.

These members are:

Name	Position	Age
Gil Beyen BVBA, represented by Gil Beyen	Chief Executive Officer	45
Frank Hazevoets	Chief Financial Officer	41
Heiko Breek (Breek Management Consultancy BV)	Vice-President Commercial Development	53
Luc Dochez (Primix Bio Ventures BVBA)	Head Business Development	33
Koen Huygens	Director Manufacturing Operations	36
Peter Tomme	Director Research & Development (R&D)	44
Nancy Veulemans (4C Partner BVBA)	Vice-President Clinical and Regulatory Affairs	46

The executive management will not constitute an executive committee (*directiecomité / comité de direction*) within the meaning of Article 524bis of the Belgian Company Code.

Following are biographies of the executive management.

**Gil Beyen:** representative of Gil Beyen BVBA, Chief Executive Officer

Gil Beyen holds an MSc degree in Bioengineering from the Katholieke Universiteit Leuven (Belgium) in 1984 and obtained an MBA from the University of Chicago (U.S.) in 1990. Before founding TiGenix, he worked as a management consultant at Arthur D. Little (ADL) in Brussels, where he was a Partner, responsible for their Healthcare and Biotechnology Practice. In this function, he has assisted a broad range of companies in the biomedical and biotech industries through different stages of their growth. Before his MBA, he worked three years as a research engineer in environmental biotechnology.



**Frank Hazevoets:** Chief Financial Officer

Frank Hazevoets holds a Commercial Engineering degree and a Master of Artificial Intelligence and Cognitive Sciences from the Katholieke Universiteit Leuven.

Before joining TiGenix, he worked during 15 years in Corporate Finance at different international companies such as ING and InBev. During his career he was involved in financial management and structuring, accompanied several IPO transactions and lead more than ten M&A deals.

**Heico Breek:** VP Commercial Development, representative of Breek Management Consultancy

Heico Breek, MD, MBA, joined TiGenix as representative of Breek Management Consultancy mid 2004 as its Chief Commercial Officer. Heico holds a Medical Doctor's degree from the University of Amsterdam. Before joining TiGenix, Heico held senior management positions in both Europe and the United States at Aventis Pharma (previously at Roussel and HMR). As VP Global marketing for Aventis' Arthritis & Bone group, he was responsible for the alliance of Aventis with Procter & Gamble and for the global launch of Actonel™, a blockbuster in osteoporosis. In 2001-2003 he was the General Manager of Aventis AB Sweden.

**Luc Dochez:** Head Business Development, representative of Primix Bio Ventures BVBA

Luc Dochez holds a M.Sc. degree in Pharmacy from the Katholieke Universiteit Leuven, a postgraduate degree in Business Economics from the same university and an MBA from Vlerick Management School. Before joining TiGenix as representative of Primix Bio Ventures BVBA in 2003, he was a consultant within Arthur D. Little's Biotechnology practice and he worked as a business development manager for Methexis Genomics.

**Koen Huygens:** Director Manufacturing Operations

Koen Huygens joined TiGenix in July 2001 to set up and head the Company's first GMP cell expansion facility. Koen Huygens holds a M. Sc. degree in Pharmacy from the Katholieke Universiteit Leuven and a Master of Advanced Studies in Industrial Pharmacy from the University of Antwerp. Before joining TiGenix, he worked in GMP quality assurance and process validation with Schering Plough in Belgium.

**Peter Tomme:** Director Research & Development (R&D)

Peter Tomme holds a Ph.D. degree in chemistry/biochemistry from the Universiteit Gent. Before joining TiGenix, he was R&D Director and co-founder of Galapagos where he was responsible for the daily operations and science strategy at the Belgian headquarters. The many R&D programmes for which he was responsible included therapeutic programmes in osteoarthritis, rheumatoid arthritis and osteoporosis. Prior to Galapagos he worked at Tibotec (now part of J&J) as Director Molecular Biology. There he was responsible for assay development as part of the drug discovery team. Peter started his career as an academic holding a staff position at the University of British Columbia, Vancouver, Canada where he specialised in engineering of pharmaceutical and industrial proteins, enzymes and biologicals.

**Nancy Veulemans:** VP Clinical and Regulatory Affairs, representative of 4C Partner BVBA

Nancy is a senior executive in the pharmaceutical and biotech industry with extensive experience in clinical and regulatory affairs. As representative of 4C Partner BVBA she has been involved with TiGenix since its foundation. Prior to that, she held the position of Director Clinical Operations Europe with a global contract research organization. Before this she was Business Unit manager Oncology-Hematology portfolio of Lederle Labs (now Immunex and AHP) and International Clinical Research Associate with Bristol Myers Squibb, responsible for clinical research in Belgium, France, Spain and Portugal. She holds a M.Sc. degree in Bioengineering from the Katholieke Universiteit Leuven.

#### **4.5. SCIENTIFIC ADVISORY BOARD AND CLINICAL ADVISORS**

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To ensure that its scientific strategy and clinical development programmes are aligned with the scientific developments in the field of regenerative medicine, the Company has appointed a scientific advisory board and a number of clinical advisors.



The main tasks of the scientific advisory board and the clinical advisors are the following:

- advise the Company on ways to improve its product research and development programmes;
- keep the Company informed on novel technologies and research ideas;
- act as a sounding board for new ideas; and,
- expand the Company's network for accessing new technology, samples, industry experts, and know-how;
- advise the Company on clinical development programmes.

The scientific advisory board will not constitute an executive committee (*directiecomité / comité de direction*) within the meaning of Article 524bis of the Belgian Company Code, nor will it constitute a committee organised by the board pursuant to Article 522, §1 of the Belgian Company Code. Current members of the Scientific Advisory Board are:

Name	Institute	Position
Frank Luyten, MD, PhD	Katholieke Universiteit Leuven (Belgium)	Professor of Rheumatology
August Verbruggen, MD, PhD	Universiteit Gent (Belgium)	Professor of Rheumatology
Stefan Lohmander, MD, PhD	University of Lund (Sweden)	Professor of Orthopaedic Surgery
Hari Reddi, PhD	University of California at Davis (US)	Professor of Orthopaedics, Director of Center for Tissue Engineering
Richard Coutts, MD, PhD	University of California, San Diego (US)	Professor of Orthopaedic Surgery,
Daniel Grande, PhD	North Shore Hospitals, NY (US)	Director of Orthopaedic Research

The clinical advisors to the Company include:

Name	Institute	Position
René Verdonk, MD, PhD	Universiteit Gent (Belgium)	Professor Orthopaedic Surgery
Johan Bellemans, MD, PhD	Katholieke Universiteit Leuven (Belgium)	Professor Orthopaedic Surgery
Bert Mandelbaum, MD	Santa Monica Orthopaedic and Sports Medicine Group (US)	Orthopaedic Surgeon
Matthias Steinwachs, MD	University of Freiburg (Germany)	Orthopaedic Surgeon
Nicholas Sgaglione, MD	North Shore Hospitals, Long Island (US)	Orthopaedic Surgeon
Jan Victor, MD	St Lucas Hospital Bruges (Belgium)	Orthopaedic Surgeon
Riley Willams, MD	Hospital Special Surgery, NY (US)	Orthopaedic Surgeon

The scientific and clinical advisors are remunerated for their services to the Company. In addition, some of them have consulting agreements with the Company and some hold shares or warrants in the Company.

## **4.6. REMUNERATION OF DIRECTORS AND EXECUTIVE MANAGEMENT**

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### **4.6.1. Directors**

Only the independent directors shall receive a fixed remuneration in consideration of their membership of the board of directors and their attendance at the meetings of committees of which they are members. They will not receive any performance related remuneration, nor will any option or warrants be granted to them in their capacity as director. However, upon advice of the nomination and remuneration committee, the board of directors may propose to the shareholders' meeting to deviate from the latter principle in case in the board's reasonable opinion the granting of option or warrants would be necessary to attract independent directors with the most relevant experience and expertise

None of the other directors will receive any remuneration in consideration of their membership of the board.

Notwithstanding the above, all directors (including those who are not independent) will keep the warrants and options granted to them prior to the completion of the offering and listing of the Company's shares.

The nomination and remuneration committee recommends the level of remuneration for independent directors, including the chairman of the board, subject to approval by the board and, subsequently, by the shareholders' meeting.

The nomination and remuneration committee benchmarks independent directors' compensation against peer companies to ensure that it is competitive. Remuneration is linked to the time committed to the Board and its various committees. The remuneration package for the independent directors approved by the shareholders meeting of February 26, 2007 is as follows. A fixed annual fee of €15,000.00 is based on six board meetings and two committee meetings a year. The fee is supplemented with an amount of €1,500.00 for each additional meeting. The chairman's fee is twice that of the other directors. Changes to these fees will be submitted to the shareholders' meeting for approval.

Apart from the above remuneration for independent directors, all directors will be entitled to a reimbursement of out-of-pocket expenses actually incurred to participate to board meetings.

The board sets and revises, from time to time, the rules and level of compensation for directors carrying out a special mandate or sitting on one of the board committees and the rules for reimbursement of directors' business-related out-of-pocket expenses. Remuneration for directors will be disclosed to shareholders in accordance with applicable laws and stock exchange rules.

The directors' mandate may be terminated "ad nutum" (at any time) without any form of compensation.

TiGenix has not made any loans to the members of the board of directors.

The total remuneration and benefits paid to the directors in 2006, 2005 and 2004 was €16,497, €14,873 and €13,146 respectively (gross amount, excluding VAT and warrants).

#### 4.6.2. Executive management

The remuneration of the members of the executive management is determined by the CEO or by the board of directors upon recommendation by the nomination and remuneration committee, after recommendation by the CEO to such committee.

The remuneration of the executive management is designed to attract, retain and motivate executive managers.

The remuneration of the members of the executive management currently consists of the following elements:

- Each member of the executive management is entitled to a basic fixed remuneration designed to fit responsibilities, relevant experience and competences, in line with market rates for equivalent positions.
- The Company pays a variable remuneration dependent on the executive management member meeting individual and/or team objectives.
- Each member of the executive management may be offered the possibility to participate in a stock based incentive scheme, in accordance with the recommendations set by the nomination and remuneration committee, after recommendation by the CEO to such committee.
- Each member of the executive management who is a salaried employee may be entitled to a number of fringe benefits, which may include participating in a defined contribution pension or retirement scheme (see also section 7.1.5.18 in chapter 7), disability insurance, a company car, a mobile telephone, a laptop computer and/or a forfaitary expense allowance according to general Company policy, and other collective benefits (such as hospitalisation insurance and meal vouchers).

Frank Hazevoets (CFO), Koen Huygens and Peter Tomme, are engaged on the basis of an employment contract. The employment contracts are generally for an indefinite term, with a trial period. The employment contracts may be terminated at any time by the Company, subject to a severance payment not exceeding market standards. The employment contracts include, where appropriate, non-competition undertakings, as well as confidentiality and IP transfer undertakings (that will try to seek maximum protection of the Company's interests, under applicable laws and subject to the employee's agreement).

Gil Beyen BVBA (Gil Beyen) (CEO) is engaged on the basis of a service agreement, which can be terminated at any time, subject to certain pre-agreed notice periods and/or compensations. Breek Management Consultancy BV (Heico Breek), Primix Bio Ventures BVBA (Luc Dochez) and 4C Partner BVBA (Nancy Veulemans) are also engaged on the basis of services agreements which can be terminated at any time, subject to certain pre-agreed notice periods and/or compensations. The service agreements include, where appropriate, non-competition undertakings, as well as confidentiality and IP transfer undertakings.

Executive members who are engaged on the basis of a service agreement do not receive fringe benefits, except that they may be provided with a mobile phone and laptop computer according to general Company policy.

The total remuneration and benefits paid to the aforementioned 7 persons in 2006 was €1.15 million (gross amount, excluding VAT and stock based compensation).

For income year 2007, the total remuneration and benefits for the 7 members of the executive management will likely increase to approximately €1.3 million (gross amount, including fringe benefits but

excluding stock based compensation). Contrary to the Belgian Code on Corporate Governance, the board of directors has currently opted not to disclose the individual remuneration of the CEO, due to privacy reasons and as the board of director believes that the remuneration of the CEO is set at reasonable market standards.

## 4.7. SHARES AND WARRANTS HELD BY DIRECTORS AND EXECUTIVE MANAGEMENT

### 4.7.1. Shares and warrants held by directors

The table below provides an overview (as at February 26, 2007) of the shares and warrants held by the independent directors. Executive directors holding shares or warrants are included in section 4.7.2 below). Some of the institutional shareholders (see section 3.7.1 of chapter 3) also serve as a board member (see section 4.2.4). None of their respective permanent representatives, however, own any shares or warrants in the Company. This overview must be read together with the note referred to below.

	Shares		Warrants <sup>(1)</sup>		Total shares and warrants <sup>(1)</sup>	
	Number	%	Number	%	Number	%
Marie-Hélène Plais	0	0%	60,000	4.89%	60,000	0.39%
Sven Andréasson	0	0%	60,000	4.89%	60,000	0.39%
<b>Total</b>	<b>0</b>	<b>0%</b>	<b>120,000</b>	<b>9.79%</b>	<b>120,000</b>	<b>0.78%</b>

*Note*

(1) This overview does not include the “existing shareholders” and new “personnel” warrants issued by the extraordinary shareholders’ meeting on February 26, 2007 since they were issued subject to the completion of the offering and the listing of the Company’s shares and the number of new warrants depends on the final offering price and the number of shares that are issued pursuant the offering. These new warrants are included in the overview in section 3.7.2 of chapter 3.

### 4.7.2. Shares and warrants held by executive management

The table below provides an overview (as at February 26, 2007) of the shares and warrants held by the executive management, including the executive directors. This overview must be read together with the notes referred to below.

	Shares		Warrants <sup>(1)</sup>		Total shares and warrants <sup>(1)</sup>	
	Number	%	Number	%	Number	%
Gil Beyen BVBA, represented by Gil Beyen, CEO <sup>(2)</sup>	0	0%	195,000	15.90%	195,000	1.27%
Other members of the executive management <sup>(3)</sup>	9,750	0.07%	418,750	34.15%	428,500	2.78%
<b>Total</b>	<b>9,750</b>	<b>0.07%</b>	<b>613,750</b>	<b>50.06%</b>	<b>623,500</b>	<b>4.05%</b>

*Notes*

(1) This overview does not include the “existing shareholders” and new “personnel” warrants issued by the extraordinary shareholders’ meeting on February 26, 2007 since they were issued subject to the completion of the offering and the listing of the Company’s shares and the number of new warrants depends on the final offering price and the number of shares that are issued pursuant the offering. These new warrants are included in the overview in section 3.7.2 of chapter 3.

(2) Gil Beyen BVBA is controlled by Gil Beyen, who also controlled Axxis V&C BVBA, one of the founding shareholders. Axxis V&C BVBA holds 320,000 shares (2.26% of the total number of outstanding shares). Therefore Gil Beyen controls through

*Gil Beyen BVBA and Axxis V&C BVBA in aggregate 320,000 shares and 195,000 "personnel" warrants (3.35% of the total number of shares and warrants).*

(3) *The other members of the executive management are identified in section 4.4.*

#### **4.7.3. Stock option plan**

The Company created several warrants within the context of stock option plans for employees, consultants or directors of the Company, as well as to persons who in the scope of their professional activity have made themselves useful to the Company. For a description of the different stock option plans, see also section 3.5 of chapter 3.

### **4.8. THE STATUTORY AUDITOR**

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BDO ATRIO Bedrijfsrevisoren - BDO ATRIO Réviseurs d'Entreprises CVBA/SCRL, a civil company, having the form of a cooperative company with limited liability (*coöperatieve vennootschap met beperkte aansprakelijkheid / société coopérative à responsabilité limitée*) organised and existing under the laws of Belgium, with registered office at The Corporate Village, Da Vincilaan 9 - Box E.6, Elsinore Building, 1935 Zaventem, Belgium, represented by Luc Annick, or in his absence Lieven Van Brussel, has been re-appointed statutory auditor of the Company on February 26, 2007 for a term of 3 years, ending immediately after the closing of the shareholders' meeting to be held in 2010 that will have deliberated and resolved on the financial statements for the financial year ended on December 31, 2009. The annual remuneration of the statutory auditor for the performance of its three-year mandate for the audit of the Belgian statutory GAAP accounts and the consolidated IFRS accounts of the Company amounts to to €25,000 (excl. VAT).

### **4.9. TRANSACTIONS WITH AFFILIATED COMPANIES**

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#### **4.9.1. General**

Each director and executive manager is encouraged to arrange his personal and business affairs so as to avoid direct and indirect conflicts of interest with the Company. The Company's corporate governance charter contains specific procedures to deal with potential conflicts.

#### **4.9.2. Conflicts of interest of directors**

Article 523 of the Belgian Company Code provides for a special procedure within the board of directors in the event of a possible conflict of interest of one or more directors with one or more decisions or transactions by the board of directors.

In the event of a conflict of interest, the director concerned has to inform his fellow directors of his conflict of interest before the board of directors deliberates and takes a decision in the matter concerned. Furthermore, the conflicted director cannot participate in the deliberation and voting by the board on the matter that gives rise to the potential conflict of interest. The minutes of the meeting of the board of directors must contain the relevant statements by the conflicted director, and a description by the board of the conflicting interests and the nature of the decision or transaction concerned.

The minutes must also contain a justification by the board for the decision or transaction, and a description of the financial consequences thereof for the Company. The relevant minutes must be included in the (statutory) annual report of the board of directors. The conflicted director must also notify the statutory auditor of the conflict. The statutory auditor must describe in his annual (statutory) audit report the financial consequences of the decision or transaction that gave rise to the potential conflict.

In case of non-compliance with the foregoing, the Company may request the annulment of the decision or the transactions which have taken place in breach of these provisions if the counterparty to the decision or the transaction was, or should have been, aware of such breach.

The procedure does not apply to decisions or transactions in the ordinary course of business at customary market conditions. It also does not apply to transactions or decisions between companies of which one holds (directly or indirectly) at least 95% of the voting financial instruments of the other, and transactions or decisions between companies whereby at least 95% of the voting financial instruments of both companies are (directly or indirectly) held by another company.

Article 524ter of the Belgian Company Code provides for a similar procedure in the event of conflicts of interest of executive committee members. In the event of such conflict, only the board of directors will be authorised to take the decision that has led to the conflict of interest. The Company's executive management team does not qualify as an executive committee in the sense of article 524bis of the Belgian Company Code.

Currently, the directors do not have a conflict of interest within the meaning of article 523 of the Belgian Company Code that has not been disclosed to the board of directors. Other than potential conflicts in relation with the present offering, as a result of ING Belgium NV/SA acting as one of the lead managers, the Company does not foresee any other potential conflicts of interest in the near future.

#### **4.9.3. Transactions with affiliates**

Article 524 of the Belgian Company Code, which will apply to the Company following completion of the offering, provides for a special procedure that applies to intra-group or related party transactions with affiliates. The procedure applies to decisions or transactions between the Company and affiliates of the Company that are not a subsidiary of the Company. It also applies to decisions or transactions between any of the Company's subsidiaries and such subsidiaries' affiliates that are not a subsidiary of the Company. Prior to any such decision or transaction, the board of directors of the Company must appoint a special committee consisting of three independent directors, assisted by one or more independent experts. This committee must assess the business advantages and disadvantages of the decision or transaction for the Company. It must quantify the financial consequences thereof and must determine whether or not the decision or transaction causes a disadvantage to the Company that is manifestly illegitimate in view of the Company's policy. If the committee determines that the decision or transaction is not manifestly illegitimate, but is of the opinion that it will prejudice the Company, it must clarify which advantages are taken into account in the decision or transaction to compensate the disadvantages. All these elements must be set out in the committee's advice. The board of directors must then take a decision, taking into account the opinion of the committee.

Any deviation from the committee's advice must be motivated. Directors who have a conflict of interest are not entitled to participate in the deliberation and vote (as set out in section 4.9.2 above). The committee's advice and the decision of the board of directors must be notified to the Company's statutory auditor, who must render a separate opinion. The conclusion of the committee, an excerpt from the minutes of the board of directors and the opinion by the statutory auditor must be included in the (statutory) annual report of the board of directors.



The procedure does not apply to decisions or transactions in the ordinary course of business at customary market conditions, and transactions or decisions with a value of less than 1% of the consolidated net assets of the Company.

Apart from the foregoing procedure, the Company must also report in its annual report substantial restrictions or burdens imposed or maintained by the controlling parent Company if any, during the previous financial year.

#### **4.10. RELATIONS WITH SIGNIFICANT SHAREHOLDERS**

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ING Belgium NV/SA holds 4,261,452 of shares in the Company and is one of the main shareholders of the Company (see also section 3.7.1 of chapter 3). ING Belgium NV/SA, corporate finance division, is also one of the lead managers in connection with the offering as described in this prospectus.

In 2003 existing shareholders of the Company concluded shareholders' agreements, in which they agreed, as confirmed in a shareholders' agreement of 2005, to approve, in case of an initial public offering of the shares in the Company meeting certain conditions, an issuance of warrants (herein referred to as the "existing shareholders" warrants) to Axxis V&C BVBA, Prof. Dr. Frank Luyten, Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven), Gemma Frisius-Fonds K.U.Leuven NV, Johan Bellemans, Etienne Schacht and Universiteit Gent, as consideration for the representations and warranties given by some of them and the waiver of their preferential subscription rights with respect to the capital increases in the Company of September 15 and 30, 2003. In accordance with these agreements, the extraordinary shareholders' meeting of the Company approved on February 26, 2007 the issuance to the aforementioned persons of in aggregate the following number of "existing shareholders" warrants, subject to completion of the offering and listing of the Company's shares: (i) 494,065 "existing shareholders" warrants, in case the final offering price is higher than €4.89 per share but lower than €7.84; or (ii) 1,012,833 "existing shareholders" warrants in case the final offering price is higher than €7.83 per share. Subject to the applicable lock-up and standstill arrangements, these "existing shareholders" warrants can be exercised at any time and entitle their holder to acquire one ordinary share in the Company per exercised warrant at an exercise price of €0.01 per warrant or, in case of exercise in blocks of 10 warrants, €0.001 per warrant. See also section 3.5 of chapter 3.

The Company has entered into a management services contract with its CEO, Gil Beyen BVBA, represented by Gil Geyen. Gil Beyen BVBA does not hold shares but does hold 195,000 "personnel" warrants. Furthermore, Gil Beyen BVBA is controlled by Gil Beyen, who also controls Axxis V&C BVBA, one of the founding shareholders. Axxis V&C BVBA holds 320,000 shares. Therefore Gil Beyen, controls through Gil Beyen BVBA and Axxis V&C BVBA in aggregate 320,000 shares and 195,000 "personnel" warrants.

The Company and the Katholieke Universiteit Leuven entered into (i) a lease agreement pursuant to which with the Katholieke Universiteit Leuven puts premises located in UZ Gasthuisbergen to the disposal of the Company and (ii) a number of commercial agreements, including subcontracting agreements, service level agreements, and research agreements. The Katholieke Universiteit Leuven (including its division Universitaire Ziekenhuizen Leuven) holds 295,685 shares in the Company.

The Company and the Universiteit Gent entered into a number of commercial agreements, including service agreements, subcontracting agreements, service level agreements, collaboration agreements, research agreements, and option agreements for technology evaluation. The Universiteit Gent holds 371,498 shares in the Company.

The Company has no knowledge of any shareholders' agreement that would be effective upon completion of the offering and listing, other than the specific lock-up and standstill agreement described in section 2.8.2 of chapter 2.





## 5. ACTIVITIES OF TIGENIX

*Most of the information contained in this chapter is based on the Company's own estimates, believed by the Company to be reasonable. Certain market size data and certain other information contained in this chapter are based on publications by leading organisations and scientific journals. A bibliography of the sources used is attached to this prospectus as Appendix 2. The information published by such organisations and journals has been accurately reproduced and as far as the Company is aware and able to ascertain, no facts have been omitted which would render the reproduced information inaccurate or misleading. The Company and the lead managers and their respective advisors have not independently verified this information. Furthermore, market information is subject to change and cannot always be verified with complete certainty due to limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties inherent in any statistical survey of market information. As a result, prospective investors should be aware that market share, ranking and other similar data in this prospectus, and estimates and beliefs based on such data, may not be reliable.*

### 5.1. INTRODUCTION

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TiGenix is a late-stage<sup>9</sup> biomedical company that focuses on innovative local treatments for damaged and osteoarthritic joints. The Company is exploiting the power of regenerative medicine to develop durable treatments, validated through controlled clinical trials, for these indications. The Company's lead product for cartilage repair, ChondroCelect, has successfully completed a randomised Phase III clinical trial and will be launched in Europe and/or in the United States, if and when all necessary regulatory approvals have been obtained. Subject to obtaining such approval, the Company aims to commercially launch ChondroCelect in Europe in 2008. To the best of the Company's knowledge, ChondroCelect is the first cell-based medicinal product that has generated positive data in randomised controlled clinical trials for this indication and as such the Company expects the product to be well positioned for regulatory approval.

Based in Leuven, Belgium, TiGenix was founded in 2000 by Prof. Dr. Frank P. Luyten, rheumatologist and renowned scientist, and Gil Beyen<sup>10</sup>, bioengineer and MBA, and CEO of the Company since its inception. The Company is built on technologies developed at both the Katholieke Universiteit Leuven and the Universiteit Gent and its scientific background lies in its expertise in the developmental biology of cartilage, bone and other connective tissues. The insights that the scientific founders gained into the biology of cartilage, namely how a stem cell transforms into a healthy cartilage cell and what happens when this cartilage cell gets injured or degenerates into an arthritic cell, led to the development of a technology platform focused on finding solutions for damaged and diseased cartilage.

TiGenix is developing a portfolio of products that address specific musculoskeletal problems. The lead indication among these is cartilage damage, which is a debilitating affliction affecting the mobility and functioning of patients. Western societies are characterised by ageing populations that place an increasing emphasis on high quality of life and life-long mobility, and, as such, cartilage problems represent a large and growing unmet medical need. Current therapies do not provide satisfying, long-term durable repair and the Company therefore believes there is a need for more effective treatments for cartilage damage. Furthermore, given the naturally heterogeneous nature of cartilage damage, the Company believes that a personalised medicine approach has significant potential to be more effective in the treatment of the condition.

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<sup>9</sup> Late-stage refers to the fact that TiGenix' lead product, ChondroCelect, has completed Phase III clinical trials. It is common practice among investors to label biomedical companies with a Phase III product as late-stage companies.

<sup>10</sup> Through his company Axxis V&C BVBA. Gil Beyen also controls Gil Beyen BVBA, the current Chief Executive Officer of the Company.

TiGenix' lead product, ChondroCelect, uses the patient's own cells as a basis for a quality-controlled product for cartilage repair, characterised by its biological potency. The Company has identified a specific set of genetic markers to identify potent cartilage-forming cells. These cells can form good cartilage when reimplanted into the patient's joint, which is critical in preventing degeneration of the joint, since cartilage defects that have not been properly treated are more likely to lead to osteoarthritis ("OA"). In January 2007, the Company entered into a strategic partnership with Fidia Advanced Biopolymers ("FAB"), based in Italy. FAB has developed a biological scaffold on which the ChondroCelect cells can be seeded to form a three-dimensional (3D) implantable construct. The combined product will enable arthroscopic implantation, which should facilitate the handling of the product for orthopaedic surgeons.

Regulatory changes in both Europe and the United States have greatly raised the efficacy threshold and burden of proof required for the approval of cell-based therapies. From its inception, the Company anticipated such an increasingly strict regulatory framework for new cell-based therapies and so developed ChondroCelect as a medicinal product according to the principles of 'evidence-based medicine'. With a product that has generated positive data from controlled Phase III clinical trials, TiGenix believes that it is well positioned to capitalise on this changing regulatory environment. This approach differentiates the Company from the majority of its competitors.

In addition, the Company' researchers are working to address more advanced stages of OA as well as to effect the repair of other tissues, such as meniscal tissue. TiGenix has recently identified novel cell culture methods that have the potential to further enhance the potency of its cell-based products. This opens the possibility of addressing larger cartilage defects and, in combination with the implantable 3D biomaterial, to treat more advanced and osteoarthritic joint surface lesions.

## 5.2. COMPETITIVE STRENGTHS

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The Company believes its competitive strengths are:

- **A clear focus on a major unmet medical need.** TiGenix has a clear and singular focus on joint disorders and OA, which are among the largest and fastest growing disease areas in Western societies, due to the ageing demographic of those societies. To date, no satisfactory medical solution exists for the treatment of cartilage damage or OA, making them indications with major unmet medical needs.
- **Leading cellular technology platform.** The Company has developed a leading cellular technology platform to identify and characterise cell populations with specific biological functions, through a combination of its core cell culture and genetic marker technologies. Such quality control of cell populations is essential in the development of efficacious cellular medicinal products, since it is the cells which constitute the essential bio-active agent. The platform enables the Company to further develop such cellular medicinal products which have a predictable *in vivo* behaviour.
- **ChondroCelect trial represented a first in class.** ChondroCelect, the Company's lead product for cartilage repair, has successfully completed a randomised Phase III clinical trial in which it demonstrated clear structural superiority combined with clinical non-inferiority over microfracture, currently the most common procedure for repairing cartilage damage.
- **Solid regulatory expertise.** Due to the novel nature of the field, regulations surrounding the approval of cell-based therapies are still in the process of being finalised. The Company anticipated such a rapidly changing regulatory environment and so developed solid regulatory expertise.
- **Access to leading biomaterials.** Through its strategic partnership with Fidia Advanced Biopolymers and its distribution agreement with Geistlich (a Swiss developer and manufacturer of

collagen-based biomaterials for use in medical applications), TiGenix has access to proven biomaterial solutions which can be used to facilitate the implantation of its ChondroCelect product, thus increasing the product's ease of use.

- **Innovative treatments in the pipeline.** TiGenix' in-depth know-how of the biology of stable cartilage formation and the signalling pathways associated with OA forms the basis of the ChondroCelect product platform. It also offers the potential to broaden the product's applications towards osteoarthritic joints, as well as to develop similar products for the repair of other musculoskeletal tissues such as meniscus, for which applications are currently being examined by the Company.
- **Solid intellectual property.** TiGenix has built a strong intellectual property portfolio consisting of patents and trade secrets surrounding the Company's genetic markers, cell culture methods and stem cell technology. The two core patents have been granted in Europe, while several others are pending. In addition, TiGenix has recently identified, and filed a patent application on, novel cell culture methods that can further enhance the potency of its cell-based products.
- **Experienced management team.** TiGenix' management team contains a strong mix of highly experienced professionals with a track record in the biomedical and pharmaceutical fields.

### 5.3. HISTORY AND DEVELOPMENT OF THE COMPANY

Between its inception in February 2000 and September 2003, the Company raised approximately €1 million in two seed rounds. In September 2003, the Company closed a second financing round of €12 million. During this round, four institutional venture capital (VC) companies invested in TiGenix' (ING Belgium NV/SA, Auriga Ventures II FCPR, Fagus NV and Capricorn Venture Fund II NV). In November 2005, TiGenix completed a third financing round of €16 million, with both existing and new investors. In this last round, international investors from the United States (HSS Ventures Inc.) and Japan (ITX Corporation) were among the new investors. Other sources of funding in the first years include two technology grants by the Flemish government, as well as income from licences and research collaborations.

An overview of key milestones and achievements since the Company's inception is presented below in chronological order.

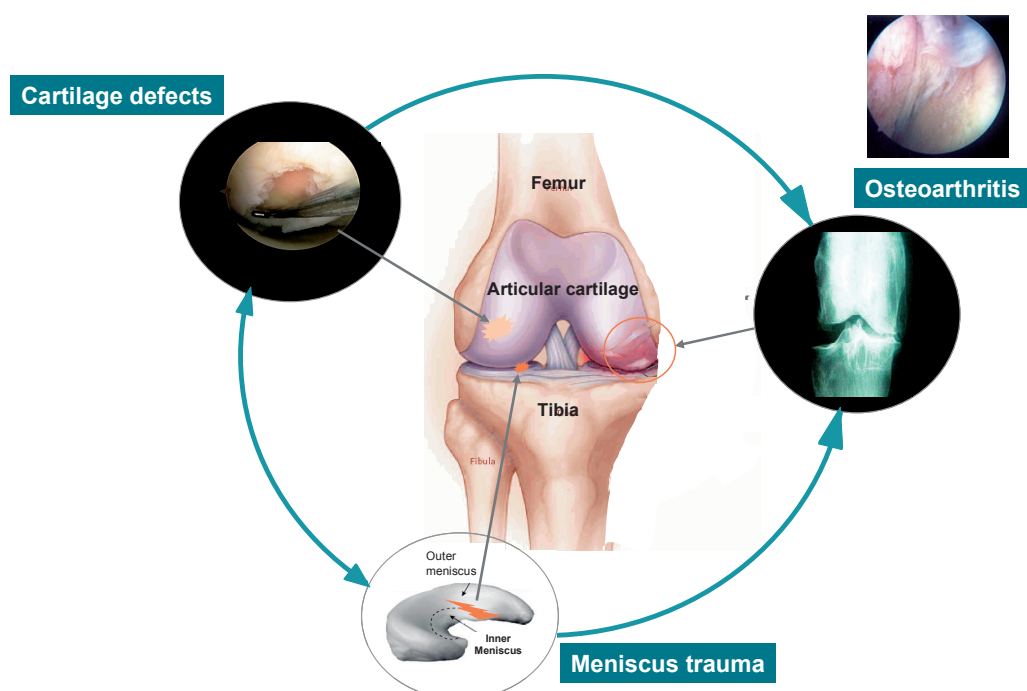
Year	Key milestones & achievements
2000	Incorporation of TiGenix NV/SA.
2001	TiGenix Cell Expansion Facility operational.
2002	Start of randomised, prospective, controlled Phase III clinical trial for ChondroCelect.
2003	Closing of a second financing round (€12 million)
2004	Completion of patient enrolment of the ChondroCelect Phase III clinical trial. Core patents protecting TiGenix' IP granted in Europe. GMP approval of TiGenix Cell Expansion Facility for production for clinical investigation.
2005	Investigational New Drug ("IND") application submitted to the FDA for the ChondroCelect trial. Closing of a third financing round (€16 million).
2006	Incorporation of TiGenix Inc. and opening of offices in New York. Patent application filed on improved cell culture methods.
2007	Positive Phase III clinical data for ChondroCelect presented. Strategic collaboration signed with Fidia Advanced BioPolymers ("FAB").

## 5.4. DESCRIPTION OF THE MARKET

Musculoskeletal conditions are a major burden on individuals, health systems and social care systems. They are the most common cause of severe long-term pain and physical disability, and they affect hundreds of millions of people all around the world<sup>11</sup>. The overall prevalence of musculoskeletal conditions in the Western adult population is estimated to be above 25%<sup>12</sup>, with OA and soft tissue disorders (which include cartilage and meniscal damage) representing the most common musculoskeletal afflictions.

The Company focuses on the development of innovative solutions for these three indications, represented in the diagram below (Figure 5.1).

**Fig. 5.1: Focus of TiGenix development activities**



### Cartilage damage

The initial marketing authorisation that TiGenix will be seeking for ChondroCelect, based on the results of its Phase III clinical trial, will be the repair of symptomatic defects of articular cartilage in the otherwise healthy knee (not yet affected by OA). Widespread adoption of currently available cartilage implantation technology has been limited, due, in part, to the fact that these technologies have not been clinically validated. Worldwide approximately 2 million articular cartilage defects are diagnosed every year in the knee alone. Although not all of these defects can be treated with cartilage implant techniques, the proportion eligible for treatment still represents a large and predominantly underserved market opportunity. TiGenix estimates the potential market for its ChondroCelect product to be 130,000 procedures per year in the United States and Europe, representing a market opportunity of over €1 billion.

Articular cartilage is a tough, elastic tissue that covers the ends of bones in joints and enables the bones to move smoothly over one another. When articular cartilage is damaged through injury, it does not heal

<sup>11</sup> Bulletin of the WHO, September 2003, Woolf et al.

<sup>12</sup> The Mapping Study, November 2005, Salaffi et al.

as rapidly or effectively as other tissues in the body. Instead, the damage tends to spread, allowing the bones to rub directly against each other, resulting in pain and reduced mobility. As such, injuries to cartilage surfaces can lead to painful and restrictive joint function and eventually to OA. Such symptoms can severely hinder a person's normal activities and occupation.

As the natural healing capacity of damaged articular cartilage is limited, cartilage injuries represent a prime opportunity for the application of regenerative medicine. When left untreated, cartilage injuries predispose the sufferer to OA, which is a major cause of disability and represents a huge socio-economic burden to society. Today, there is a belief amongst many medical professionals that repairing cartilage defects at an early stage can slow down or even prevent progression to OA.

### **Meniscal damage**

Meniscal tears are the most common injury of the knee and, like cartilage defects, their spontaneous healing capacity is very low. According to a 2005 article in the *American Journal of Sports Medicine*, approximately one million people in the United States have surgical procedures, known as a menisectomies, to remove a damaged or torn meniscus. Extrapolating these data to Europe suggests more than 1.2 million menisectomies are performed annually in Europe.

It is generally accepted that patients who have had this procedure are more likely to develop OA. Furthermore, very few products are approved which address meniscal regeneration.

### **Osteoarthritis ("OA")**

OA, also known as degenerative joint disease, is a very common disease that is associated with the loss of the ability of joint tissue to repair and maintain itself. OA particularly affects tissues such as articular cartilage and underlying bone, and progression of the disease is the result of several biomechanical, biological and genetic factors. OA is one of the leading causes of disability with more than 25 million Americans affected today. This number is expected to grow to over 30 million by 2020 and similar trends are projected for Europe.

OA has a very substantial economic impact on society, both in terms of direct and indirect costs. Recent studies in the United States and Canada estimated the total impact at approximately US\$250 billion. Another study in Germany estimated that the total costs associated with OA in that country were approximately €19 billion per year: €4 billion in direct costs and €15 billion in indirect costs such as productivity losses. In addition, Reuters identifies OA as one of the prime therapeutic areas with new blockbuster potential in its 2003 Blockbuster Drug Outlook report

The prevalence of symptomatic OA of the knee is estimated between 2.5 and 5 % of the Western adult population<sup>13 14</sup>. Both cartilage and meniscal damage are leading causes of knee OA. If not properly treated at an early stage, patients suffering from meniscal or cartilage damage run a high risk of developing OA later in life. TiGenix' initial focus has been the regeneration of these tissues through the application of its cell-based products, in order to stop or delay further progression towards OA and hence lead to longer mobility for patients. Very few products are approved for the regeneration of cartilage or meniscus tissue and none, to the best of the Company's knowledge, has been validated in randomised prospective clinical studies.

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<sup>13</sup> American Academy of Orthopaedic Surgeons, 2004

<sup>14</sup> The Mapping Study, Salaffi e.a. 2005

## Key factors required for success in this market

As a result of the absence of validated treatments, many patients with these conditions are left untreated. The Company believes that cell-based therapies have significant potential to be effective in their treatment. To be successful in the treatment of these diseases, a cell- or tissue-based medicinal product has to demonstrate the following characteristics:

- **Strong scientific basis leading to a proven technology.** The product needs to be able to show its potency, *i.e.* that it can make or reform stable cartilage or functional meniscus in the patient.
- **Solid clinical validation.** The product's efficacy needs to be demonstrated in well-designed, rigorous clinical studies. This will be necessary to convince the medical community, the Regulatory Authorities and the reimbursement authorities of the product's benefits, all of which will be necessary to create a wide-spread acceptance of such products.
- **Ease of use.** The product should ideally be administered in a simple, non time-consuming and preferably minimally invasive manner.
- **Efficient manufacturing and supply.** Cell-based products require rapid, effective and easily validated procedures for cell extraction, expansion and delivery.

The sections below outline how the Company has addressed these challenges.

## 5.5. TECHNOLOGY

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### *Introduction*

TiGenix' product pipeline, including ChondroCelect, is based upon the application of cell and tissue-based therapies to treat musculoskeletal soft tissue disorders and OA. The concept of cell- and tissue-based therapies, or the use of human cells as therapeutic agents to regenerate and repair the body, is not new. However, this area of medicine has been marked in the past by a cycle that has often characterised novel medical research: initial hype, then a subsequent trough of disappointment, followed finally by the emergence of a viable technology and industry. There are signs that cell therapy is now emerging from such a trough to become a rational and successful component of modern medicine.

Part of the initial problem was a failure to appreciate and understand fully the technical hurdles which needed to be overcome before cell therapy could be considered commercially viable. Initial media coverage tended to overstate what was feasible, using the techniques then available that often resulted in clinical failures. However, lessons from these failures combined with further advances in the fundamental science have created a more mature and realistic industry. Comparisons could be drawn with the commercial exploitation of monoclonal antibodies, a field which required a similar period of development but which has now become an established and growing industry.

There is increasing evidence that a key criterion for the successful application of cell therapy is to use populations of cells that exhibit clearly defined genetic, or other, markers. These markers should link the cells to specific tissue-forming potencies and ultimately predispose them to a durable tissue regeneration and successful clinical outcome. Furthermore, full clinical validation is now required in thorough, well-designed studies.

As a recent review article in the *New England Journal of Medicine* illustrated, cells taken from undefined, heterogeneous populations fail to deliver consistent clinical outcomes. The paper discusses the outcomes of three different clinical studies in which stem cells were tested in heart muscle repair, and illustrates that



there is a need for well characterised cell populations developed using validated potency assays. These requirements have also been highlighted by the FDA, as discussed further in section 5.7.1.

### ***TiGenix' Technology Platform***

TiGenix' in-depth understanding of the biology of stable cartilage and the biological pathways associated with OA form the basis of the Company's technology platform. Prof. Dr. Frank P. Luyten, the Company's scientific founder, has a long history in and extensive experience with cartilage and bone biology research. His research efforts have focused on the behaviour of cells in soft and musculoskeletal tissues. In the course of these investigations he has helped improve the understanding of the biological changes that drive the development of stem cells into fully functional cartilage cells. Furthermore, he has helped to clarify the various factors that differentiate stable, cartilage-forming cells from cells that form less durable, scar-like fibro-cartilagenous tissue, and has elucidated many of the processes that cause cartilage tissue to become osteoarthritic.

This research and subsequent development by TiGenix has resulted in the Company's core technology platform, the key elements of which are:

- **Selection and characterisation of cell populations with specific biological function.** TiGenix has patented a set of well-defined positive and negative molecular markers, capable of predicting the ability of cell populations to form stable hyaline cartilage *in vivo*. These molecular markers were identified by monitoring the expression of molecules known to play a role in the formation and maintenance of the cells' ability to produce cartilage. TiGenix' molecular marker technology is a direct response to the regulatory authorities' demand for clear characterisation of cellular products. This marker technology can also be applied to characterise and select other types of cell populations and potentially also to identify individuals at risk of developing OA.
- **Validated potency assay for cartilage formation *in vivo*.** TiGenix is using a proprietary potency assay for assessing the cartilage forming capacity of human cells in a pre-clinical model. This means that the Company has developed a test that can discriminate between stable chondrocytes, which form high-quality cartilage tissue, and cells that have poor or no capacity to do so. To the best of the Company's knowledge, this is currently the only validated assay in this area.
- **Optimised cell culture methods.** By monitoring molecular markers that are expressed during the growth of cartilage-forming cells, the Company has been able to optimise the process by which the cells are grown (known as cell culture). In addition, TiGenix has recently identified and filed for patent protection on novel cell culture methods that further enhance the potency of ChondroSelect. The Company is also using its technology to predict the point up to which the cell culture is able to generate cartilage, and continues to focus on further improvements to address larger cartilage defects and more advanced osteoarthritic lesions.
- **Identification and selection of specific adult mesenchymal stem cells (precursor cells).** The Company has identified selected populations of joint tissue-forming stem cells that can be used for the repair of connective tissues *in vivo*. These precursor cells are easily obtained and can be used to generate cartilage, bone, meniscus, tendon and muscle tissue. In its stemcell research, TiGenix focuses on populations of human adult stem cells that are committed to develop into one or a limited number of these tissue types, rather than pluri- or multipotent stem cells that can develop into many tissue types depending on the growth conditions.
- **Identification of targets for the discovery of compounds that may prevent or treat OA.** The Company's analysis of the genetics of stable cartilage formation has led it to identify a number of biochemical signalling pathways associated with the development of OA. This has enabled TiGenix to define several potential targets for OA drug discovery. In addition, the Company has developed a series of tests which can be used to assess the most promising drug candidates.

## 5.6. PRODUCT PORTFOLIO OVERVIEW

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TiGenix' approach is to offer a comprehensive solution for the treatment of damaged and diseased joints with the ultimate goal of preventing OA and treating osteoarthritic joints. The product portfolio is focused on:

- treatment of articular cartilage defects;
- the development of easier surgical procedures for such articular cartilage defects;
- the repair of cartilage defects in patients with early OA; and
- the repair of traumatic lesions in meniscus.



The figure below outlines the product portfolio, the intended area or indication of use, the development steps that have been completed and the steps that are still to be completed.

Since the development of cell-based medicinal products is a relatively new area, there is at present not a standard development path as is the case for classic pharmaceutical products. The steps that need to be taken to bring a cell- and tissue-based medicinal product from idea to patient are, however, to a large extent similar to the phases of development of a classic pharmaceutical product. It starts with a research phase in which the key tasks are the identification and the characterisation of the cells or tissues that are suitable to treat a certain indication, followed by the development of a potency assay, required to demonstrate the cell-product's biological function and activity. Once the product has been characterised and the biological activity confirmed, the step of pre-clinical testing can start. The duration of pre-clinical testing can vary considerably. Typically, it will take between 1 and 3 years, but it should be noted that this step can often overlap with the other development steps. Once the safety profile of the product has been confirmed in pre-clinical testing, the clinical development can be initiated. The length of this step is dependent upon the indication, the number of studies to be performed and duration of the patient follow-up required. For ChondroCelect, the clinical development phase has taken 5 years. Upon completion of these clinical trials, the sponsor prepares and submits an application for registration or marketing authorisation to the relevant Regulatory Authorities, after which a review process will start which on average today takes about one year, but this period can be shorter or longer in function of the indication, the quality of the dossier, etc. In total, the time between the end of the clinical trials and registration of the product is believed to be in the order of 1.5 to 2 years.

Fig. 5.2: Overview of products in development

Product	Indication	Product characterisation	Development of potency assay	Preclinical development	Clinical development	Registration & launch
ChondroCelect	Articular cartilage defects					
ChondroCelect-3D <sup>1)</sup>	Articular cartilage defects				1)	
ChondroCelect-3D <sup>1)</sup>	Cartilage defects in (early) OA					
MeniscoCelect	Traumatic meniscus lesions					

1) Combination of ChondroCelect with proven biomaterial (Hyalograft C) may allow faster start of pivotal clinical development

**LEGEND:**  Development steps completed  
 Development steps to be completed

The Company's different products, together with a short overview of its main research projects are given below.

### 5.6.1. ChondroCelect

#### 5.6.1.1. Market Opportunity

ChondroCelect is a cell-based medicinal product, derived from the patients' own cartilage tissue, that is designed to realise functional and durable repair of full-thickness cartilage defects in knee joints. ChondroCelect is currently intended for the regeneration of symptomatic defects of the articular cartilage in the otherwise healthy knee (not affected by OA). Roughly 2 million articular cartilage defects of the knee are diagnosed worldwide every year. TiGenix estimates that in Europe and the United States around 130,000 of these cases are eligible for treatment with cartilage regeneration products such as ChondroCelect.

#### Current surgical treatments for cartilage defects in knee joints

Various surgical procedures are currently available for the local treatment of cartilage defects in the knee, including debridement and lavage, microfracture and osteochondral grafting (also called mosaicplasty). However, none of these surgical treatments has been unequivocally proven to create functional and durable repair of cartilage in prospective, randomised clinical trials.

The figure below gives an overview of the most common surgical procedures used today, with a brief description of their main characteristics.

**Fig. 5.3.: Surgical procedures for the treatment of cartilage defects**

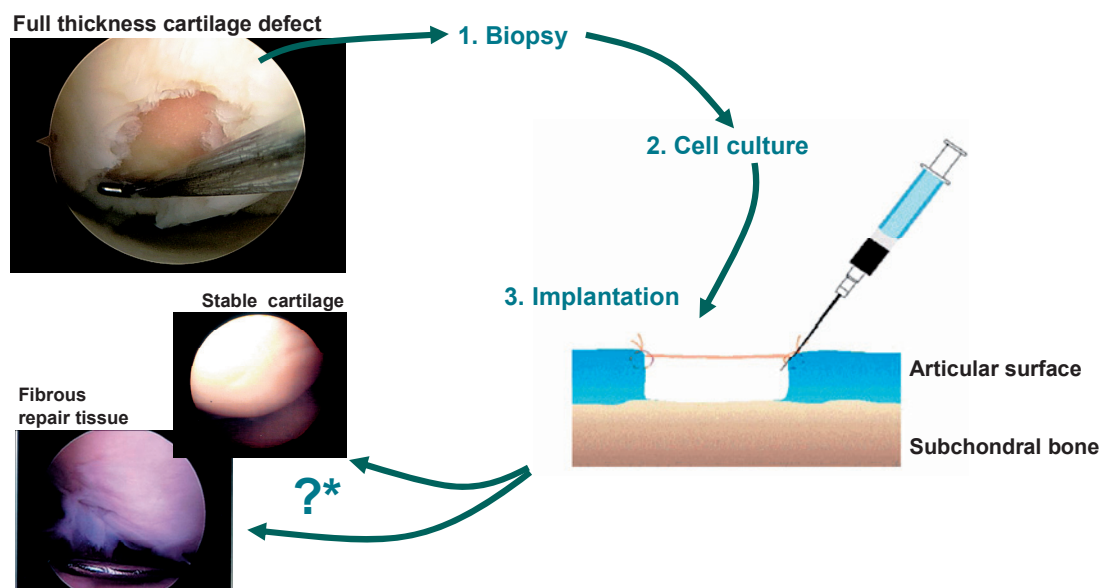
Surgical procedure	Description	Main Characteristics	Frequency of Use
Debridement and lavage	Shaving of the edges, debridement of loose cartilage and lavage to remove loose tissue debris.	Easy, arthroscopic procedure, but no repair tissue formed.	Most frequently used procedure for cartilage damage.  Current use in the U.S. is estimated at 550,000 cases/year
Microfracture	Perforation of the subchondral bone plate to create a blood clot which, mixed with bone marrow stem cells, tends to form a scar-like fibro-cartilaginous repair tissue.	Easy arthroscopic procedure, but since the repair tissue is not hyaline-like cartilage, its functional quality is limited and cannot withstand wear over time.	Microfracture is considered today the standard of care for smaller cartilage defects up to 2-3 cm <sup>2</sup> .  Current use (including abrasion arthroplasties) in the U.S. is estimated at ca. 75,000 cases/year
Osteochondral grafting (mosaicplasty)	Osteochondral grafting is a technique in which one or more plugs of cartilage and bone are harvested from a lesser weight-bearing area in the joint and subsequently transplanted into the defect.	Implants tend to give immediate mechanical support. Harvest site co-morbidity is, however, very large and chances of failure are high.	The use of osteochondral grafting is limited and decreasing.  Current use in the U.S. is estimated to be below 5,000 cases/year

While debridement and lavage is the most frequently used procedure, microfracture appears to be the currently accepted standard of care for small-sized cartilage defects. However, it is recognised that microfracture often leads to the formation of scar-like fibro-cartilaginous repair tissue, which, unlike stable hyaline-like cartilage, has not been associated with successful long-term clinical outcomes.

### **Autologous Chondrocyte Implantation (“ACI”)**

ACI is a technique designed to regenerate articular cartilage by implanting the patient's own expanded cartilage cells, and was developed in order to address the limitations of the surgical procedures described above. ACI was invented in the early 1980s by researchers at the Hospital for Joint Diseases in New York and was subsequently improved at the University of Göteborg in Sweden. Figure 5.4. gives an overview of the ACI procedure. When a patient is diagnosed with a symptomatic cartilage defect eligible for ACI treatment, a small cartilage biopsy is taken arthroscopically from a healthy, non-weight bearing area of the joint. The cells are subsequently transported to a cell expansion laboratory and, after approximately 3-5 weeks of cell culture, the expanded cells are sent back to the surgeon for re-implantation in the patient. In conventional ACI, the cells are implanted underneath a periosteal flap, which has been harvested from the patient's tibia and sewn onto the cartilage defect. Newer techniques employ a collagen membrane rather than a periosteal flap, or use a 3-D matrix in which the cells are seeded.

**Fig. 5.4.: Autologous Chondrocyte Implantation (“ACI”)**



\* The question mark indicates an important unknown in the ACI procedure: will the cells, after expansion be able to make stable cartilage or will they form a scar-like fibrous or fibrocartilaginous tissue?

Although over 15,000 patients have been treated using ACI since the 1980s, only a fraction of patients suffering from cartilage defects are currently treated in this way. The Company believes that the limited market share of ACI procedures is attributable to several factors, most notably the following:

- **There is insufficient histological proof that ACI leads to formation of stable hyaline-like cartilage.** It is known that cartilage cells have the tendency to dedifferentiate (lose their specific characteristics) during cell culture. Conventional culturing techniques will normally yield a sufficiently high number of cells to fill the defect, but these cells have often lost their original cartilage phenotype and so may lack the capacity to form stable cartilage. In many cases the re-implanted cells will produce fibrous tissue instead of stable cartilage.
- **ACI lacks validation from well-controlled clinical trials.** There is still insufficient evidence that ACI provides good structural and clinical outcome in prospective, randomised, controlled clinical trials, which the Company believes has inhibited adoption of the procedure by medical professionals.
- **ACI is a relatively complex surgical procedure.** The current procedures in most cases involve open knee surgery for the implantation of the cells.

The ChondroCelect development programme has focused on providing solutions for these hurdles and thus aims to exploit the potential of the ACI market.

### **Cartilage defects: prevalence and incidence**

According to current medical practice, ICRS Grade 3-4 full-thickness cartilage defects (lesions in which underlying bone is exposed) are eligible for treatment with ACI. No accurate market data are available for this specific indication. TiGenix estimates the incidence of such focal cartilage defects (in otherwise healthy joints) in Europe and the United States to be around 130,000 cases annually. This estimate is

based on an analysis of the number of arthroscopies and the incidence of different types of cartilage defects. Studies have shown that full-thickness cartilage defects are detected in approximately 11% of all knee arthroscopies (*The American Journal of Sports Medicine*).

It is the Company's experience that practically all full-thickness cartilage lesions, following debridement, are larger than 1 cm<sup>2</sup> and consequently are eligible for ACI treatment. In the United States, 680,000 arthroscopies are performed every year. Assuming that full thickness cartilage defects are present in 11% of these cases, a total number of 75,000 eligible patients are implied. By conducting a similar analysis, and taking into account a more conservative diagnostic approach in Europe (proportionally fewer diagnostic arthroscopies), the Company believes there are approximately 55,000 eligible patients for ACI in the European Union.

Opportunities in other markets such as Japan, Australia and China have not been taken into account in the Company's market analysis, but it is believed there may be potential in these markets that could be addressed after FDA or EMEA regulatory approval has been obtained.

#### **5.6.1.2. Product & Technology**

ChondroCelect is a cell-based medicinal product, derived from the patient's own cartilage tissue, which is designed to realise functional and durable repair of full-thickness cartilage defects in knee joints. ChondroCelect is applied through ACI, but uses a well characterised and more potent cell population than standard ACI procedures. When a patient is diagnosed with a symptomatic cartilage defect, a small cartilage biopsy is taken from a healthy, non-weight bearing area of the joint. The cells are transported in a specially designed biopsy kit to TiGenix' GMP cell expansion laboratory. After approximately 3-4 weeks of cell culture, employing TiGenix' proprietary methods, the cells are quality controlled and sent back to the surgeon for re-implantation into the patient's joint. The implantation is done underneath a membrane (periosteal flap harvested from the patient's tibia or a collagen membrane) that is sewn onto the cartilage defect.

ChondroCelect significantly improves the ACI procedure, moving it from a cell culture service into a consistent and quality-controlled cell-based medicinal product. The key differences between ChondroCelect and other ACI procedures are:

- ChondroCelect is associated with a well-characterised, more potent cell population, which is able to make stable hyaline-like cartilage *in vivo* and therefore aims to create functional and durable repair; and
- ChondroCelect benefits from extensive clinical validation. As far as TiGenix is aware, ChondroCelect is the only ACI product to have proven structural superiority over microfracture in a prospective, randomised, controlled clinical trial.

ChondroCelect has been developed to exhibit features that address the most important aspects of cartilage biology.

#### **Selection of more potent and better characterised cell population**

By applying TiGenix' core cell culture and proprietary molecular marker technology, ChondroCelect uses a specific cell population that has a proven capability of forming stable hyaline-like cartilage *in vivo*. Cartilage comprises a complex mixture of active cells, known as chondrocytes, circa 5%, embedded in a scaffold-like matrix. In order to obtain sufficient cells for cell implantation, the small number of chondrocytes harvested from the patient has to be increased (expanded) in culture, a process in which the cells undergo a number of doublings. It is known that chondrocytes easily lose their biological

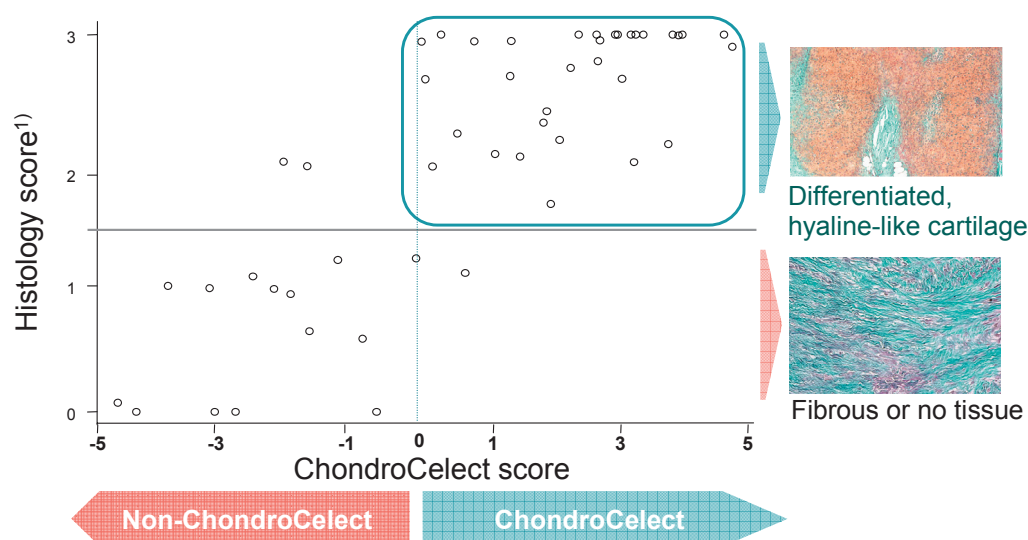


characteristics, or phenotype, during cell culture. Once implanted back into the patient, they will often no longer be able to make stable hyaline-like cartilage *in vivo*. Instead, they are more likely to form less durable, fibro-cartilagenous tissue or bone-like tissue.

The ChondroCelect cell culture method has been optimised to enable the harvested chondrocytes to retain their biological characteristics during cell expansion. The Company has identified and patented several proprietary genetic markers, the presence or absence of which can be correlated with the ability of chondrocytes to form stable, hyaline-like cartilage. In two patent filings, already granted in Europe and pending in the United States and Canada, TiGenix has filed for protection of approximately 200 such marker genes (see section 5.10).

The figure below illustrates the correlation between the molecular marker profile identified by the Company, known as the ChondroCelect score, and the type of cartilage formed after implantation of cells in an environment which models the *in vivo* situation found in articular cartilage defects (ectopic environment). A histology score of two or three means the formation of well-differentiated, hyaline-like cartilage, while a score below two means that an undifferentiated fibrous or fibrocartilagenous tissue is formed. TiGenix uses the ChondroCelect score as a measure of quality control to ensure that only potent cartilage-forming cells are implanted into the patient.

**Fig. 5.5.: Correlation between the molecular marker profile and type of cartilage formed *in-vivo***



1) Type of tissue found in *in-vivo* assay: 3 = hyaline-like cartilage; 2 = differentiated cartilage tissue; 1 = fibro-cartilagenous tissue; 0 = no tissue

### 5.6.1.3. Clinical validation – Pivotal trial results

#### Introduction

In 2002, the Company initiated a multi-centre, prospective, randomised, controlled clinical trial with a view to obtaining approval for ChondroCelect as a first-line treatment for symptomatic cartilage defects of the knee. The trial, known as TIGACT01, was designed to compare ChondroCelect to the current standard of care, microfracture. By the end of 2004, patient enrolment was completed, with 118 patients<sup>15</sup> treated in

<sup>15</sup> This is the number of patients that entered the clinical trial (i.e., were “enrolled”). It should be noted that the number of patients in the following graphs (Fig. 5.7) is less than 118 due to the fact that (i) 9 patients ended the study before the one-year endpoint had been reached, (ii) for some patients not all the outcome data could be collected (this was subsequently handled as missing data in the statistical analysis), and (iii) some patients refused to enter the long-term follow-up (beyond 12 months).



nine Belgian and three international centres (The Netherlands, Germany, Croatia). The Company designed the study to demonstrate short term structural superiority (at 12 months) with a long-term patient follow-up period of up to five years.

The TIGACT01 trial results at 12 and 18 months demonstrate that the primary objective of the study has been achieved:

- (a) at 1 year following treatment, ChondroCelect formed regenerated tissue that was superior to the repair tissue formed following microfracture;
- (b) at 6, 12 and 18 months clinical outcome was similar for both treatment groups.

In addition, a sub-group of patients treated within two years since the onset of symptoms showed a statistically significant superior clinical outcome at 18 months follow up in patients treated with ChondroCelect, and a correlation was noted between the ChondroCelect gene score and the clinical outcome (measured by overall KOOS) at 12 and 18 months post treatment.

The trial results have been presented at the yearly meeting of the American Academy of Orthopedic Surgeons in February 2007 in the United States.

As far as the Company is aware, TiGenix is currently the only company to have completed a GCP-controlled, prospective, randomised multi-centre clinical trial for a cell-based therapy product intended for cartilage repair. The Company believes that a trial of this level of stringency is necessary for cell- and tissue-based products, in order to obtain marketing authorisation in Europe and the United States.

The pivotal TIGACT01 trial data has been complemented by supplementary information from an open label trial and other clinical programmes:

- an open label trial for the treatment of complex cases at the Belgian military hospital;
- an expanded access programme for the treatment of complex and salvage cases at three hospitals in Belgium;
- a compassionate use (named patient) programme in Belgium, the Netherlands, Germany, UK and Luxemburg.

## TIGACT01 Trial Results

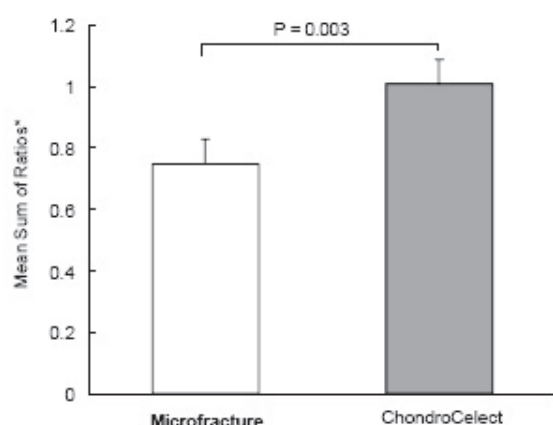
The analysis of the TIGACT01 trial at 12 and 18 months post-surgery demonstrates that the primary endpoint of the study has been achieved.

### a) Structural superiority at 12 months post surgery

The TIGACT01 study demonstrated that treatment with ChondroCelect resulted in superior structural repair compared to microfracture, as determined by histological analysis of biopsies taken 12 months after treatment (Figure 5.6.A and B). The repair tissue formed by patients treated with ChondroCelect was found to be less fibrous and to display features indicative of more durable hyaline-like cartilage.

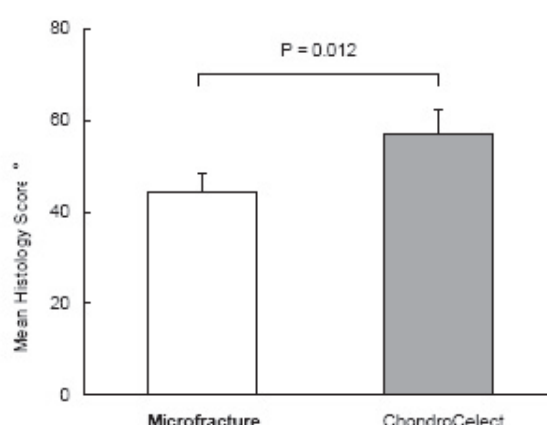
**Fig. 5.6.: Structural outcome at 12 months**

#### A. Computer-Assisted Histomorphometry



\* Sum of staining intensities for Collagen II and Safranin-O, indicators of characteristics of hyaline-like cartilage

#### B. Overall Histology Assessment



\* Mean histological scores of two blinded histopathologists

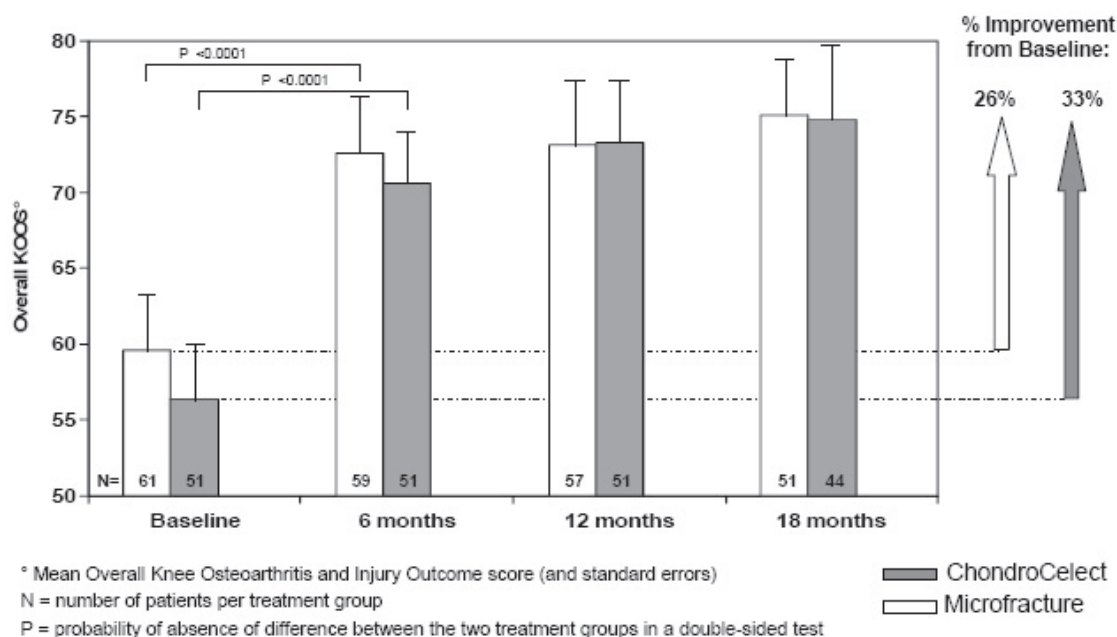
P = probability of absence of difference between the two treatment groups in a double-sided statistical test

### b) Clinical non-inferiority with microfracture and strong improvement compared to baseline

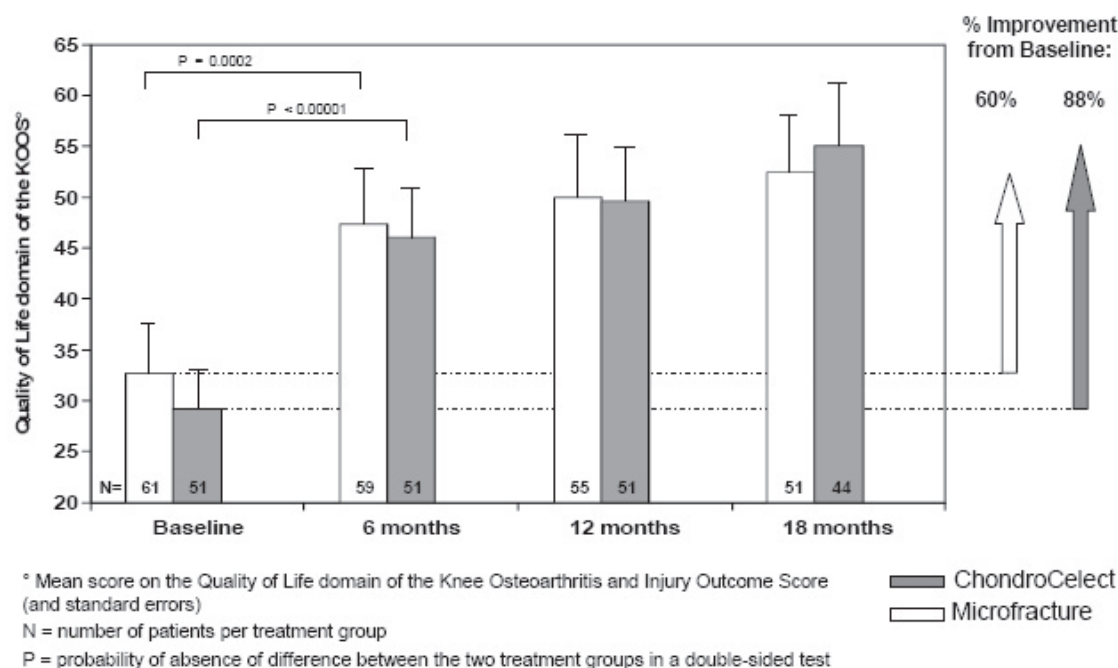
In addition to confirming the superior quality of the cartilage formed following treatment with ChondroCelect, versus the more traditional microfracture procedure, a further objective of the trial set out to compare the differences in the rates of improvement on clinical outcome parameters, such as pain and function, witnessed between the two groups. Patients studied in the ChondroCelect group required both an arthroscopy (to perform the harvest biopsy), and open knee surgery (to implant the therapeutic cells), whereas patients in the microfracture group only required an arthroscopy. Due to these inequalities, it remained a possibility that open surgery with ChondroCelect would be disadvantageous to the pace of recovery and clinical benefit displayed by patients in the ChondroCelect group. However, the results from this study demonstrated that six months following treatment, patients in the ChondroCelect group had improved significantly ( $p < 0.0001$ ) compared to the baseline, and that patients receiving ChondroCelect recorded similar clinical outcomes to those patients treated by microfracture treatment. Furthermore, the average improvement scores recorded at 12 and 18 months post-surgery confirmed that the clinical outcomes remained similar in both treatment groups, with a slight advantage in improvement from baseline witnessed in patients treated using ChondroCelect (Figure 5.7.).

**Fig. 5.7.: Clinical outcome at 6, 12 and 18 months**

**A. Evolution of Overall KOOS during the first 18 months post-surgery follow-up**



**B. Evolution of Quality of Life during the first 18 months post-surgery follow-up**



**c) Discussion of results**

TiGenix has completed its Phase III clinical trial with both the structural and clinical endpoints being reached. Furthermore, not only did the Company demonstrate that it is possible to conduct these types of

studies, it also showed that its well-characterised and potency-based product, ChondroCelect, can regenerate hyaline-like cartilage.

In conclusion, the use of characterised chondrocytes in autologous cartilage repair represents a new class of treatment which is associated with superior structural repair of cartilage tissue, compared to microfracture. In the short-term, the risk-benefit profile for ChondroCelect and microfracture appears to be similar, and supporting a first-line use.

The improved structural repair recorded in patients receiving ChondroCelect, during the TIGACT01 Phase III clinical trial, confirms the results obtained earlier in pre-clinical experiments. In all, the results have confirmed the Company's development strategy and further demonstrated the importance of a well-characterised product, defined using tests for specific potency markers. Based on these data, the Company believes that ChondroCelect has the potential to significantly increase the success rate of cartilage regeneration procedures.

Patients in the study will be followed up to 5 years in order to assess the longer-term clinical response.

#### 5.6.1.4. Next Steps

Having described the successful outcome of the TIGACT01 study, the next steps in the development of ChondroCelect remain:

- **To achieve regulatory approval.** The data from the TIGACT01 study and from the additional studies form the basis for the regulatory submissions the Company is currently preparing.
- **To develop a successful commercialisation strategy.** By building early support from key opinion leaders in the field, in the years prior to launch, TiGenix aims to ensure a rapid and wider acceptance of ChondroCelect.
- **Scale-up of manufacturing and logistics.** Whilst manufacturing capabilities exist to cope with the projected initial demand, in anticipation of the further supplies expected, the Company is both negotiating with contract manufacturers as well as considering the acquisition of its own manufacturing facility.

In addition, the Company continues to further improve the product to:

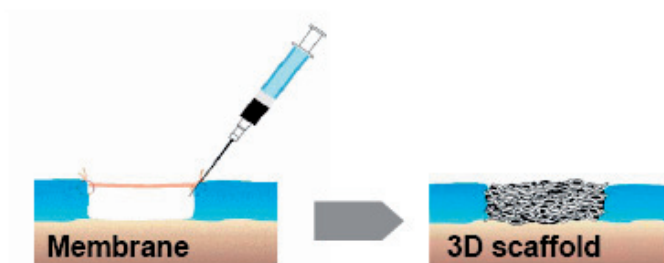
- increase its ease of implantation by combining it with a biological 3D scaffold in view of enabling arthroscopic or minimally invasive implantation of the cells (ChondroCelect-3D); and
- broaden its indication towards defined cartilage damage in joints that are affected by (early) OA. TiGenix is in the process of developing novel ways to boost certain of these biological features, through cell enrichment or through *ex vivo* stimulation with pharmaceutical compounds, and believes this will allow it one day to broaden the product's indication into functional regeneration of cartilage defects in the osteoarthritic joint.

#### 5.6.3. ChondroCelect 3D

In addition to the quality of the cells and clinical validation of the technology, an important driver believed to be necessary for the broader application of cell-based cartilage repair products, such as ChondroCelect, is to make the implantation procedure easier and faster for both the surgeon and patient alike. It is the Company's belief that surgeons who perform these operations would prefer that implantation of the cell product into the cartilage defect can be achieved through the use of minimally

invasive or arthroscopic procedures, which require no stitching. To enable such implantation, the cells would need to be delivered in a biomaterial-based scaffold.

**Fig. 5.8: From injection to arthroscopic implantation of the cells**



TiGenix has acknowledged the importance of such an approach and evaluated different biomaterials for their suitability. In its evaluation, TiGenix has searched for a biomaterial that does not negatively influence the biology and potency of the ChondroCelect product (cells) and that allows for the integration of the cells into the surrounding tissue of the joint environment following implantation.

The material which has been selected is a hyaluron-based scaffold, Hyalograft-C, developed by the Italian company Fidia Advanced Biopolymers ("FAB"). This scaffold is the same as that used in their current cartilage repair product, HyaloGraft-C AutoGraft, which has been used to treat over 4,000 patients in selected European countries. TiGenix and FAB have recently decided to join forces in a strategic partnership, to develop a combined product which is expected to have a strong competitive position in the cartilage repair landscape.

The combination of a potent and efficacious cell product (ChondroCelect) with a scaffold which further enhances the product's regenerative capabilities, and which has already demonstrated its clinical suitability, is believed to be the main characteristics of a preferred cartilage repair product, as was indicated by close to 200 surgeons when asked in a recent survey (at the meeting of the ESSKA, the European Society of Sports Traumatology, Knee Surgery and Arthroscopy, in May 2006).

On January 10, 2007, TiGenix entered into a strategic partnership with FAB. The partnership consists of a License Agreement for HyaloGraft-C, covering all territories outside of Europe, a Cross-License Agreement on ChondroCelect and HyaloGraft-C in Europe and a Worldwide Supply Agreement. TiGenix will pay FAB a license-fee, milestone payments and royalties and will itself receive royalties from sales made by FAB in selected European countries.

#### **5.6.4. MeniscoCelect**

TiGenix initially focused its development efforts on cartilage regeneration products. The expertise gained during the development of ChondroCelect is now being applied to related joint tissues, such as meniscus. Meniscus tissue displays a number of similarities to cartilage tissue, including a limited degree of regeneration, a (fibro-) cartilage-like appearance and the involvement of cells with similar characteristics to those of chondrocytes.

The menisci of a human knee joint are formed by two fibro-cartilaginous, crescent shaped wedges of tissue, which were historically believed to be of little importance to knee-joint functionality. However, it is now clear that they are required for knee stability. Furthermore, their importance is such that even partial meniscal loss is thought to be one of the major reasons for earlier development of OA. Repair of knee-joint menisci is, therefore, essential in the prevention of this disease, as is true of articular cartilage damage.

MeniscoCelect is the Company's biological product in development for the regeneration of meniscus. The development strategy mirrors closely that followed for ChondroCelect. The Company has identified and characterised cells and cell populations isolated from meniscus tissue with respect to the presence or absence of selected molecular markers relevant to the biology of meniscus. A key step is the development of a potency assay, which is currently being finalised by the Company. In addition, the Company has initiated a series of pre-clinical experiments in view of initiating an exploratory clinical study.

### **5.6.5. Research projects**

#### **5.6.5.1. Allogeneic applications**

A number of the Company's research programmes are focused on the development of technology to exploit allogeneic therapies, which use cells derived from a donor source rather than from the patients themselves. Whilst regulatory and technical hurdles remain, including the potential for rejection due to immunogenicity, allogeneic applications have the advantage that they can be prepared in advance and can be used in acute indications, immediately following diagnosis. Such applications could further broaden the market acceptance and use of cell-based therapies, together with simplifying the associated logistics, resulting in possible cost reductions.

#### **5.6.5.2. Adult stem cell platform**

Another research programme of the Company aims at developing a proprietary stem cell platform. Stem cells might be better suited for allogeneic applications and in this context the Company has set up a research programme to further explore their potential. TiGenix' stem cell platform, which focuses on adult mesenchymal stem cells ("MSCs") isolated from the synovial membrane of the knee, is protected by a granted patent. Initial findings have indicated that specific subpopulations of these MSCs are responsible for particular biological characteristics, with further work currently ongoing to identify and select optimal traits.

#### **5.6.5.3. Targeted therapeutics**

A further research programme is underway to identify novel targets associated with OA, with the intention of using the information to develop pharmaceutical products, including both small molecules and biologicals, which could be used to slow or prevent progression of the disease. Based on its understanding of the biology of cartilage, the Company has identified, in collaboration with the Katholieke Universiteit Leuven, a set of potential OA targets. The first of these targets have been functionally validated with additional verification experiments planned.

In addition, TiGenix has developed a set of high-content screening assays which use human chondrocytes and stem cells to assess the effect of compounds on the different aspects of cartilage biology. The use of these assays in a testbank enables the biologically intelligent screening of compounds, in order to identify those with a potential therapeutic effect in OA.

The progression of this targeted therapeutics programme will require the application of complementary technologies, in particular those of medicinal chemistry and rational drug design. Since this will utilise different skills and resources outside of the Company's main focus, the Company has initiated discussions with other parties, including the Katholieke Universiteit Leuven, to access such complementary technologies and to possibly jointly create a new drug discovery company. TiGenix would maintain a stake in this new company and keep a first right to use any potential compounds to be used in combination with its cell-based therapy portfolio (ex vivo applications).

## 5.7. REGULATORY & REIMBURSEMENT

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### 5.7.1. Regulatory

#### 5.7.1.1. Introduction

The Company believes that the key to success in cell- and tissue-based therapies is to excel in “evidence-based medicine”. Only by proving efficacy in prospective randomised clinical trials and by demonstrating the health-related economic benefits in well-designed pharmacoeconomic studies, will it be possible to convince Regulatory Authorities of the overall benefits provided by the use of these products. Under “evidence-based medicine”, it is no longer sufficient just to demonstrate the safety of cellular products, as their efficacy and potency also must be demonstrated and validated. The Company anticipated this early on and so positioned its cell-based products as defined medicinal products.

Since cell-based therapies are a relatively new field, the regulatory framework for these products is continuously developing. When TiGenix started designing its first clinical trials for ChondroCelect, no clear regulatory framework for cell-based products existed in Europe. The Company therefore looked to the FDA for guidance, who had made the choice to regulate these products for cartilage repair as biologics. TiGenix decided to set up a fully controlled, prospective randomised clinical trial in compliance with Good Clinical Practice (“GCP”) requirements deriving from Directive 2001/20/EC<sup>16</sup> as well as related implementation measures and applicable guidelines, thus anticipating the increasing regulatory requirements of the European Regulatory Authorities.

#### 5.7.1.2. General background

Regulation by governmental authorities worldwide is a significant factor in the development, manufacture, commercialisation and reimbursement of TiGenix’ product portfolio. All of the Company’s products will require marketing approval, or licensure, by governmental agencies prior to commercialisation.

In particular, human medicinal products are generally subject to rigorous preclinical and clinical testing and approval procedures of the U.S. Food and Drug Administration (“FDA”) in the United States, the European Medicines Agency (“EMA”) in Europe and similar Regulatory Authorities in other countries. Various governmental statutes and regulations also govern or influence testing, manufacturing, safety, labeling and record keeping related to such products and their marketing. State, local or other authorities may also regulate pharmaceutical manufacturing facilities. The process of obtaining such approvals and the subsequent compliance with the appropriate statutes and regulations require the expenditure of substantial amounts of time and money and there can be no guarantee that approvals will be obtained.

For classic pharmaceutical products, the pre-clinical and clinical development paths are broadly similar in Europe and in the United States. Initially, pre-clinical studies are conducted to evaluate the mode of action and *in vivo* tests are conducted until adequate proof of safety is established. Upon successful completion of pre-clinical studies, Regulatory Authorities may grant approval for clinical trials, which are typically conducted in three sequential phases that may overlap. In Phase I clinical trials, which consists of the initial introduction of the pharmaceutical into healthy human volunteers, the emphasis is on testing for safety and adverse effects, dosage tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase II clinical trials consist of studies in a limited patient population to determine the initial efficacy of the pharmaceutical for specific targeted indications, to determine dosage tolerance and optimal dosage and to identify possible adverse side effects and safety risks. Once a compound shows evidence of effectiveness and is found to have an acceptable safety profile in Phase II clinical trials, Phase III clinical trials are undertaken to more fully evaluate clinical outcomes.

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<sup>16</sup> Directive 2001/20/EC of the European Parliament and of the Council of April 4, 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.



For cell-based products, the clinical development paths are today less standardised than for classic pharmaceutical or biological products. Especially for autologous cell-based products, the distinction between Phase I, Phase II and Phase III clinical trials is in most cases not relevant or possible. Moreover, phases can often be combined. Both the EMEA and the FDA are aware of the specificities of cell-based products. Increasingly, a distinction is made between so-called “exploratory” studies (*i.e.*, studies to confirm the proof of concept and establish the safety profile of the product) and so-called “confirmatory” studies (*i.e.*, studies to establish the proof of efficacy in view of potential approval on the market). On the other hand, more attention is given to the upfront part, the characterisation of cell-based products and the development of assays to measure the biological activity (potency) of cell-based products.

#### **5.7.1.3. United States – FDA approval process**

The U.S. Food and Drug Administration (“FDA”) was the first to adopt a clear regulatory framework for cell therapy products. With the exception of cell-based products for skin repair, most cell therapy products are now being regulated as biologics (medicinal products) by the Center for Biologics Evaluation and Research (“CBER”), requiring product characterisation and solid clinical validation in prospective randomised clinical trials.

TiGenix believes that its products will be regulated as biological products. The FDA generally requires the following steps for pre-market approval or licensure of a new biological product:

- pre-clinical laboratory and animal testing, conducted to assess a product’s biological activity, to identify potential safety problems and to fully characterise and document the product’s manufacturing controls, formulation and stability;
- submission to the FDA of an Investigational New Drug (“IND”) application, which must become effective before clinical testing in humans can begin in the United States;
- obtaining approval of Institutional Review Boards (“IRBs”) of research institutions or other clinical sites to introduce the biological drug candidate into humans in clinical trials;
- adequate and well-controlled human clinical trials to establish safety and efficacy of the product for its intended indications, conducted in compliance with the FDA’s Good Clinical Practice (“GCP”) requirements;
- compliance with all Good Manufacturing Practice (“GMP”) regulations and standards;
- submission to the FDA of a biologics license application (“BLA”) for marketing that includes adequate results of pre-clinical testing and clinical trials;
- FDA review of the BLA in order to determine, amongst other things, whether the product is safe, effective and potent for its intended uses; and
- obtaining FDA approval of the BLA, including inspection and approval of the product’s manufacturing facility as being compliant with cGMP requirements, prior to any commercial sale or shipment of the product.

Typically, clinical testing involves a three-phase process. Phases may however overlap.

#### **Phase I Clinical Trials**

In the United States, Phase I clinical trials can only start after an Investigational New Drug (“IND”) application has been submitted and has become effective. Phase I clinical trials can be performed outside the United States if the relevant Ethics Committee and Regulatory Authority approvals are obtained. Phase I clinical trials are initially conducted in a limited population to evaluate a drug candidate’s safety profile and the range of safe dosages that can be administered to the patient.

## Phase II Clinical Trials

As in Phase I clinical trials, relevant Ethics Committee and Regulatory Authority approvals are required before initiating Phase II clinical trials. These trials are conducted in a limited patient population to further determine the possible adverse effects and safety risks for the drug candidate, evaluate its initial efficacy for specific indications and determine dose-tolerance and optimal dosage. The first Phase II clinical trials – which are sometimes referred to as Phase IIa clinical trials – may be conducted in few patients to demonstrate preliminary safety and efficacy. Additional Phase II clinical trials – which may be termed Phase IIb clinical trials – may be conducted in a larger number of patients to confirm the safety and efficacy data generated in the Phase IIa studies and to refine optimal dosing.

## Phase III Clinical Trials

As in Phase I and Phase II clinical trials, relevant Ethics Committee and Regulatory Authority approvals are required before initiating Phase III clinical trials. These trials, which are sometimes referred to as registration or pivotal studies, are undertaken when Phase I and/or II clinical trials suggest that the drug candidate is effective and has an acceptable safety profile and an effective dosage has been identified. In Phase III clinical trials, the drug candidate is usually tested in a blinded controlled randomised trial comparing the investigational new drug to an approved form of therapy in an expanded and well-defined patient population and at a number of hospitals and medical practices. When no alternative is available, investigational new drugs are tested against placebo. The goal of these studies is to obtain statistical evidence of safety and efficacy of the investigational new drug as compared to an approved standard treatment or placebo, as the case may be, in defined patient populations with a given disease and stage of illness.

Upon successful completion of the above-referred clinical trials, the sponsor may submit an application for marketing authorisation to the relevant Regulatory Authority. After review of the application, the Regulatory Authority may grant marketing authorisation, deny the application or request additional information, including further clinical testing of the drug candidate. When granting marketing authorisation, a Regulatory Authority may impose upon the sponsor an obligation to conduct additional clinical testing, referred to as Phase IV clinical trials or post-approval commitments, to monitor the drug after commercialisation. Additionally, marketing authorisation may be subjected to limitations on the indicated uses for the drug.

After marketing authorisation has been obtained, the marketed drug and its manufacturer will continue to be subject to regulations and review. The conditions for marketing authorisation include requirements that the manufacturer of the drug complies with current Good Manufacturing Practices (“cGMP”) as well as ongoing inspection of manufacturing and storage facilities.

As indicated above, the development path for cell-based products is today less standardised and less guidance exists than for classic pharmaceutical products. In 1996, the FDA developed a guidance document for products comprised of living autologous cells intended for structural repair (MAS-cells; Docket No. 95N-0200). This document states that *“the Agency recognises that a flexible approach for the clinical investigations of MAS-cells may be feasible because of certain attributes of structural defects and MAS cell therapies”*.

### 5.7.1.4. Europe – EMEA approval process

Although different terminology is sometimes used, the general approval process for medicinal products by the European Medicines Agency (“EMA”) in Europe is quite similar to the process in the United States described above.

Similar to the United States, prior regulatory approval is required in EU Member States for the commencement of clinical trials on human healthy volunteers. Currently, in each EU Member State, following successful completion of Phase I clinical trials, data is submitted in summarised format to the

relevant Regulatory Authority in the Member State in respect of applications for the conduct of later Phase II clinical trials. The Regulatory Authorities in the EU typically have between one (1) and three (3) months from the date of receipt of the application to raise any objections to the proposed clinical trial and they often have the right to extend this review period at their discretion. The authorities may require additional data before allowing the studies to commence and could demand that the studies be discontinued at any time if there are significant safety issues. In addition to obtaining regulatory approval, clinical trials must receive Ethics Committee approval. The exact composition and responsibilities of the Ethics Committees differ from one EU Member State to another. In each EU Member State, one or more independent Ethics Committees (depending on whether the study is a monocentre or multicentre clinical trial) will review the ethics of conducting the proposed research.

Upon successful completion of Phase III clinical trials, the sponsor may submit a Marketing Authorisation Application (“MAA”) for the drug candidate to EMEA. After obtaining EMEA Marketing Authorisation, the product may be commercially launched. In practice, effective launch is often conditioned upon completion with each national authority of pricing and reimbursement negotiations.

No uniform regulatory framework or well-defined regulatory path exists at present in Europe for cell-based products. To date, cell-based products are (wholly or partially) subject to various legislations. The current lack of an EU-wide framework leads to divergent national approaches as to the legal classification and authorisation of advanced therapy products. Since 2004, steps have been taken towards the development of a framework, which is more in line with the FDA approach to regulating cell-based products. Although the EU is trying to harmonise the applicable rules as the industry further matures, there is still a way to go before a situation similar to that in the United States will be achieved.

An important piece of future EU legislation in the area of cell-based products is the proposed Advanced Therapies Regulation<sup>17</sup>. With this proposal, the EU Commission intends to cover all advanced therapies (i.e., gene-, cell- and tissue-based therapies) within a single, integrated and tailored European regulatory framework. A first draft thereof did not pass the vote in the European Parliament in the last quarter of 2006 but an amended version received an almost unanimous positive vote in the Environment Committee of the European Parliament on January 30, 2007. A new plenary vote is planned for March 2007. The proposed Advanced Therapies Regulation will require authorisation, supervision and post-authorisation vigilance for cell-based products on the market. It will provide a uniform and direct access to the market, which will be welcomed by industry, and requires demonstration of quality, safety and efficacy of the products. As a result, the bar will become significantly higher for cell-based products, requiring clinical trials, GMP manufacturing and marketing approval for entry on the market.

#### **5.7.1.5. Regulatory situation of ChondroCelect**

The Company’s lead product, ChondroCelect, has completed a randomised Phase III clinical trial and is currently preparing the submissions for market approval as a medicinal product.

Taking into account the uncertain regulatory framework in Europe, TiGenix chose to base its regulatory strategy for ChondroCelect on the existing regulations in the United States and to follow a similar process in Europe.

In June 2005, ChondroCelect was ruled as a cell therapy medicinal product by EMEA. This designation makes the ChondroCelect eligible for central approval with EMEA, thus providing a more direct access to the markets of the EU Member States, as approval, if and when granted, is automatically valid in all the EEA countries. To date, TiGenix has received Scientific Advice from EMEA and had a Pre-Submission MAA meeting. The Company intends to submit its MAA dossier to EMEA in the first half of 2007.

In the future, ChondroCelect is likely to fulfill the definition of a human Tissue Engineered Product (“hTEP”) and thus to fall within the scope of the proposed Advanced Therapies Regulation. Article 29 of the proposed Advanced Therapies Regulation indeed stipulates that advanced therapy medicinal

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<sup>17</sup> Proposal for a Regulation of the European Parliament and of the Council COM(2005) 567 final 2005/0227 (COD) on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004, dated November 16, 2005.

products (including tissue-engineered products) which were on the Community market at the time of entry-into-force of the Regulation, will have to comply with this Regulation within a certain period of time. The definition of hTEP is, however, not final. In addition, the Company cannot predict when the Advanced Therapies Regulation will be enacted nor can it estimate at present the potential impact on the Company's business.

In the United States, the Company has taken the necessary steps to start the procedure with the FDA to obtain a marketing authorisation for ChondroCelect. In 2004, the Company had a pre-IND meeting with the FDA. This meeting had been requested by the Company to ask the FDA's advice on the regulatory path towards obtaining approval for ChondroCelect, taking into account that the clinical trial had been ongoing for some time and patient enrollment was approaching its end. The FDA encouraged TiGenix to file an IND application, with a view to obtaining a potential Biological License Approval ("BLA") based on the results from the European patients in the trial. This IND application was submitted in 2005. Discussions are currently ongoing with respect to the timing of the possible filing of an application for obtaining a BLA. TiGenix aims to file the BLA in 2008.

### 5.7.2. Reimbursement

#### Europe

Pricing and reimbursement are not harmonised in Europe and fall within the exclusive competence of the national authorities, provided that basic transparency requirements described in Directive 89/105/EEC of December 21, 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems are met. As a consequence, reimbursement mechanisms by private and public health insurers vary from country to country. In public health insurance systems, reimbursement is determined by guidelines established by the legislator or a competent national authority. In general, inclusion of a product in reimbursement schemes is dependent upon proof of the product efficacy, medical need, and economic benefits of a product to patients and the healthcare system in general. Acceptance for reimbursement comes with cost, use and often volume restrictions, which again vary from country to country.

TiGenix is currently performing an analysis of the pricing and reimbursement landscape in Europe. Initial findings show that there is no general reimbursement for ACI products in Europe due to a lack of robust data from clinical trials. However, several countries have established processes to reimburse novel therapies like ACI, although the stakeholder and decision-making pathway varies significantly between territories.

In free-price markets, pricing and reimbursement will be managed primarily at the local level, with national-level input likely to be influential in terms of guidelines. E.g. in the UK, ACI is being reimbursed as long as patients are included in one of the two large scale trials initiated by the National Institute for Health and Clinical Excellence ("NICE"), which assesses cost effectiveness in the UK, while in Germany the public healthcare insurance (*Krankenkassen*) will officially reimburse membrane-covered (periosteum, collagen) autologous chondrocyte implantation ("ACI") on the knee joint as of July 2007 if the quality control criteria and documentation requirements defined by the Common Federal Committee (*Gemeinsame Bundesausschuss*) are met.

In price-controlled markets, pricing and reimbursement will be set at the national level, with restrictions in place to manage use. In absence of clear reimbursement policies, ACI is often being reimbursed by public and private payers after prior authorisation.

The ChondroCelect pricing and reimbursement track will differ from the route conventional ACI therapies have taken until now, since ChondroCelect will follow the pricing and reimbursement track for medicinal products. Similar to pharmaceutical products, a pricing and reimbursement dossier must be submitted to the national authorities. Price and reimbursement level will depend on the strength of the clinical data set and, as for most novel therapies, restrictions may apply. The Company is performing further analysis to

understand how restrictions change as the price increases. The ultimate goal is to define the optimal point in this range.

## United States

In the US, only one cell-based product for cartilage repair is on the market. This product, Carticel® from Genzyme (Cambridge, MA), is thought to be reimbursed by 85% of the payers. The target population for ACI are persons between 18 and 55 years, for which worker compensation plans and private insurers are the main payers. Also Medicare, the federal healthcare programme for the elderly and disabled, initiated reimbursement of ACI in 2005. Genzyme has obtained a special reimbursement code (HCPCS J-code 7330) for the Carticel® product. The current in-market price for Carticel in Medicare is US\$18,285 and the National Average Payment<sup>18</sup> for commercial reimbursement of the cells is US\$29,625. In order to ease the administrative burden on facilities and to remove financial considerations from the mind of physicians, Genzyme contracted with US Bioservices, a specialty pharmacy that manages the full reimbursement process for Carticel®.

In 2007, the Company will engage in a detailed dialogue with key decision makers at different payers in order to identify unique preferences and concerns by payer type and to obtain insight in the perceived value drivers, reimbursement barriers and price elasticity for ChondroCelect. Based on this information, the Company will create its pricing and reimbursement strategy and infrastructure before the launch of the product.

## 5.8. COMMERCIALISATION STRATEGY

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TiGenix aims to obtain central approval in the United States and Europe and will commercially launch ChondroCelect once all regulatory approvals will have been obtained. In anticipation of the commercial launch, ChondroCelect is already being made selectively available to key reference surgeons in Europe in the context of a compassionate use (named patient) programme, thereby building early support from key opinion leaders for the Company.

Furthermore, TiGenix focuses on ensuring a strong scientific dissemination and communication to both the medical community and general public in the years before the launch. A key event is the publication of the Phase III study results and the subsequent presentation of these data at the AAOS (AANA Specialty Day Meeting), the largest orthopaedic congress in the world, in February 2007. In addition, TiGenix will be present at the key events in its industry to build brand equity and generate a strong interest in order to ensure an early adoption of its ChondroCelect product after the commercial launch.

For the ChondroCelect launch, TiGenix will follow a reference centre strategy. The Company has already identified top reference centres in Europe and the United States. The clinics will become international reference centres and the opinion leaders will be involved in activities to support and broadly disseminate the clinical trial results. In the first years, the Company intends to develop the market with an internal direct sales force, assisted where necessary by selected local players (agents and distributors).

The Company has started to build its own specialised sales force, taking into consideration the specific needs and requirements when marketing cell therapy products. Next to selling ChondroCelect, the training and education of surgeons and hospital staff are a key priority for the sales team and one which also requires such a specialised rep profile. When the market expands, the distribution of the product is likely to require a broader commercialisation effort and distribution partnership with larger companies with specialised orthobiological sales teams will be considered.

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<sup>18</sup> Ingenix, HCPCS Level II Updateable 2006.



## 5.9. MANUFACTURING & LOGISTICS

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The Company has established its own central cell expansion facility (“CEF”), located at the University Hospital in Leuven, Belgium. In 2005, this facility was GMP-approved for the production of clinical trial batches. Based on the Company’s current operational plan, the CEF’s capacity is believed to be sufficient to serve customers in Europe for the initial years of commercialisation. However, at this stage, the Company has not received a manufacturing authorisation for commercial production, import and export of ChondroCelect. An application in respect of this will be made in due course.

Furthermore, upon transposition into Belgian law of Directive 2004/23/EC<sup>19</sup>, a recognition of the Company as a tissue establishment or, alternatively, a collaboration between the Company and a tissue establishment may be required.

Efficient manufacturing is of strategic importance within the Company as it utilises some of the Company’s core know-how (specific culture methods). During the first years of operation, TiGenix has developed and improved its cell culture technologies and related operations. As the demand for its products grows, TiGenix will evaluate different manufacturing expansion options, which may include outsourcing of certain activities.

In Europe, TiGenix has initiated the process of identifying a new centralised production location as it anticipates a need for additional capacity in the coming years. In the United States, the Company is evaluating different manufacturing options. In parallel with a search for an in-house facility, discussions are ongoing with specialised contract manufacturing organisations. Scalability and control of the cell culture process, as well as a strategic logistic location, will be the key decision drivers.

In a ChondroCelect-treatment procedure, logistics are an important success factor for which TiGenix has worked out a standardised procedure. To this end, the Company has installed a support desk at its head office that manages all logistics arrangements. Transportation of biological samples (patient biopsies) and final products (ChondroCelect) are handled by selected ISO 9001 certified courier services. The biological samples and ChondroCelect are packed in sterile and tamper proof packaging, and conditioned at the appropriate temperature.

## 5.10. INTELLECTUAL PROPERTY

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From its creation, the Company has implemented an intellectual property protection policy with the objective of protecting its integrated and proprietary tissue engineering platform in the broadest possible way. In general, the Company pursues a strategy of protecting its core technologies and products by broadly filing patent applications and by securing some of the key processes used in cell production and in-house research programmes as proprietary know-how.

The Company’s patent portfolio and all intellectual property related matters are managed by an in-house IP manager in close collaboration with an external patent counsel, Bird Goën & Co.

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<sup>19</sup> Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

### 5.10.1. Patents

To date, TiGenix' patent portfolio consists of two granted European patents and seven pending applications. The figure below gives an overview of TiGenix' patents and patent applications.

**Fig. 5.9.: Overview of TiGenix' patents**

Title	Country/region	Patent/application number (publication number)
<b>Granted patents</b>		
<i>In vivo</i> assay and molecular markers for testing the phenotypic stability	Europe	EP1 218 037 B1
Isolation of precursor cells and their use for tissue repair	Europe	EP1 282 690 B1
<b>Pending Patents</b>		
<i>In vivo</i> assay and molecular markers for testing the phenotypic stability of cell populations for autologous transplantation	U.S.	US 10/089,932 (WO01/24833)
<i>In vivo</i> assay and molecular markers for testing the phenotypic stability of cell populations for autologous transplantation	U.S.	US 10/422,475 (US2003/0235813)
<i>In vivo</i> assay and molecular markers for testing the phenotypic stability of cell populations, and selected cell populations for autologous transplantation	Europe	EPA 04077642.9 (EP-A-1,498,146)
<i>In vivo</i> assay and molecular markers for testing the phenotypic stability of cell populations, and selected cell populations for autologous transplantation	Hong-Kong	HK 05106052.7 (EP-A-1,498,146)
<i>In vivo</i> assay and molecular markers for testing the phenotypic stability of cell populations, and selected cell populations for autologous transplantation	Canada	CA 2,397,610 (WO01/24833)
Isolation of precursor cells and their use for tissue repair	U.S.	US 10/089,994 (WO01/25402)
Isolation of precursor cells and their use for tissue repair	Canada	CA 2,386,506 (WO01/25402)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Europe	EPA 04761478.9 (EP-A-1,653,994)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	U.S.	US 10/595,072 (US2006/0246031)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Canada	CA 2,533,124 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Australia	WO05/014026
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Japan	JP522,851/2006 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Russia	RU2006107536 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Norway	NO20060464 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Israel	IL173,544 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Singapore	SG200600211-7 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	Hong-Kong	HK06105628.3 (WO05/014026)
Use of CXCL6 chemokine in the prevention or repair of cartilage defects	New Zealand	NZ545,702 (WO05/014026)
Compositions comprising muscle progenitor cells and uses thereof	Europe	EPA 03766397.8 (EP-A-1 539 934)
Compositions comprising muscle progenitor cells and uses thereof	U.S.	US 10/522,362 (WO2004/012503)
Methods to maintain, improve and restore the cartilage phenotype of chondrocytes	U.S. provisional	US60/783,986
Identification and use of biologicals for the treatment of OA and related disorders of cartilage	U.S. provisional	US60/820,429



Title	Country/region	Patent/application number (publication number)
Marker genes for use in the identification of chondrocyte phenotypic stability and in the screening of factors influencing cartilage production	U.S. provisional	US60/867,152
<b>Gebrauchsmusters</b>		
Molekulare Marker zum Testen der phänotypischen Stabilität von Zellpopulationen und Zellpopulationen für die autologe Transplantation	DE	200 23 659.8
Isolierung von Vorläuferzellen und deren Verwendung zum Wiederaufbau von Bindegewebe	DE	200 23 640.7

### 5.10.2. Granted patents

The two granted European patents broadly cover the Company's lead cartilage repair product ChondroCelect and its stem cell technology platform. The European patent (EP1 218 037 B1, which patent can remain in force for up to 20 years from its priority date, *i.e.* until October 6, 2019), entitled “*In vivo* assay for testing the phenotypic stability”, protects the tools and methods used to determine novel functional and molecular parameters that define mature cartilage-forming chondrocytes, as well as the use of these parameters as quality control markers in the preparation of cells used for autologous chondrocyte transplantation. The claimed methods and markers form the basis of the potency assay, the product optimisation and the quality control procedures used in the production of ChondroCelect. The equivalent filings in the United States (US 10/089,932) and in Canada (CA 2,397,610) are pending.

The second granted European patent (EP1 282 690 B1, which patent can remain in force for up to 20 years from its priority date, *i.e.* until October 6, 2019), entitled “Isolation of precursor cells and their use for tissue repair”, protects TiGenix' stem cell technology platform. The patent broadly covers methods for the isolation of adult mesenchymal precursor cells that are able to form skeletal or connective tissue such as cartilage, bone, ligament, tendon, meniscus, joint capsule, intervertebral discs or teeth. Further claims relate to cultures of these isolated precursor cells and the use thereof for pharmaceutical purposes or for the production of specific growth factors. The equivalent filings in the United States (US 10/089,994) and in Canada (CA 2,386,506) are pending.

### 5.10.3. Pending patent applications

TiGenix has two additional pending applications that relate to ChondroCelect. The pending application (US 10/422,475) entitled “*In vivo* assay and molecular markers for testing the phenotypic stability of cell populations for autologous transplantation” is filed as a United States continuation-in-part and represents an expansion of the claims granted in EP1 218 037 B1, covering a large number of additional genes associated with the phenotype of stable hyaline cartilage, their use as quality control markers and cell populations characterised by these markers.

The patent application (EP-A-1 498 146) entitled “*In vivo* assay and molecular markers for testing the phenotypic stability of cell populations, and selected cell populations for autologous transplantation” is filed as a divisional European patent application and includes claims to cell populations of chondrocytes with a defined marker profile, pharmaceutical compositions and implants comprising these cell populations. TiGenix in-house target discovery programme has resulted in the identification of a number of novel molecules which influence the proper development of chondrocyte precursors into high quality cartilage. These novel molecules can have an application as marker but also have revealed a number of potential therapeutic targets related to improper development and repair of cartilage with potential applications in the field of OA.

In the U.S. provisional application entitled “Marker genes for use in the identification of chondrocyte phenotypic stability and in the screening of factors influencing cartilage production” (US60/867,152), the use of specific genetic marker sets for determining the phenotypic stability of cultured chondrocyte populations and in screening systems for identifying compounds of use in the treatment of cartilage defects and cartilage related diseases are claimed.

The United States provisional application entitled “Methods to maintain, improve and restore the cartilage phenotype of chondrocytes” (US60/783,986) claims a novel regulatory cell population that can be used to maintain, restore or improve the cartilage phenotype of chondrocytes and chondrocyte precursor cells. The invention also relates to methods for isolating the regulatory cell populations from cartilage.

A patent application (WO2005/014026) entitled “Use of CXCL6 chemokine in the prevention or repair of cartilage defects” was filed and claims the use of CXCL6 for the promotion of cartilage and bone formation *in vitro* and *in vivo* and especially for the repair of cartilage or osteochondral defects or for the formation of bone or cartilage in cosmetic surgery. Other molecules which were considered of particular interest are being evaluated for further testing and will be considered for patenting as soon as further data become available.

TiGenix has also identified novel biologicals that can penetrate the cartilage microstructure and can target surface markers on chondrocytes or chondroprogenitors or enzymes and proteins residing within the articular cartilage in order to modulate their activity. A patent application entitled “Identification and use of biologicals for the treatment of OA and related disorders of cartilage” (US 60/820,429) was filed claiming these novel biologicals and methods of using these biologicals for the local treatment of cartilage defects.

#### **5.10.4. Freedom to operate**

Parallel to the development of TiGenix’ own intellectual property, patent literature related to cartilage repair in general and, more specifically, patents of competing companies, are permanently updated and evaluated, in order to avoid infringement and to explore the space of patentable subject matter.

To date, no patent infringement claims have been made against TiGenix nor by TiGenix against third parties. It is however the aim of TiGenix to take action against any third party products or processes, whether or not protected by patents, that could be considered infringing and, where appropriate, enforce intellectual property rights of TiGenix.

#### **5.10.5. Trade secrets**

TiGenix’ inventions are based on the Company’s expertise in developmental skeletal biology, leading to cell isolation and cultivation procedures for which in some cases only common tools and techniques are used. The experience of TiGenix’ researchers has taught that isolation protocols, growth conditions, cell density and passaging protocols are extremely important in the production process of quality controlled products such as ChondroCelect. For some of these procedures patenting (and thus publication) is neither appropriate nor desirable. However, this is part of TiGenix’ proprietary know-how, and is treated as such within TiGenix. For this purpose, procedures have been installed to maintain the confidentiality and ownership of such proprietary information. These procedures include that all internal and key external researchers and associates sign confidentiality agreements. In addition, the know-how is fragmented between different people according to standard industry practice in order to optimally protect these trade secrets.

### 5.10.6. Trademarks

The Company has secured protection on the “TiGenix” and “ChondroCelect” names by having these registered as trademarks in the most relevant European countries and in the United States. The Company has also filed for trademark protection of the “CCI” and “Chondroboost” names and the “CCI” logo within the Benelux.

## 5.11. COMPETITION

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### 5.11.1. ChondroCelect competition

The market for treatments for cartilage repair, including ICRS grade 3-4 full thickness defects of articular cartilage, which is the label that the Company is initially seeking for ChondroCelect, is highly fragmented and immature. As described in section 5.6.1, current treatment options comprise a range of surgical treatments and conventional ACI-based therapies. The Company is not aware of any pharmaceutical based therapies that directly treat the condition. Consequently, obtaining accurate data that provide a detailed breakdown of market share by product or treatment type is very difficult. However, the Company believes that ChondroCelect’s efficacy, ease of use and novel mechanism of action should enable the product both to capture market share from existing surgical treatments and to grow the current ACI market significantly.

In the United States, only one cell-based ACI product, Carticel<sup>®</sup>, from Genzyme (Cambridge, MA), has obtained FDA-approval. In 2000, the indication for Carticel has been narrowed to second-line treatment, for use in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure.

As far as the Company is aware, several other companies in the United States are making efforts to enter the cartilage repair market. Companies such as ISTO Technologies, HistoGenics and also larger orthopaedic groups such as Depuy (a Johnson & Johnson company) have initiated research projects and started Phase I clinical trials. One other European company, ArthroKinetics, has initiated a Phase I clinical trial in the United States. To the best of the Company’s knowledge, the development and validation of an acceptable potency assay is a key requirement by the FDA in order to be allowed to start Phase III efficacy studies. No Phase III clinical trials in this field have been reported, as far as TiGenix is aware.

Alternative competition may come from cell-free products that also target the cartilage repair market, which will generally be brought to market through the medical device regulatory route. This route is less rigorous than the pharmaceutical or medicinal products regulatory route that the Company is following. The most important competitor in this space is Osteobiologics, which was acquired by Smith & Nephew in July 2006.

In Europe, where the barriers to entry for ACI services and cell-based products have so far been relatively low, different companies have been active in the field. Examples include Verigen, which was acquired by Genzyme in 2005, Codon, CellGenix, Tetec and ArthroKinetics. To the best of the Company’s knowledge, these companies have not initiated prospective, randomised, controlled clinical trials to validate their products.

### 5.11.2. Other competition

For other products in its development portfolio the Company may face competition from companies focusing on other tissues, such as Regen Biologics and Regentis for meniscal repair, or from broad-focus

stem cell companies like Osiris, Aastrom and Lifecell and from diversified regenerative medicine companies such as Curis or Geron.

As there are no therapies currently available that reverse, prevent or block the disease process involved in OA, the market targeted by TiGenix' earlier-stage pipeline, this market mainly comprises pain relieving non-steroidal anti-inflammatory agents (NSAIDs). The Company believes that functionally effective treatments could capture a significant share of this existing treatment market. Different biotech and pharmaceutical companies have set up development programs targeted at the discovery of such disease modifying drugs. In the field of targeted therapeutics for OA, TiGenix could encounter biotech companies like GeneNews and Galapagos as well as most of the larger pharmaceutical companies, in particular Pfizer, AstraZeneca and GSK.

## **5.12. HUMAN RESOURCES**

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TiGenix recognises that the Company's success largely depends on its human capital. Therefore, TiGenix selects talented people to participate and drive its development programmes and to develop its commercial strategy.

TiGenix seeks to offer a dynamic, international and entrepreneurial working environment. On December 31, 2006 TiGenix had in total 44 permanent employees and mandate contractors, 70% of whom work in research and development activities (including clinical development). All permanent employees are based in Belgium. TiGenix's scientific staff has expertise in the broad range of fields including but not limited to molecular biology, cell and developmental biology, immunology, biochemistry, histopathology, rheumatology, surgery and intellectual property.

For further details of the headcount evolution, reference is made to section 7.1.5.5 of chapter 7.

## **5.13. FACILITIES**

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### **5.13.1. Facilities in Belgium**

The Company's registered and main office and research & development site, based in the Technologielaan 3 in Leuven, Belgium, is currently leased pursuant to a number of separate lease agreements.

The Company leases additional premises from the Katholieke Universiteit Leuven (Universitaire Ziekenhuizen Leuven) for its production facility, and also some premises in Herentals for pre-clinical research activities.

For future expansion, the Company intends to move to larger office and R&D facilities in the coming one to two years. Additional manufacturing capacity will be added in response to developing requirements, as discussed in section 5.9.

### **5.13.2. Facilities in the United States**

TiGenix Inc., the Company's U.S. subsidiary, currently leases office facilities located at One Battery Park Plaza, 4th Floor, New York, NYC 10004, U.S.A., from the Partnership for New York City Inc. The current lease agreement expires on April 30, 2007 and negotiations have already been initiated to enter into a new (or renew the current) lease agreement.

The Company executed an option agreement relating to the potential acquisition of certain personal property and leasehold rights in and to a production facility in the United States. TiGenix, together with a U.S. partner has an option until the end of March 31, 2007 to buy the equipment of a manufacturing facility in Memphis, Tennessee (U.S.) and to take over the leasehold rights to this facility consisting of ca. 1,500 m<sup>2</sup> equipped for cell culture and 2000 m<sup>2</sup> expansion space.

#### **5.14. GRANTS & SUBSIDIES**

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Since its incorporation TiGenix has been awarded two research and development grants from the Flemish government. To the extent the granting conditions are met, these grants must not be refunded. Information on these grants is provided in chapter 7. It is the Company's intention to request additional grants from different sources in the coming years.

#### **5.15. LITIGATION**

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On the date of this prospectus and since the incorporation of the Company, TiGenix is and has not been involved in any legal proceeding.

## 6. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULT OF OPERATIONS

*The following outlook discussion contains forward-looking statements, including statements about the Company's beliefs and expectations. Forward-looking statements involve inherent risks and uncertainties and speak only as of the date they are made. The Company cautions investors that a number of important factors could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements. See also "Forward-looking information" on page 38.*

*With respect to the expectations for 2007 there can be no assurance that such expectations will occur due to a number of factors including, among others, general economic and business conditions, industry trends, availability and the terms of funding available, competition, currency fluctuations, failure to achieve the expected research and development results and regulatory approvals to commercialize the product as a medicinal product, the loss of key personnel, availability of suitably qualified personnel on commercially reasonable terms and other factors, some of which are referred to elsewhere in this prospectus. See also "Risk factors", beginning on page 21. All financial information set out in this chapter has been derived from the audited consolidated financial statements of TiGenix as of December 31, 2006 and from the audited financial statements of TiGenix as of December 31, 2005 and December 31, 2004 and for the financial years then ended. The financial information has been presented in accordance with International Financial Reporting Standards ("IFRS").*

### 6.1. OVERVIEW

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Section 5.1 of chapter 5 contains a general overview of the Company's activities.

Since its inception, TiGenix has focused on research and development for damaged and osteoarthritic joints. This has led the Company (1) to hire personnel to work primarily on research and development projects, (2) to collaborate with orthopaedic surgeons and rheumatologists worldwide for technology, product improvements and clinical validation, (3) to conduct research and development of characterising cell populations with a specific biological function, (4) to develop and optimise cell culture methods, and (5) to patent and in-license key technology on a worldwide basis.

Despite the numerous achievements since inception, the Company has not achieved profitability. The Company incurred a cumulated loss of €21,911k. TiGenix expects to incur further losses in the coming years as it continues (i) to expand its research and development projects, (ii) to invest in clinical validation of its products and (iii) to increase its commercialisation and manufacturing efforts.

TiGenix expects to perform the following in the coming few years:

- continue to collaborate with universities and other third parties, orthopaedists and rheumatologists and medical centres in order to develop and validate the technology and products of the Company;
- expand the research and development teams and internal support organization of the Company so as to enlarge and bring forward the product pipeline of the Company;
- expand the sales and marketing team so to commercialise its lead product ChondroCelect;
- ensure the necessary production capacity to be in a position to manufacture its lead product according to the GMP requirements; and
- expand the intellectual property portfolio via further patent filings and in-licensing.

## 6.2. INCOME STATEMENT

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
<b>CONSOLIDATED INCOME STATEMENT</b>			
Sales	0	0	0
Other revenues	416	784	567
<b>Revenues</b>	<b>416</b>	<b>784</b>	<b>567</b>
Research and development expenses	5,765	3,817	3,025
Selling, general and administrative expenses	3,201	1,845	1,338
Other operating income	0	0	0
Other operating expenses	0	0	0
<b>Total operating charges</b>	<b>8,966</b>	<b>5,662</b>	<b>4,364</b>
<b>Operating Result (EBIT)</b>	<b>(8,550)</b>	<b>(4,878)</b>	<b>(3,797)</b>
Financial result	304	75	50
<b>Profit/(Loss) before taxes</b>	<b>(8,246)</b>	<b>(4,803)</b>	<b>(3,747)</b>
Income taxes	0	0	0
<b>Net Profit/(Loss)</b>	<b>(8,246)</b>	<b>(4,803)</b>	<b>(3,747)</b>

### 6.2.1. Sources of revenues and revenue recognition

The Company has generated revenues from the following sources:

- **Grants and subsidies.** Such items are recognized as income when the conditions for their approval and payment have been met and in the period during which the subsidised cost has occurred.
- **License and deal revenues.** License fees are recognized when the Company has fulfilled all conditions and obligations. The license fee will not be recognised if the amount cannot be reasonably estimated and if the payment is doubtful.
- **Contribution to costs.** The Company received a contribution to costs for its ChondroCelect product manufactured on request. This is recognised as income at the moment the invoice is sent to the medical centre.

### 6.2.2. Revenues

Since its inception, the Company has generated a significant part of its revenues to date and in the coming few years will come from government grants and collaborative research and licence deals, leading to significant volatility in revenues. Prior to the launch of its lead product, ChondroCelect, this volatility is likely to remain. Only after the successful commercialisation of ChondroCelect, will the Company's revenues potentially become more predictable. However, revenues generated from sales of ChondroCelect are not expected to become a significant part of the Company's overall revenues for at least another two years. In view of this volatility and of its limited operating history, the Company believes that period-to-period comparisons of its historical operating results are not meaningful and should not therefore be relied upon as being indicative of future performance.



### **6.2.3. Research and development expenses**

Research and development costs consist primarily of costs associated with:

- research pursued internally and externally in the domain of cartilage repair and OA;
- internally funded product development efforts;
- expansion and maintenance of the intellectual property portfolio;
- clinical validation of a product; and
- regulatory filing of a product with the authorised bodies.

These costs mainly consist of:

- direct personnel costs and material expenses;
- laboratory consumables;
- subcontracting expenses for research, development, validation, analysing of results, medical writing and regulatory advice; and
- depreciation charges on research and development equipment.

To date, no internally-generated development expenditures have been capitalized in the IFRS consolidated financial statements.

An increase in the research and development expenses is expected in the coming years as the Company expands its operations and seeks to develop further products.

To date, the Company has primarily spent research and development costs on the following projects:

- development and validation of a potency assay for cartilage formation;
- identification of predictive genes for cartilage formation and set-up of the ChondroCelect-score, a quality control assay based on PCR technology;
- development of cell culture methods;
- set-up and validation of pre-clinical models for cartilage repair;
- pre-clinical experiments with ChondroCelect technology;
- setting up a manufacturing facility that is GMP-approved for the production of clinical batches;
- development of an adult stem cell platform;
- development of potency assay for meniscal repair;
- evaluation of different allogeneic approaches; and
- set-up of test bank for screening of compounds in osteoarthritis.

The Company spends a significant portion of its research and development budget on external collaboration agreements. The Company utilizes such collaborations to access key orthopaedists and scientific and clinical experts on a worldwide basis so as to improve the research and development and clinical programs of the Company.

### **6.2.4. Selling, general and administrative expenses**

Selling, general and administrative expenses consist primarily of sales and marketing costs, professional services (such as financial, legal, accounting, auditing, IT administration expenses, insurances), salaries and other personnel-related expenses, general expenses and office rental payments.

We expect that selling expenses will increase significantly with the pre-marketing and commercialisation of ChondroCelect. General and administrative costs are also expected to increase as a result of hiring additional personnel and further growth of the organisation.

## 6.3. ANALYSIS OF RESULTS OF OPERATIONS

### 6.3.1. Year ended December 31, 2006 compared to year ended December 31, 2005

#### 6.3.1.1. Revenues

Total revenues were €416k in 2006 compared to €784k in 2005, a decrease of 47%. The decrease was the result of a decrease in grant revenues and license & deal revenues compared to 2005. The contribution to costs increased as more patients were treated with ChondroCelect under the compassionate use programme compared to 2005.

#### 6.3.1.2. Research and development expenses

Research and development expenses were €5,765k in 2006 compared to €3,817k in 2005, an increase of 51%.

The main components of the research and development expenses were as follows for the years ended December 31:

<i>Thousands of Euro (€)</i>	Years ended December 31	
	2006	2005
Personnel costs	2,620	1,764
Operating costs	2,455	1,479
Production costs	293	246
General costs	284	248
Depreciation	113	80
<b>Total</b>	<b>5,765</b>	<b>3,817</b>

The major part of this increase was due to (i) personnel related costs as the numbers of employees (mandate contractors included) increased from 24 in 2005 to 32 at year end in 2006 and (ii) operating costs as the costs related to the analysis of the results of the TIGACT01 study together with R&D costs increased significantly compared to 2005. Production costs increased further as more ChondroCelect batches were manufactured.

#### 6.3.1.3. Selling, general and administrative expenses

Selling, general and administrative expenses were €3,201k in 2005 compared to €1,845k in 2005, an increase of 73%. The main components of the selling, general and administrative expenses were as follows for the years ended December 31:

	Years ended December 31	
	2006	2005
Thousands of Euro (€)		
Personnel costs	1,498	1,072
Operating costs	1,338	503
General costs	252	219
Depreciation	113	51
<b>Total</b>	<b>3,201</b>	<b>1,845</b>

The major part of the increase was due to (i) personnel related costs as the number of people increased from 9 in 2005 to 12 in 2006 at year end and (ii) operating costs as the pre-marketing costs increased significantly together with the IT related costs and the advisory and legal costs related to the FAB transaction.

#### 6.3.1.4. Financial results

As the Company realised a capital increase end 2005, the Company had a higher financial result of €304k in 2006 as compared to €75k in 2005.

#### 6.3.1.5. Net loss

The net loss was €8,246k in 2006 compared to €4,803k in 2005, an increase of 72%. As highlighted the decrease in revenues and the increase of operating charges both in research and development expenses and selling, general and administrative expenses explained the increase in net loss.

### 6.3.2. Year ended December 31, 2005 compared to year ended December 31, 2004

#### 6.3.2.1. Revenues

Total revenues were €784k in 2005 compared to €567k in 2004, an increase of 38%. The difference mainly came from an increase in the number of ChondroCelect products offered at the request of surgeons. A significant part of the revenues in 2005 and 2004 resulted from license & deal revenues that mainly consisted of two payments under the collaboration agreement between TiGenix, AlphaGen and the Katholieke Universiteit Leuven for the research project "recellurisation of no-react-treated tissue heart valve prosthesis".

#### 6.3.2.2. Research and development expenses

Research and development expenses were €3,817k in 2005 compared to €3,025k in 2004, an increase of 26%.

The main components of the research and development expenses were as follows for the years ended December 31:

<i>Thousands of Euro (€)</i>	Years ended December 31	
	2005	2004
Personnel costs	1,764	1,187
Operating costs	1,479	1,607
Production costs	246	115
General costs	248	24
Depreciation	80	92
<b>Total</b>	<b>3,817</b>	<b>3,025</b>

The major part of this increase was due to personnel related costs as the numbers of employees (mandate contractors included) increased from 17 in 2004 to 24 at year end in 2005. Operating costs decreased as there were less Contract Research Organisation costs related to the TIGACT01 study in 2005. Production costs almost doubled as the number of batches to manufacture ChondroCelect increased.

#### 6.3.2.3. Selling, general and administrative expenses

Selling, general and administrative expenses were €1,845k in 2005 compared to €1,338k in 2004, an increase of 38%.

The main components of the selling, general and administrative expenses were as follows for the years ended December 31:

<i>Thousands of Euro (€)</i>	Years ended December 31	
	2005	2004
Personnel costs	1,072	730
Operating costs	503	273
General costs	219	306
Depreciation	51	29
<b>Total</b>	<b>1,845</b>	<b>1,338</b>

The major part of the increase was due to personnel related costs as the number of people (mandate contractors included) increased to 9 at year end. Operating costs mainly increased due to initial marketing costs and IT related services.

#### 6.3.2.4. Financial results

In 2005, the Company had a financial result of €75k as compared to €50k in 2004.

### 6.3.2.5. Net loss

The net loss was €4,803k in 2005 compared to €3,747k in 2004, an increase of 28%. As highlighted the increase of operating charges both in research and development expenses and selling, general and administrative expenses explained the increase in net loss.

## 6.4. CASH FLOW STATEMENT

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
<b>CASH FLOWS FROM OPERATING ACTIVITIES</b>			
Operating Result	(8,550)	(4,878)	(3,797)
Depreciation, amortization and impairment results	226	131	121
Share-based compensation	277	215	184
Other financial result	(6)	(10)	(6)
Income taxes	0	0	0
Increase/(decrease) in Trade payables	(39)	208	(120)
Increase/(decrease) in Other current liabilities	441	9	10
(Increase)/ decrease in Receivables	(107)	(100)	(53)
(Increase)/ decrease in deferred charges&accrued income	15	(119)	283
Total Adjustments	807	334	419
<b>Net cash provided by/(used in) operating activities</b>	<b>(7,743)</b>	<b>(4,544)</b>	<b>(3,378)</b>
<b>CASH FLOWS FROM INVESTING ACTIVITIES</b>			
Interest received	311	85	56
Interest paid	(1)	(1)	(1)
Purchase of tangible assets	(203)	(119)	(180)
Purchase of intangible assets	(332)	(19)	(29)
<b>Net cash provided by/(used in) investing activities</b>	<b>(225)</b>	<b>(54)</b>	<b>(154)</b>
<b>CASH FLOWS FROM FINANCING ACTIVITIES</b>			
Payments cash deposits	2	(1)	(16)
Payments on long-term leases	(5)	0	0
Proceeds of subordinated loan	391	0	0
Proceeds from long-term leases	0	18	0
Proceeds from issuance of shares (net of issue costs)	422	16,684	4,073
<b>Net cash provided by/(used in) financing activities</b>	<b>810</b>	<b>16,701</b>	<b>4,057</b>
<b>Net increase/(decrease) in cash and cash equivalents</b>	<b>(7,158)</b>	<b>12,103</b>	<b>525</b>
Cash and cash equivalents at beginning of year	14,899	2,796	2,271
Effect on exchange rate changes	(3)	0	0
<b>Cash and cash equivalents at end of period</b>	<b>7,738</b>	<b>14,899</b>	<b>2,796</b>

#### **6.4.1. Cash flows from operating activities**

Net cash used in operating activities increased in 2006 to €7,743k from €4,544k in 2005 primarily due to a higher net loss compared to 2005 as explained above and only partly compensated by higher adjustments of €807k in 2006 compared to €334 in 2005.

Cash used in operating activities increased in 2005 to €4,544k from €3,378k in 2004 primarily due to a higher net loss as explained above and to an increase in receivables and deferred charges & accrued income that was only partially compensated by an increase in trade payables.

Cash used in operating activities of €7,743k in 2006 was mainly due to the operating loss of €8,550k that was partly compensated by several adjustments totalling €807k. The most important adjustments were the depreciation, the share-based compensation and the increase in other current liabilities.

Cash used in operating activities of €4,544k in 2005 was due to the operating loss of €4,878k that was partly compensated by several adjustments totalling €334k as referred in the table above.

Cash used in operating activities of €3,378k in 2004 was due to the operating loss of €3,797k that was partially compensated by several adjustments totalling €419k as referred in the table above.

#### **6.4.2. Cash flows from investing activities**

Cash used in investing activities increased in 2006 to €225k from a net use of cash of €54k in 2005 primarily due to higher net investments in tangible and intangible assets compared to 2005 that were only partly compensated by the higher interests received compared to 2005.

Cash used in investing activities decreased in 2005 to €54k from a net use of cash of €154k primarily due to lower investments in 2005.

Cash used in investing activities of €225k in 2006 was primarily due to (i) investments in tangible assets (equipment and IT material) and intangible assets (mainly the development cost of an ERP system) and (ii) interests received from the available cash and cash equivalents resulting from the capital increase of €16,684k (net of issuance cost) in 2005.

In 2005, the net cash out due to the purchase of tangible and intangible assets was partly compensated by the cash in from interest received, resulting in a net cash out of €54k.

Cash used in investing activities of €154k in 2004 was primarily attributable to the purchase of extra lab equipment and the purchase of software rights, only partly compensated by interest received.

#### **6.4.3. Cash flows from financing activities**

Net cash provided by financing activities in 2006, 2005 and 2004 was mainly due to the issuance of new shares, resulting from several capital increases and exercises of warrants (see section 7.1.5.14. in chapter 7 for more details). In 2006, the Company received a subordinated loan from IWT of €391k.

## 6.5. BALANCE SHEET

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
<b>CONSOLIDATED BALANCE SHEET – ASSETS</b>			
Intangible assets	311	32	27
Tangible assets	437	374	345
Other non current assets	32	34	33
<b>Non-current assets</b>	<b>780</b>	<b>440</b>	<b>405</b>
Receivables	444	337	237
Cash and cash equivalents	7,738	14,899	2,796
Deferred charges & Accrued income	117	132	13
<b>Current assets</b>	<b>8,299</b>	<b>15,368</b>	<b>3,046</b>
<b>TOTAL ASSETS</b>	<b>9,079</b>	<b>15,808</b>	<b>3,451</b>

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
<b>CONSOLIDATED BALANCE SHEET – EQUITY AND LIABILITIES</b>			
Share capital	13,044	12,645	8,259
Share premium	15,335	15,312	3,014
Accumulated profit/(loss)	(13,665)	(8,862)	(5,115)
Result of the year	(8,246)	(4,803)	(3,747)
Share-based compensation	693	416	201
Translation reserves	(3)		
<b>Equity attributable to equity holders</b>	<b>7,158</b>	<b>14,707</b>	<b>2,612</b>
<b>Total equity</b>	<b>7,158</b>	<b>14,707</b>	<b>2,612</b>
Subordinated loan	391	0	0
Finance lease obligations	8	13	0
<b>Non-current liabilities</b>	<b>399</b>	<b>13</b>	<b>0</b>
Current portion of lease debt	5	5	0
Trade payables	749	775	540
Other current liabilities	768	308	299
<b>Current liabilities</b>	<b>1,522</b>	<b>1,088</b>	<b>839</b>
<b>TOTAL EQUITY AND LIABILITIES</b>	<b>9,079</b>	<b>15,808</b>	<b>3,451</b>

Cash and cash equivalents is the main asset class of the Company as expressed on the balance sheet in each of the years ended December 31.

Besides the cash position, tangible assets (mainly consisting of laboratory and IT equipment) and receivables (mainly consisting of trade receivables and recoverable taxes) were the other main assets of the Company. In 2006, the development costs of an integrated ERP system were booked as an intangible asset.



### **6.5.1. Off-balance sheet commitments**

The Company has off-balance sheet commitments related to the rent for leased facilities, vehicles and equipment. At December 31, 2006, these commitments amounted to €1,373k (see also section 7.1.5.16. of chapter 7). There are no other off-balance sheet commitments.

### **6.5.2. Taxation**

Since its inception, TiGenix has not made profits and has thus not paid corporate taxes. Its accumulated losses amounted to €21,911k at December 31 2006. These losses can be offset against future profits if and when they are made. However, no deferred tax assets were recorded so far due to the development stage of the Company and the lack of guarantees that it will generate profits in the future which could be offset against current losses.

## **6.6. CAPITAL EXPENDITURES**

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### **6.6.1. Investments in tangible assets**

Investments in tangible assets of €216k in 2006 mainly consisted of investments in IT equipment (€180k) and furniture (€28k).

Investments in tangible assets of €144k in 2005 mainly consisted of investments in furniture (€37k) and IT equipment (€74k).

Investments in tangible assets of €197k in 2004 mainly consisted of investments in laboratory equipment (€98k) and IT equipment (€55k).

### **6.6.2. Investments in intangible assets**

Investments in intangible assets consist of software rights purchased and software development costs and amounted to €351k in 2006, €21k in 2005 and €32k in 2004.

## **6.7. CASH AND FUNDING SOURCES**

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Since its inception, the Company has obtained funding primarily via private placements of its shares and via government grants. The issuance of shares has generated total proceeds of €28,379k, net of issuance costs. Until December 31, 2006, the Company had received €1,446k in grants.

As of December 31, 2006, the Company had non-current liabilities of €399k consisting of a subordinated IWT loan of €391k and financial lease debts of €8k. The Company had no ongoing commercial commitments, such as lines of credit or guarantees which would affect its liquidity over the next five years, other than rent payments related to leased facilities, vehicles and equipment.

## **6.8. LONG-TERM CONTRACTUAL OBLIGATIONS**

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At December 31, 2006, the Company had no long term contractual obligations.

## **6.9. FUTURE FUNDING REQUIREMENTS**

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The present and future funding requirements will depend on many factors, including, among other things:

- the amount of proceeds actually raised in this offering;
- the level of research and development needed to bring the Company's products in development to the market;
- the level of clinical validation required to obtain regulatory approval in the different markets of the Company's products;
- the level of success of commercialising its own products;
- the level of manufacturing costs needed to obtain regulatory authorisation and to reach the GMP requirements;
- the costs associated with maintaining, defending, and expanding the Company's intellectual property position;
- the regulatory, reimbursement, and competitive environment in which the Company operates; and
- the ability and the costs associated with attracting and maintaining key personnel and key scientific collaborators.

The Company intends to expand (i) its research and development capabilities, (ii) the number of products in the development pipeline, (iii) its sales and marketing team, (iv) its manufacturing capabilities and develop, in-license and acquire additional intellectual property rights and know-how.

These expansion intentions will likely increase the net losses and cash consumption of the Company in the coming years. There is a possibility that the Company will require additional funds in connection with its expansion, on-going activities and possible acquisitions.

## **6.10. FINANCIAL RISKS**

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### **6.10.1. Credit risk**

The Company is not commercialising its product yet. For the medical centres that receive the products and that need to pay a contribution to costs, the credit risk is limited.

### **6.10.2. Interest risk**

The Company is not subject to material interest risk. All leases have fixed interest rates.

### **6.10.3. Currency risk**

The Company may be subject to limited currency risk as certain of its invoices need to be paid in U.S. Dollars and for the operations of its U.S. wholly-owned subsidiary. The Company has not engaged in hedging of the foreign currency risk via derivative instruments.

## **6.11. RECENT BUSINESS DEVELOPMENTS**

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In the first quarter of 2007, the Company has entered into a strategic partnership with FAB to start the development and clinical validation of the next generation product, combining the hyaluronan-based

Hyalograft-C scaffold from FAB as a carrier for the ChondroCelect cells. The partnership consists of a License Agreement for HyaloGraft-C, covering all territories outside of Europe, a Cross-License Agreement on ChondroCelect and HyaloGraft-C in Europe and a Worldwide Supply Agreement. TiGenix will pay FAB a license-fee, milestone payments and royalties and receive royalties from sales made by FAB in selected European countries (see section 5.6.3. of chapter 5).

The Company, together with a U.S. partner, has an option until March 31, 2007 to buy the equipment of a manufacturing facility in the United States and to take over the leasehold rights of this facility (see section 5.13.2 of chapter 5).

## **6.12. OUTLOOK**

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### **6.12.1. Outlook 2007**

In 2007, the Company expects to increase expenditure in the following areas and to achieve the following milestones:

- to file a marketing authorisation application (MAA) for its lead product ChondroCelect with the EMEA;
- to increase efforts in the pre-marketing of and preparation for commercialisation of ChondroCelect;
- to expand its capacity to be able to produce its products in the United States and Europe according to GMP requirements;
- to develop the protocol and design of the clinical trial for the next generation product (ChondroCelect-3D); and
- to expand its R&D activities in the area of meniscal repair and other pipeline products.

Furthermore, the Company expects that, prior to the launch of ChondroCelect, it will continue to generate limited revenues, primarily derived from government grants and collaborative research and licence fees. The Company also expects to incur significant additional administrative expenses related to its growth, particularly in connection with the activities related to this offering and the entering into of new collaborative research and development agreements.

As a result, the net loss of the Company is expected to increase in 2007.

### 6.12.2. Outlook beyond 2007

In the coming two to three years, an increasing part of TiGenix' revenues should be generated from the sale of its lead product ChondroCelect. However, the timing of and growth in these revenues will depend, among other things, on:

- the Company obtaining timely regulatory marketing approvals in different geographic markets, particularly the US and Europe;
- the pricing and reimbursement status of the product in these different markets;
- the ability of TiGenix to introduce and distribute the product within different markets; and
- the prevailing and future competitive environment.

The Company will continue to expand its research and development capabilities and facilities to cope with the development of its product pipeline, in particular to manage the products that reach the validation phase. The Company will also continue to expand its selling, general and administrative capabilities to cope with the Company's growth and the number of projects to follow-up.

The Company will likely continue with its business model of (i) partnering with external collaborators for research and development and (ii) manufacturing and commercialising certain products. The Company will evaluate this strategy from time to time, and could adapt its business model if deemed appropriate by management.



## 7. FINANCIAL INFORMATION

### 7.1. CONSOLIDATED ANNUAL ACCOUNTS 2004 - 2005 - 2006

The following accounts are drawn up in accordance with International Financial Reporting Standards ("IFRS") as adopted in the EU. The accounting policies and notes are an integral part of these financial statements. The following accounts differ from the statutory annual accounts of the Company, which have been prepared in accordance with Belgian GAAP.

Since the Company's sole subsidiary, TiGenix Inc., has only been incorporated in 2006, the financial statements for each of the financial years ended December 31, 2005 and 2004 are not consolidated financial statements and only relate to TiGenix NV/SA. As required under IFRS, the financial statements for the financial year ended December 31, 2006 are consolidated financial statements, relating to TiGenix NV/SA and TiGenix Inc., even though although TiGenix Inc. did not yet have operational activities in 2006. The TiGenix Inc. results have limited impact (€54k) on the consolidated accounts 2006.

#### 7.1.1. Income statement

		Years ended December 31		
Thousands of Euro (€)	Notes	2006	2005	2004
CONSOLIDATED INCOME STATEMENT				
Sales		0	0	0
Other revenues	7.1.5.3.	416	784	567
Revenues		416	784	567
Research and development expenses	7.1.5.4.a.	5,765	3,817	3,025
Selling, general and administrative expenses	7.1.5.4.b.	3,201	1,845	1,338
Other operating income		0	0	0
Other operating expenses		0	0	0
Total operating charges		8,966	5,662	4,364
Operating Result (EBIT)		(8,550)	(4,878)	(3,797)
Financial result	7.1.5.6.	304	75	50
Profit/(Loss) before taxes		(8,246)	(4,803)	(3,747)
Income taxes		0	0	0
Net Profit/(Loss)		(8,246)	(4,803)	(3,747)

### 7.1.2. Balance sheet

		Years ended December 31		
Thousands of Euro (€)	Notes	2006	2005	2004
CONSOLIDATED BALANCE SHEET – ASSETS				
Intangible assets	7.1.5.9.	311	32	27
Tangible assets	7.1.5.10.	437	374	345
Other non current assets		32	34	33
Non-current assets		780	440	405
Receivables	7.1.5.11.	444	337	237
Cash and cash equivalents	7.1.5.12.	7,738	14,899	2,796
Deferred charges & Accrued income		117	132	13
Current assets		8,299	15,368	3,046
TOTAL ASSETS		9,079	15,808	3,451

		Years ended December 31		
Thousands of Euro (€)	Notes	2006	2005	2004
CONSOLIDATED BALANCE SHEET – EQUITY AND LIABILITIES				
Share capital	7.1.5.14.	13,044	12,645	8,259
Share premium		15,335	15,312	3,014
Accumulated profit/(loss)		(13,665)	(8,862)	(5,115)
Result of the year		(8,246)	(4,803)	(3,747)
Share-based compensation	7.1.5.19.	693	416	201
Translation reserves		(3)	0	0
Equity attributable to equity holders		7,158	14,707	2,612
Total equity		7,158	14,707	2,612
Subordinated loan	7.1.5.15.	391	0	0
Finance lease obligations	7.1.5.16.	8	13	0
Non-current liabilities		399	13	0
Current portion of lease debt	7.1.5.16.	5	5	0
Trade payables	7.1.5.17.a.	749	775	540
Other current liabilities	7.1.5.17.b.	768	308	299
Current liabilities		1,522	1,088	839
TOTAL EQUITY AND LIABILITIES		9,079	15,808	3,451



### 7.1.3. Cash flow statement

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
<b>CASH FLOWS FROM OPERATING ACTIVITIES</b>			
Operating Result	(8,550)	(4,878)	(3,797)
Depreciation, amortisation and impairment results	226	131	121
Share-based compensation	277	215	184
Other financial result	(6)	(10)	(6)
Income taxes	0	0	0
Increase/(decrease) in Trade payables	(39)	208	(120)
Increase/(decrease) in Other current liabilities	441	9	10
(Increase)/ decrease in Receivables	(107)	(100)	(53)
(Increase)/ decrease in deferred charges & accrued income	15	(119)	283
Total Adjustments	807	334	419
<b>Net cash provided by/(used in) operating activities</b>	<b>(7,743)</b>	<b>(4,544)</b>	<b>(3,378)</b>
<b>CASH FLOWS FROM INVESTING ACTIVITIES</b>			
Interest received	311	85	56
Interest paid	(1)	(1)	(1)
Purchase of tangible assets	(203)	(119)	(180)
Purchase of intangible assets	(332)	(19)	(29)
<b>Net cash provided by/(used in) investing activities</b>	<b>(225)</b>	<b>(54)</b>	<b>(154)</b>
<b>CASH FLOWS FROM FINANCING ACTIVITIES</b>			
Payments cash deposits	2	(1)	(16)
Payments on long-term leases	(5)	0	0
Proceeds of subordinated loan	391	0	0
Proceeds from long-term leases	0	18	0
Proceeds from issuance of shares (net of issue costs)	422	16,684	4,073
<b>Net cash provided by/(used in) financing activities</b>	<b>810</b>	<b>16,701</b>	<b>4,057</b>
<b>Net increase/(decrease) in cash and cash equivalents</b>	<b>(7,158)</b>	<b>12,103</b>	<b>525</b>
Cash and cash equivalents at beginning of year	14,899	2,796	2,271
Effect on exchange rate changes	(3)	0	0
<b>Cash and cash equivalents at end of period</b>	<b>7,738</b>	<b>14,899</b>	<b>2,796</b>

#### 7.1.4. Statement of changes in shareholders' equity

Thousands of Euro (€)	Attributable to equity holders of the Company							
	Number of shares	Issued capital	Issuance cost	Share premium	Retained loss	Share- based compen- sation	Trans- lation reserves	Total Equity
Balance at January 1, 2004	7,347,904	7,348	(437)	290	(5,115)	17	0	2,103
Issuance of shares	1,358,024	1,358	(10)	2,724				4,072
Net Profit/(Loss)					(3,747)			(3,747)
Share-based compensation						184		184
Translation reserves							0	0
<b>Balance at Dec. 31, 2004</b>	<b>8,705,928</b>	<b>8,706</b>	<b>(447)</b>	<b>3,014</b>	<b>(8,862)</b>	<b>201</b>	<b>0</b>	<b>2,612</b>
Balance at 1 January 2005	8,705,928	8,706	(447)	3,014	(8,862)	201	0	2,612
Issuance of shares	5,048,586	5,007	(621)	12,298				16,684
Net Profit/(Loss)					(4,803)			(4,803)
Share-based compensation						215		215
Translation reserves							0	0
<b>Balance at Dec. 31, 2005</b>	<b>13,754,514</b>	<b>13,713</b>	<b>(1,068)</b>	<b>15,312</b>	<b>(13,665)</b>	<b>416</b>	<b>0</b>	<b>14,707</b>
Balance at January 1, 2006	13,754,514	13,713	(1,068)	15,312	(13,665)	416	0	14,707
Issuance of shares	402,500	402	(3)	23				422
Net Profit/(Loss)					(8,246)			(8,246)
Share-based compensation						277		277
Translation reserves							(3)	(3)
<b>Balance at Dec. 31, 2006</b>	<b>14,157,014</b>	<b>14,115</b>	<b>(1,071)</b>	<b>15,335</b>	<b>(21,911)</b>	<b>693</b>	<b>(3)</b>	<b>7,158</b>

## **7.1.5. Notes to consolidated financial statements**

### **7.1.5.1. General information**

TiGenix NV/SA is a limited liability company incorporated in Belgium.

TiGenix is a biotechnology company founded in 2000 as a spin-off company of the Katholieke Universiteit Leuven and the Universiteit Gent. The Company focuses on the development of innovative local treatments for damaged and osteoarthritic joints. The research and development work is done both in-house and through collaboration agreements with an extensive international network of leading experts and medical centres.

The TiGenix group of companies has its parent company, headquarters, and main production facility and laboratory in Belgium, but also operates via one wholly-owned subsidiary in the United States. The consolidated financial statements are presented in Euro because that is the currency of the primary economic environment in which the Company operates.

### **7.1.5.2. Accounting policies**

#### **Basis of preparation**

The consolidated financial statements have been prepared in accordance with International Financial Reporting Standards ("IFRS") as adopted in the EU. The principle accounting policies adopted when preparing these consolidated financial statements are set out below.

The financial statements have been prepared on the historical cost basis. Any exceptions to the historical cost convention are disclosed in the valuation rules described hereafter.

The financial statements have been established assuming the Company is a going concern. The Company has generated losses since its inception, which is inherent to the current stage of the Company's business life cycle as a biotech company. Sufficient funds have been raised since inception.

#### **Basis of consolidation**

The consolidated financial statements incorporate the financial statements of TiGenix NV/SA (Belgium legal entity) made up to December 31, each year and of TiGenix Inc. (United States legal entity) made up to December 31, 2006. TiGenix NV incorporated TiGenix Inc. as a wholly-owned subsidiary in 2006 but TiGenix Inc. does not yet have any operational activities at this stage. The subsidiary is included following the full consolidation method. All intra-group transactions, balances, income and expenses are eliminated in consolidation.

#### **Foreign currency translation**

#### **Functional and presentation currency**

Items included in the financial statements of each of the group's entities are measured using the currency of the primary economic environment in which the entity operates (*functional currency*). The consolidated financial statements are presented in Euro, which is the Company's functional and presentation currency.

### **Transactions and balances**

Transactions in currencies other than Euro are recorded at the rates of exchange prevailing on the dates of the transactions. At each balance sheet date, the monetary assets and liabilities that are denominated in foreign currencies are translated at the rates prevailing on the balance sheet date. Non-monetary assets and liabilities carried at fair value that are denominated in foreign currencies are translated at the rates prevailing at the date when the fair value was determined. Gains and losses arising on translation are included in net profit or loss for the period, except for exchange differences arising on non-monetary assets and liabilities where the changes in fair value are recognised directly in equity.

On consolidation, the assets and liabilities of the group's foreign operations are translated at exchange rates prevailing on the balance sheet date. Income and expense items are translated at the average exchange rates for the period. Exchange differences arising, if any, are classified as income or as expense in the period in which the operation is disposed of.

### **Segment information**

The Company does not distinguish different segments, neither business nor geographical segments.

### **Revenue recognition**

The Company is not actively commercialising any of its products yet. Under the current legislation, the Company is allowed to offer its products to medical centres. The price asked for these products is recognised as a contribution to cost in other revenues.

License fees are recognised when the Company has fulfilled all conditions and obligations. The license fee will not be recognised if the amount cannot be reasonably estimated and if the payment is doubtful. License up-front (signature fees) and non-refundable fees for access to prior research results and databases are recognised when earned, if the Company has no continuing performance obligations and all conditions and obligations are fulfilled (this means after the delivery of the required information).

If the Company has continuing performance obligations towards the fees, the fee will be recognised on a straight line basis over the contractual performance period.

Research and development service fees are recognised as revenue over the life of the research agreement as the required services are provided and costs are incurred. These services are usually in the form of a defined number of full-time equivalents ("FTE") at a specified rate per FTE.

Government grants are recognised as revenue over the life of the grant as the required or planned activities are performed and the related costs incurred and when there is reasonable assurance that the Company will comply with the conditions of the grant. The grants are usually in the form of periodic progress payments.

Deferred revenue represents amounts received prior to revenue being earned.

### **Research & development costs**

Development costs are capitalised to the extent that all conditions for capitalisation have been satisfied. The Company considers that the regulatory and clinical risks inherent to the development of its products preclude it from capitalising development costs. In the consolidated IFRS financial statements of the Company, no research and development costs have been capitalised.

### **Property, plant and equipment**

Property, plant and equipment are stated at historical cost less accumulated depreciation and impairment. Repair and maintenance costs are charged to the income statement as incurred. Gains and losses on the disposal of property, plant and equipment are included in other income or expense. Depreciation is charged so as to write off the cost or valuation of assets over their useful lives, using the straight-line method pro rata in the year of purchase, on the following basis:

- equipment: 5 years;
- IT hardware: 3 years;
- furniture: 5 years; and
- leasehold improvements: in line with the lease agreement period.

### **Intangible assets**

Software licenses and software development costs are measured internally at purchase cost and are amortised on a straight-line basis over 3 years and pro rata in the year of purchase.

Costs related to patents which are in-licensed are expensed as incurred. Costs related to the filing, maintenance and defence of patents are expensed as incurred. Internal and external research and development programme costs are expensed as incurred.

### **Leases**

Leases are classified as finance leases whenever the terms of the lease transfers substantially all the risks and rewards of ownership to the lessee. All other leases are classified as operating leases.

Assets held under finance leases are recognised as assets of the Company at their fair value or, if lower, at the present value of the minimum lease payments, each determined at the inception of the lease. The corresponding liability to the lessor is included in the balance sheet as a finance lease obligation so as to achieve a constant rate of interest on the remaining balance of the liability. Finance charges are expensed.

Rentals payable under operating leases are charged to income on a straight-line basis over the term of the relevant lease. Benefits received and receivable as an incentive to enter into an operating lease are also spread on a straight-line basis over the lease term.

### **Impairment of tangible and intangible assets**

At each balance sheet date, the Company reviews the carrying amount of its tangible and intangible assets to determine whether there is any indication that those assets have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss (if any). Where the asset does not generate cash flows that are independent from other assets, the Company estimates the recoverable amount of the cash-generating unit to which the asset belongs. An intangible asset with an indefinite useful life is tested for impairment annually, and whenever there is an indication that the asset might be impaired. Recoverable amount is the higher of fair value less costs to sell and value in use. The estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset.

If the recoverable amount of an asset or cash generating unit is estimated to be less than the carrying amount, the carrying amount of the asset is reduced to its recoverable amount. An impairment loss is recognised as an expense immediately, unless the relevant asset is carried at re-valued amount, in which

case the impairment is treated as a revaluation decrease. Where an impairment loss subsequently reverses, the carrying amount of the asset is increased to the revised estimate of its recoverable amount, but so that the increased carrying amount does not exceed the carrying amount that would have been determined had no impairment loss been recognised for the asset in prior years. A reversal of an impairment loss is recognised as income, unless the relevant asset is carried at re-valuated amount, in which case the reversal of the impairment is treated as a revaluation increase.

### **Inventories**

All purchases are expensed as incurred. The Company does not account for work in progress and finished products, as the production process is short and finished goods are shipped to customers immediately thereafter, resulting in no such items on the balance sheet at year-end for any of the periods reported.

### **Trade receivables**

Trade receivables do not carry any interest and are stated at their nominal value.

### **Cash and cash equivalents**

Cash and cash equivalents are carried in the balance sheet at nominal value. For the purposes of the cash flow statements, cash and cash equivalents comprise cash on hand and deposits held on call with banks. In the balance sheet, bank overdrafts, if any, are included in borrowings in current liabilities.

### **Taxation**

Deferred income tax is provided in full using the “balance sheet liability method”, on temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes.

The amount of deferred tax provided is based on the expected manner of realisation of settlement of the carrying amount of assets and liabilities, using tax rates enacted or substantially enacted at the balance sheet date. Deferred tax assets relating to tax losses carried forward are recognised to the extent that it is probable that the related tax benefits will be realised.

### **Trade payables**

Trade payables are not interest bearing and are stated at their nominal value.

### **Equity instruments**

Equity instruments issued by the Company are recorded in the amount of the proceeds received, net of direct issue costs.

### **Derivative instruments**

The Company has not used any derivative financial instruments.

### **Retirement benefit schemes and employee savings schemes**

Payments to defined contribution retirement benefit schemes are charged as an expense as they fall due. The Company does not offer nor operate any defined benefit schemes for its employees.

### Share-based compensation plans for personnel

The Company has share-based compensation plans for both personnel, directors and business associates. The fair value of the employee services received for the granted compensation plans are measured as an expense. The corresponding credit is recorded directly into equity.

The total cost to be charged as an expense over the vesting period is measured at the fair value of the granted compensation plans. The estimate of the number of compensation plans which will be vested is revised at each reporting date. The change in estimates will be recorded as expense with a corresponding correction in equity.

The received amount, less directly attributable transaction costs, will be recorded as share capital and share premium when the compensation plans are exercised.

### 7.1.5.3. Revenues

The revenues consist of other revenues that can be split into:

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Grant revenues	94	180	85
License & deal revenues	15	355	390
Contribution to costs	307	249	92
<b>Total</b>	<b>416</b>	<b>784</b>	<b>567</b>

### 7.1.5.4. Operating result

Result from operations has been arrived at after charging:

### Research and development expenditures

<i>Thousands of Euro (€)</i>		Years ended December 31		
		2006	2005	2004
Personnel costs	7.1.5.5.	2,620	1,764	1,187
Depreciations		113	80	92
Operating costs		2,455	1,479	1,607
General costs		284	248	24
Production costs		293	246	115
<b>Total</b>		<b>5,765</b>	<b>3,817</b>	<b>3,025</b>

The operating costs mainly consist of lab consumables, subcontracting and collaboration agreements with the Katholieke Universiteit Leuven, the Universiteit Gent and other third parties, IP services, cost related to the managing of the trial and the analysis of the results, regulatory advice fees, medical writing costs and the rent of the R&D facilities.

The general costs are the costs related to training and seminars, membership and literature, hiring and executive search, insurance and the office.



The production costs mainly consist of the direct production cost, such as the reagentia to culture the cells and the quality control analysis performed at the different stages of the process, and logistic costs.

### Selling, general and administrative expenses

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Personnel costs 7.1.5.5.	1,498	1,072	730
Depreciations	113	51	29
Operating costs	1,338	503	273
General costs	252	219	306
<b>Total</b>	<b>3,201</b>	<b>1,845</b>	<b>1,338</b>

The operating costs mainly consist of expenses for congresses, symposia and trade exhibitions, advisory and legal fees, travel expenses, audit and accounting fees, consultancy costs for pricing & reimbursement and IT related costs for the development of an ERP system.

The general costs are the costs related to training and seminars, membership and literature, hiring and executive search, insurance and the office.

### 7.1.5.5. Personnel costs

The number of employees and mandate contractors at the end of the year was:

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
The number of employees and mandate contractors at the end of the year was:			
R&D staff	32	24	17
SG&A staff	12	9	6
<b>Total</b>	<b>44</b>	<b>33</b>	<b>23</b>
Their aggregate remuneration comprised:			
Wages, salaries, fees and bonuses	3,336	2,337	1,535
Social security cost	420	241	140
Group & Hospitalisation insurance	58	35	32
Other costs	304	224	210
<b>Total</b>	<b>4,118</b>	<b>2,837</b>	<b>1,917</b>

#### 7.1.5.6. Financial result

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Interest on bank deposits	311	85	56
Interest paid	(1)	(1)	(1)
Other finance costs	(6)	(10)	(5)
<b>Total financial results</b>	<b>304</b>	<b>75</b>	<b>50</b>

#### 7.1.5.7. Taxes

There is no current tax accounted for in any of the periods presented.

	Income statement			Balance at
	2006	2005	2004	01-Jan-04
Tax losses carried forward	(21,310)	(13,274)	(8,712)	(5,092)
Issuance cost	(1,081)	(1,068)	(447)	(437)
Depreciation of issuance cost	438	230	135	46
Purchase of intangible assets	(117)	(103)	(20)	(19)
Depreciation of intangible assets	48	30	17	13
Total deductible temporary difference	(22,022)	(14,185)	(9,027)	(5,489)
Deferred taxes @ 34%	7,487	4,823	3,069	1,866
Deferred tax of the year	2,664	1,754	1,203	1,866

The Company has not recorded deferred net tax assets on the basis that at December 31, 2006, 2005 and 2004 no profits were realised and the lack of guarantees that it will generate profits in the future which could be offset against current losses.

The deferred taxes are calculated on the following items:

- tax losses as per tax return. The financial figures under IFRS are not necessarily the same as the local GAAP financial figures used for tax declarations. Tax losses as per tax return refers to accounting rules of the tax authorities which in certain cases differ from IFRS accounting rules;
- in the statutory accounts the issuance cost are capitalised and amortised on a straight-line basis pro rata in the year of purchase and over a period of 5 years. In the IFRS statements the issuance costs related to realised capital increases are deducted directly from the share capital, the others are directly expensed in the income statement; and
- in the statutory accounts certain intangible assets are capitalised and amortised on a straight-line basis over a period of 5 years. According to IAS 38, these intangible assets need to be expensed directly in the income statement.

#### 7.1.5.8. Loss per share

Basic loss per share is calculated by dividing the net result attributable to shareholders by the weighted average number of shares outstanding during the year.

<i>Thousands of Euro (€)</i>	<b>Years ended December 31</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
Result for the purpose of basic loss per share, being net loss	(8,246)	(4,803)	(3,747)
Number of shares (common and preferred)	13,836,493	9,378,769	8,196,669
<i>Weighted average number of shares for the purpose of basic loss per share</i>			
Basic loss per share (in Euro (€))	(0.60)	(0.51)	(0.46)

At December 31, 2006, 2005 and 2004, the Company has two classes of warrants who have a dilutive potential: "personnel" warrants and "adjustment" warrants. Under IAS 33, no disclosure is required of the diluted result per share, since as long as the Company is reporting a net loss, the warrants have an anti-dilutive effect rather than a dilutive effect.

#### 7.1.5.9. Intangible assets

<i>Thousands of Euro (€)</i>	<b>Years ended December 31</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>Gross value</b>			
At January 1	63	42	10
Additions	351	21	32
Subsidy			
Impairment			
Gross value at December 31	414	63	42
<b>Accumulated amortisation</b>			
At January 1	31	15	7
Additions	72	16	8
Disposals			
Related to subsidy			
Impairment			
Accumm. amortisation at December 31	103	31	15
<b>Net value at December 31</b>	<b>311</b>	<b>32</b>	<b>27</b>

The intangible asset consists of software rights purchased and development costs of an integrated ERP system. The amortisation period for software is 3 years pro rata in the year of purchase. The straight-line method of amortisation is used.

#### 7.1.5.10. Tangible assets

<i>Thousands of Euro (€)</i>	IT & mach equipment	Furniture	Laboratory equipment	Leasehold improvements	Leasing	TOTAL
<b>Gross value</b>						
At January 1, 2004	320	30	74	7	0	<b>431</b>
Additions	55	41	98	3	0	<b>197</b>
At December 31, 2004	375	71	172	10	0	<b>628</b>
<b>Accumulated amortisation</b>						
At January 1, 2004	164	8	0	0	0	<b>172</b>
Additions	77	11	22	1	0	<b>111</b>
At December 31, 2004	241	19	22	1	0	<b>283</b>
<b>Net value at Dec. 31, 2004</b>	<b>134</b>	<b>52</b>	<b>150</b>	<b>9</b>	<b>0</b>	<b>345</b>
<b>Gross value</b>						
At January 1, 2005	375	71	172	10	0	<b>628</b>
Additions	74	36	11	0	23	<b>144</b>
At December 31, 2005	449	107	183	10	23	<b>772</b>
<b>Accumulated amortisation</b>						
At January 1, 2005	241	19	22	1	0	<b>283</b>
Additions	55	17	35	2	6	<b>115</b>
At December 31, 2005	296	36	57	3	6	<b>398</b>
<b>Net value at Dec. 31, 2005</b>	<b>153</b>	<b>71</b>	<b>126</b>	<b>7</b>	<b>17</b>	<b>374</b>
<b>Gross value</b>						
At January 1, 2006	449	107	183	10	23	<b>772</b>
Additions	180	28	5	3	0	<b>216</b>
At December 31, 2006	629	135	188	13	23	<b>988</b>
<b>Accumulated amortisation</b>						
At January 1, 2006	296	36	57	3	6	<b>398</b>
Additions	85	25	37	2	4	<b>153</b>
At December 31, 2006	381	61	94	5	10	<b>551</b>
<b>Net value at Dec. 31, 2006</b>	<b>248</b>	<b>74</b>	<b>94</b>	<b>8</b>	<b>13</b>	<b>437</b>

#### 7.1.5.11. Receivables

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Trade accounts receivable	184	184	87
Recoverable taxes	260	153	140
Other	0	0	10
<b>Total other accounts receivable</b>	<b>444</b>	<b>337</b>	<b>237</b>

Trade receivables mainly consist of amounts due from the medical centres. The Company considers that the carrying amount of trade and other receivables approximates their fair value.

#### 7.1.5.12. Cash and cash equivalents

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Cash at bank and in hand	7,738	14,899	2,796
<b>Total cash and cash equivalents</b>	<b>7,738</b>	<b>14,899</b>	<b>2,796</b>

In November 2005, the Company issued new shares, providing the Company with about €16 million of new funds. The Company has historically kept its cash in business accounts. These cash and cash equivalents have no restriction upon them.

#### 7.1.5.13. Financial Risk Management

##### Credit risk

The Group is not commercialising its product yet. For the medical centres that receive the products and that need to pay a contribution to costs, the credit risk is limited.

##### Interest risk

The group is not subject to material interest risk. All leases have fixed interest rates.

##### Currency risk

The group may be subject to limited currency risk as certain of its invoices needs to be paid in U.S. Dollars and for the operations of its U.S. wholly-owned subsidiary. The Company has not engaged in hedging of the foreign currency risk via derivative instruments.

#### 7.1.5.14. Share capital

At December 31, the Company's share capital was represented by the following number of shares (units)

<i>Number of shares</i>	<b>Years ended December 31</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
Share class:			
Class A	1,025,943	1,025,943	890,896
Class B	640,000	265,000	265,000
Class C	667,183	667,183	594,106
Class D	71,000	43,500	30,000
Class E	11,752,888	11,752,888	6,925,926
<b>Total</b>	<b>14,157,014</b>	<b>13,754,514</b>	<b>8,705,928</b>

This results in the following share capital at December 31:

<i>Thousands of Euro (€)</i>	<b>Years ended December 31</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
Share Capital	14,116	13,713	8,706
Issuance cost	(1,071)	(1,068)	(447)

The change of the number of shares during each of the 3 years ending on December 31, 2006 is as follows:

<b>Per January 01, 2004</b>	<b>7,347,904</b>
Capital increase	1,358,024
<b>December 31, 2004</b>	<b>8,705,928</b>
Capital increase	4,998,389
Exercise of warrants	22,500
Exercise of "adjustment" warrants	27,697
<b>December 31, 2005</b>	<b>13,754,514</b>
Exercise of warrants	402,500
<b>December 31, 2006</b>	<b>14,157,014</b>

The extraordinary shareholders' meeting of May 14, 2004 approved the issuance of 1,358,024 shares of Class E for an amount of €4,074,072. The shares issued were fully paid in and subscribed;

The extraordinary shareholders' meeting of April 20, 2005 approved the issuance of 452,680 shares of Class E for an amount of €1,358,040. The shares issued were fully paid in and subscribed;

On August 23, 2005 the shareholders of Class A and C exercised 3 "adjustment" warrants issued on September 15, 2003 with a strike price of €0.01 per warrant, resulting in 11,762 additional shares of Class A and 15,935 additional shares of Class C. The shares issued were fully paid in;

On November 3, 2005 a total of 22,500 warrants issued on March 22, 2001 were exercised with a strike price of €1.25 per warrant, resulting in 22,500 additional shares of Class D. The shares were fully paid in. Subsequently, 9,000 of these Class D shares were sold to Gemma Frisius-Fonds K.U.Leuven NV and reallocated to Class A so that the end result of this operation was 9,000 additional shares of Class A and 13,500 additional shares of Class D;

The extraordinary shareholders' meeting of November 3, 2005 approved the issuance of 114,285 shares of Class A, of 57,142 shares of Class C and of 4,374,282 shares of Class E for a total amount of €15,909,982. The shares issued were fully paid in and subscribed;

On April 20, 2006 a total of 27,500 warrants issued on March 22, 2001 were exercised with a strike price of €1.25 resulting in 27,500 additional shares of Class D. The shares issued were fully paid in;

On October 31, 2006 the 375,000 warrants issued on March 13, 2000 were exercised with a strike price of €1.00 resulting in 375,000 additional shares of Class B. The shares issued were fully paid in.

#### 7.1.5.15. Subordinated loan

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Subordinated loan	391	0	0

In accordance with the agreement with respect to the project "Novel treatment approaches for Osteoarthritic joints: from stem cells to nutraceuticals" (see also section 7.1.5.21.), TiGenix and IWT entered into a subordinated loan agreement on September 29, 2006. This loan needs to be paid back in quarterly instalments partly consisting of capital and partly of interest. The first instalment of €48.4k needs to be paid back on January 31, 2010 and the last instalment of €41.2k on October 31, 2012.

#### 7.1.5.16. Finance lease obligations and other lease obligations

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
<b>Amounts payable under finance lease :</b>			
Within one year	5	5	0
In the second to fifth year	8	13	0
After five years		0	0
<b>Total</b>	<b>13</b>	<b>18</b>	<b>0</b>
Less future finance charges	0	0	0
<b>Present value of lease obligations</b>	<b>13</b>	<b>18</b>	<b>0</b>
<b>Outstanding commitments for future minimum rent payments, which fall due as follows :</b>			
Within one year	367	368	265
In the second to fifth year	611	651	569
After five years	395	473	551

The fair value of the Company's finance lease obligations approximated their carrying value. Outstanding operating lease commitments for future minimum rent payments include rental fees related to leased facilities, vehicles and equipment. These operating lease contracts can be terminated early with certain indemnity fees. All figures shown assume that the lease contracts will not be terminated early. Rentals payable under operating leases are charged to the income statement as operating charges on a straight-line basis over the term of the lease.



#### 7.1.5.17. Accounts payable

##### Trade accounts payable

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Trade accounts payable	673	632	383
Accruals for invoices to be received	76	143	157
<b>Total trade accounts payable</b>	<b>749</b>	<b>775</b>	<b>540</b>

##### Other current liabilities

<i>Thousands of Euro (€)</i>	Years ended December 31		
	2006	2005	2004
Payroll	542	232	138
Other accruals	226	76	161
<b>Total other current liabilities</b>	<b>768</b>	<b>308</b>	<b>299</b>

#### 7.1.5.18. Retirement benefit schemes

The Company operates defined contribution systems for all its qualifying employees. The assets of the schemes are held separately from those of the Company in designated funds.

A total cost of €49,249 in 2006 (€26,946 in 2005 and €23,741 in 2004) represents contributions payable to these schemes by the Company at rates specified in the rules of the plans.

### 7.1.5.19. "Stock option" plans

The Company has created several pools of "personnel" warrants for grant to employees, directors, and consultants.

The table below provides an overview as per December 31, 2006 of the outstanding warrant pools together with the activities under the different pools of warrants for the last 3 years ending on December 31, 2006.

	Weighted average exercise price	TOTAL <sup>(1)</sup>	"personnel" warrants issued in					
Creation date			Nov 03, 2005	April 20, 2005	May 14, 2004	Sept 30, 2003 Sept 15, 2003	March 22, 2001	March 13, 2000
<b>Total number created</b>		<b>454,570</b>	<b>45,268</b>	<b>135,802</b>	<b>784,290</b>	<b>120,000</b>	<b>375,000</b>	
<b>Outstanding 31 Dec 2003</b>	<b>1.02</b>	<b>989,351</b>				<b>519,351</b>	<b>95,000</b>	<b>375,000</b>
Granted	3.00	357,285			92,346	264,939		
Lapsed	-	-						
Exercised	-	-						
Expired	-	-						
<b>Outstanding 31 Dec 2004</b>	<b>1.55</b>	<b>1,346,636</b>	-	-	<b>92,346</b>	<b>784,290</b>	<b>95,000</b>	<b>375,000</b>
<b>Exercisable 31 Dec 2004</b>	<b>1.00</b>	<b>375,000</b>	-	-	-	-	-	<b>375,000</b>
Granted	3.18	70,762		29,424	41,338			
Lapsed	3.00	(9,201)			(1,358)	(7,843)		
Exercised	1.25	(22,500)					(22,500)	
Expired	-	-						
<b>Outstanding 31 Dec 2005</b>	<b>1.63</b>	<b>1,385,697</b>	<b>0</b>	<b>29,424</b>	<b>132,326</b>	<b>776,447</b>	<b>72,500</b>	<b>375,000</b>
<b>Exercisable 31 Dec 2005</b>	<b>1.04</b>	<b>447,500</b>	-	-	-	-	<b>72,500</b>	<b>375,000</b>
Granted	3.50	317,649	301,805	15,844				
Lapsed	1.74	(29,762)	(12,500)		(3,169)	(14,093)		
Exercised	1.02	(402,500)	-	-	-	-	(27,500)	(375,000)
Expired	1.25	(45,000)					(45,000)	
<b>Outstanding 31 Dec 2006</b>	<b>2.32</b>	<b>1,226,084</b>	<b>289,305</b>	<b>45,268</b>	<b>129,157</b>	<b>762,354</b>	<b>0</b>	<b>0</b>
<b>Exercisable 31 Dec 2006</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>

Notes:

(1) The column "TOTAL" disregards the warrants that technically have not yet expired but which have not been granted and will not be granted because of lack of exercise windows, more in particular 2,118 "personnel" warrants issued on May 14, 2004 and 152,765 "personnel" warrants issued on November 3, 2005 (see also the overview in section 3.5 of chapter 3).

### "Personnel" warrants issued in March 2000 for the founders

By a decision of the extraordinary shareholders' meeting of March 13, 2000, the Company issued 375,000 "personnel" warrants. On the date of this prospectus, all such warrants have been exercised.

### **"Personnel" warrant issued in March 2001 for employees, directors, and consultants**

By a decision of the extraordinary shareholders' meeting of March 22, 2001, the Company issued 120,000 "personnel" warrants. On the date of this prospectus, all such warrants either have been exercised (50,000 warrants) or have lapsed or expired (70,000 warrants).

### **"Personnel" warrants issued in September 2003 for employees, directors, and consultants**

By a decision of the extraordinary shareholders' meeting of September 15, 2003, the Company issued 632,439 warrants giving the beneficiaries the right to subscribe to shares in the Company of class B or D. By a decision of the extraordinary shareholders' meeting of September 30, 2003, the Company issued an additional 151,851 warrants giving the beneficiaries the right to subscribe to shares in the Company of type B or D. The warrants were granted with an exercise price equal to the fair market price of the underlying shares at the date of grant.

The warrants were granted to selected beneficiaries by decision of the board of directors. Under this plan, 25% of the warrants become vested on each anniversary of the date of the grant, provided that the beneficiary still has a relationship with the Company via an employment agreement, a director's mandate or another collaboration agreement. The warrants can only be exercised once vested, it being understood that they can only be exercised as from January 1 of the fourth year following the year in which they are granted (*i.e.*, from January 1, 2007 onwards for warrants granted in 2003). Non-exercisable warrants become exercisable in case of an IPO or trade sale of the Company. All warrants were granted for free. The duration of the warrants is 5 years as of the issue date of the warrants. Warrants that have not been exercised within 5 years of their creation become null and void.

### **"Personnel" warrants issued in May 2004 for employees, directors, and consultants**

By a decision of the extraordinary shareholders' meeting of May 14, 2004, the Company issued 135,802 warrants giving the beneficiaries the right to subscribe to shares of the Company of class B or D. The warrants were granted with an exercise price equal to the fair market price of the underlying common shares at the date of grant.

The warrants were granted to selected beneficiaries by decision of the board of directors. Under this plan, 25% of the warrants become vested on each anniversary of the date of the grant, provided that the beneficiary still has a relationship with the Company via an employment agreement, a director's mandate or another collaboration agreement. The warrants can only be exercised once vested, it being understood that they can only be exercised as from January 1 of the fourth year following the year in which they are granted (*i.e.*, from January 1, 2008 onwards for warrants granted in 2004). Non-exercisable warrants become exercisable in case of an IPO or trade sale of the Company. All warrants were granted for free. The duration of the warrants is 5 years as of the issue date of the warrants. Warrants that have not been exercised within 5 years of their creation become null and void.

### **"Personnel" warrants issued in April 2005 for employees, directors, and consultants**

By a decision of the extraordinary shareholders' meeting of April 20, 2005, the Company issued 45,268 warrants giving the beneficiaries the right to purchase shares of the Company of class B or D. The warrants were granted with an exercise price equal to the fair market price of the underlying common shares at the date of grant.

The warrants were granted to selected beneficiaries by decision of the board of directors. Under this plan, 25% of the warrants become vested on each anniversary of the date of the grant, provided that the beneficiary still has a relationship with the Company via an employment agreement, a director's mandate or another collaboration agreement. The warrants can only be exercised once vested, it being understood

that they can only be exercised as from January 1 of the fourth year following the year in which they are granted (*i.e.*, from January 1, 2009 onwards for warrants granted in 2005). Non-exercisable warrants become exercisable in case of an IPO or trade sale of the Company. All warrants were granted for free. The duration of the warrants is 5 years as of the issue date of the warrants. Warrants that have not been exercised within 5 years of their creation become null and void.

#### **“Personnel” warrants issued in November 2005 for employees, directors, and consultants**

By a decision of the extraordinary shareholders’ meeting of November 3, 2005, the Company issued 454,570 warrants giving the beneficiaries the right to purchase shares of the Company of class B or D. The warrants were granted with an exercise price equal to the fair market price of the underlying common shares at the date of grant.

The warrants were granted to selected beneficiaries by decision of the board of directors. Under this plan, 25% of the warrants become vested on each anniversary of the date of the grant, provided that the beneficiary still has a relationship with the Company via an employment contract agreement, a director’s mandate or another collaboration agreement. The warrants can only be exercised once vested, it being understood that they can only be exercised as from January 1 of the fourth year following the year in which they are granted (*i.e.*, from January 1, 2009 onwards for warrants granted in 2005). Non-exercisable warrants become exercisable in case of an IPO or trade sale of the Company. All warrants were granted for free. The duration of the warrants is 5 years as of the issue date of the warrants. Warrants that have not been exercised within 5 years of their creation become null and void.

#### **Accounting for share-based payment**

The warrants have been accounted for in accordance with IFRS 2 Share-based payment. In accordance with IFRS 1, the Company elected not to apply IFRS 2 to the equity instruments that were granted on or before November 7, 2002.

The share-based compensation expense recognised in the income statements as such is given below:

<i>Thousands of Euro (€)</i>	<b>Years ended December 31</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
Research and development expenses	124	104	90
Selling, general and administrative expenses	153	111	94
<b>Total for the year</b>	<b>277</b>	<b>215</b>	<b>184</b>
<b>Total per year end</b>	<b>693</b>	<b>416</b>	<b>201</b>

The fair value of each warrant is estimated on the date of grant using the binomial model by Black Scholes with the following assumptions:

- Expected stock price volatility of 40% based on the historical volatility of Benelux based biotech companies.
- Weighted average risk-free interests rates based on Belgian Sovereign Strips at the date of grant with a term equal to the expected life of the warrants, ranging between 2.6% and 3.8%.
- The expected life time of the warrants, which is on average about 4 years.

#### 7.1.5.20. Related parties

Transactions between TiGenix NV/SA and TiGenix Inc., which are related parties, have been eliminated in consolidation and are not disclosed in this note. Transactions between the Company and its employees, consultants or directors are disclosed below.

There were no other related party transactions.

#### Remuneration of key management personnel

The combined remuneration package, including employer taxes, amounted to the following:

Thousands of Euro (€)	Years ended December 31		
	2006 <sup>(1)</sup>	2005	2004
Number of management members	8	8	8
Short-term employee benefits	1,415	1,083	779
Post-employment benefits	9	10	7
Share based compensation	277	215	184
Other employment costs	39	39	22
<b>Total benefits</b>	<b>1,740</b>	<b>1,347</b>	<b>992</b>
Number of warrants offered	194,124	21,503	240,254
Cumulative outstanding warrants	661,250	551,089	552,086
Exercised warrants	3,750	22,500	0
Exercisable warrants	0	3,750	0
Outstanding receivables from persons	0	0	0
Outstanding payables to persons	0	0	0
Shares owned	17,250	13,500	0

#### Note

(1) Anne Bijlstra and Thomas Wagner left the company in 2006 and are not included anymore in the figures for the financial year ended on December 31, 2006. Frank Hazevoets and Peter Tomme joined the management team in 2006 and are included in the figures for the financial year ended on December 31, 2006.

No loans, quasi-loans or other guarantees are outstanding with members of the executive management team.

#### Transactions with non-executive directors

Non-executive directors that represent shareholders of the Company receive no compensation for their position as directors. The reimbursement for expenses in 2006, 2005 and 2004, was respectively €2,003, €2,143 and €1,977 in total.

The independent directors receive a fee for attending and preparing for meetings of the board of directors and they receive reimbursement for expenses directly related to the board meetings. In 2006, 2005 and

2004, respectively €14,494, €12,730 and €11,169 in total was paid as fees and expense reimbursement to independent members of the board of directors.

#### 7.1.5.21. Significant agreements, commitments and contingencies

##### Collaborative research agreements and clinical research agreements

The Company has entered into numerous agreements with universities, medical centres and external researchers for research and development work and for the validation of the Company's technology and products. These agreements typically have durations of one to three years. The Company must pay fixed fees to the collaborators and in exchange receives access and rights to the results of the work.

##### Intellectual property in-licensing agreements

The Company has entered into several agreements with universities and companies for in-licensing intellectual property. These agreements typically require the Company to pay an up-front fee, annual maintenance fees and/or minimum annual royalty fees, legal fees related to the patents, and certain milestone and royalty fees if the patents are eventually used in a commercialised product. In addition, the Company must provide the licensor with periodic reports.

##### Legal proceedings

On the date of this prospectus and since the incorporation of the Company, TiGenix is and has not been involved in any legal proceeding. As a result, the Company has no provisions for legal proceeding at this time.

##### Grants

Since its incorporation, TiGenix has been awarded two grants from the Belgian government.

To date, TiGenix has been approved for a total of €1,578k in grants and has received grant payments for a total of €1,446k. A total of €359k has already been recognised as revenues in the period 2004-2006. If the Company respects the conditions of the already approved grants, the Company stands to receive a further €132k in grant payments. These grants will be only recognised as revenue once paid.

The main grants are the following:

(1) Name (2) Source (3) Description (4) Applicability	Start date	End date	€ amount approved	€ amount received	Main conditions
(1) <b>Tissue engineering for joint repair</b> (2) Flemish government (IWT) (3) research into cellular treatments for cartilage defect repair (4) covers part of personnel/lab costs, and collaborator costs	1/07/00	31/10/03	992,465	992,465	Respect plans and budget. Advances paid at start of each semi-annual period, except last period paid at end
(1) <b>Novel therapeutic approaches for OA joints: from stem cells to nutraceuticals</b> (2) Flemish government (IWT) (3) research into cellular and drug treatments for OA (4) covers part of personnel/lab costs, collaborator costs	1/11/03	31/10/06	585,990	454,029	Respect plans and budget. Advances paid at start of each semi-annual period, except last period paid at end

The grants are subject to periodic reporting on the status of the projects and on the costs incurred to date by the project. The approved amounts are the maximum amounts the Company stands to receive. If the Company spends less on the projects than the original budget or deviates from the plans without consent, then it risks receiving lower grant payments than the amounts that were initially approved.

#### **7.1.5.22. Subsequent events**

On January 10, 2007, the Company entered into an agreement with the Italian company Fidia Advanced Biopolymers to join forces in a strategic partnership (see also section 5.6 of chapter 5).

During its meeting of February 26, 2007, the board of directors of the Company approved the IPO of the Company.

In addition, an extraordinary shareholders' meeting was held on February 26, 2007, with, amongst others, the following items on the agenda:

- the decision to cancel the existing classes of shares and to convert all shares into common shares, the decision to amend the terms and conditions of the existing "personnel" warrants of the Company to take into account the cancellation of the classes of shares;
- the decision to increase the Company's share capital within the framework of the proposed offering and listing, to issue warrants to certain existing shareholders subject to certain conditions, to create new "personnel" warrants, and to create the over-allotment option (see also section 2.1 of chapter 2);
- the confirmation that the existing shares and the shares to be issued upon exercise of outstanding "personnel" warrants do not have any VVPR right;
- the decision to equalise the par value of all shares;
- the decision to amend and restate the articles of association in view of the capital increase and the proposed listing of the Company, including, amongst other things, the decision to grant the board of directors the authority to increase the Company's share capital within the framework of the authorised capital.

The aforementioned resolutions of the extraordinary shareholders' meeting of February 26, 2007, including the cancellation of the existing classes of shares and related amendments of the terms and conditions of the warrants, and the amendment and restatement of the Company's articles of association, are subject to the completion of the offering and listing of the Company's shares on the Eurolist by Euronext Brussels.

#### **7.1.5.23. Reconciliation between the consolidated financial statements under local GAAP and IFRS**

The Company presents the financial statements under IFRS for the previous three years. The date of transition for the Company is as such January 1, 2004. It is planned to start preparing and filing the company's consolidated financial statements under IFRS as of December 31, 2007 and thereafter.

The statutory annual accounts presented under section 7.3 are prepared on a non-consolidated basis and under local (Belgian) GAAP.



## Equity reconciliation and profit & loss reconciliation between local GAAP and IFRS

Thousands of Euro (€)	Years ended December 31					
	2006		2005		2004	
	Equity	Loss of the year	Equity	Loss of the year	Equity	Loss of the year
<b>Under local GAAP</b>	<b>7,926</b>	<b>(8,117)</b>	<b>15,618</b>	<b>(4,613)</b>	<b>2,926</b>	<b>(3,656)</b>
Impact consolidation TiGenix Inc.	(54)	(54)				
Translation reserves	(3)					
Issuance cost	(1,081)	(10)	(1,068)	(0)	(447)	(0)
Depreciation of incorporation cost	438	208	230	96	135	89
Purchase of intangible assets	(117)	(14)	(103)	(83)	(20)	(0)
Depreciation of intangible assets	48	18	30	12	17	4
Share based compensation		(277)		(215)		(184)
<b>Total restatements</b>	<b>(711)</b>	<b>(75)</b>	<b>(911)</b>	<b>(190)</b>	<b>(315)</b>	<b>(91)</b>
<b>Under IFRS</b>	<b>7,158</b>	<b>(8,246)</b>	<b>14,707</b>	<b>(4,803)</b>	<b>2,612</b>	<b>(3,747)</b>

The 2004 and 2005 figures are non-consolidated audited figures both under local GAAP and under IFRS. The 2006 figures are audited non-consolidated figures under local GAAP (see section 7.3) and audited consolidated figures under IFRS.

### 7.1.5.24. Disclosure under Article 114 of the Belgian Royal Decree of January 30, 2001 implementing the Belgian Company Code (*Koninklijk besluit tot uitvoering van het wetboek van vennootschappen / Arrêté royal portant exécution du code des sociétés*)

#### Subsidiaries

The Company has one wholly-owned subsidiary, as follows:

TiGenix Inc.	
Registered office	1209 Orange Street Wilmington, Delaware, U.S.A.
New York address	One Battery Park Plaza, 4th Floor, New York, NYC 10004, U.S.A.
Incorporation Date	February 7, 2006
Number of employees	0

#### Remuneration of the board

The total remuneration of the board of directors in 2006, 2005 and 2004 was €16,497, €14,873 and €13,146 respectively (excluding VAT and excluding stock-based compensation). No advances or credits have been granted to any member of the board of directors. None of the members of the board of directors have received any non-monetary remuneration other than warrants as disclosed above.

## **7.2. INDEPENDENT AUDITOR'S REPORT ON THE ANNUAL ACCOUNTS AS PER DECEMBER 31, 2006, 2005 AND 2004**

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The conclusion of the independent auditor's report on the annual accounts as per December 31, 2006 (consolidated), 2005 and 2004 is as follows:

*"We have audited the attached consolidated balance sheets of TiGenix NV and its subsidiary as at December 31, 2006, the balance sheet of TiGenix NV as at December 31, 2005 and 2004 and the related income statement, cash flow statement and statement of changes in shareholders' equity for the years then ended.*

*These annual accounts are the responsibility of the Board of Directors. It is our responsibility to form an opinion on the annual accounts and to report our opinion to you.*

*We conducted our audit in accordance with Belgian auditing standards, as issued by the Institut des Réviseurs d'Entreprises/Instituut der Bedrijfsrevisoren.*

*We planned and performed our work so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to give reasonable assurance that the financial information is free from material misstatement.*

*Our audit included consideration of internal controls as a basis for designing audit procedures that are appropriate in the circumstances.*

*We examined, on a test basis, evidence supporting the amounts and disclosures in the annual accounts. We assessed the appropriateness of the accounting principles used and the significant estimates made by the Board of Directors, as well as the overall presentation of the annual accounts. We believe that our audit provides a reasonable basis for our opinion.*

*In our opinion these annual accounts present fairly, in all material aspects, the financial position of the Company as at December 31, 2006, 2005 and 2004 and the results of operations and cash flows for the years then ended in accordance with International Financial Reporting Standards as adopted in the EU.*

February 9, 2007

BDO Atrio Bedrijfsrevisoren/ Réviseurs d'Entrprises Burg.Ven. CVBA/Soc. Civ. SCRL

Represented by

Luc Annick

Statutory auditor"

### 7.3. STATUTORY ANNUAL ACCOUNTS 2004 - 2005 -2006

The statutory financial statements as filed with the Belgian National Bank are based upon Belgian GAAP. In conformity with Articles 112 and 16 of the Belgian Company Code, the 2006 accounts are not consolidated. An unqualified audit opinion has been issued by the statutory auditor on February 9, 2007 (see section 7.4).

The impact on consolidating TiGenix Inc. of €54k is not taken into account in the audited non-consolidated statutory annual account of 2006.

#### 7.3.1. Statutory income statement 2004-2006

<b>STATUTORY INCOME STATEMENT</b>		<b>Year ended December 31</b>		
	<i>Thousands of Euro (€)</i>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>I. Operating income</b>		<b>416</b>	<b>793</b>	<b>627</b>
A. Turnover		322	604	482
D. Other operating income		94	189	145
<b>II. Operating charges</b>		<b>(8,830)</b>	<b>(5,477)</b>	<b>(4,332)</b>
B. Services and other goods		6,100	3,910	3,270
C. Remuneration, social security costs, pensions		2,251	1,327	832
D. Depreciation & amounts written off formation expenses, intangible and tangible fixed assets		453	239	214
G. Other operating charges		25	1	17
<b>III. Operating profit/(loss)</b>		<b>(8,413)</b>	<b>(4,684)</b>	<b>(3,705)</b>
<b>IV. Financial income</b>		<b>317</b>	<b>85</b>	<b>57</b>
B. Income from current assets		312	85	56
C. Other financial income		4	0	0
<b>V. Financial charges</b>		<b>(21)</b>	<b>(15)</b>	<b>(7)</b>
A. Debt charges		1	1	1
C. Other financial charges		20	14	6
<b>VI. Current profit/(loss) before taxes</b>		<b>(8,117)</b>	<b>(4,613)</b>	<b>(3,656)</b>
<b>VII. Extraordinary income</b>		<b>0</b>	<b>0</b>	<b>0</b>
<b>VIII. Extraordinary charges</b>		<b>0</b>	<b>0</b>	<b>0</b>
<b>IX. Profit/(loss) before taxes</b>		<b>(8,117)</b>	<b>(4,613)</b>	<b>(3,656)</b>
<b>X. Income taxes</b>		<b>0</b>	<b>0</b>	<b>0</b>
<b>XI. Profit/(loss) for the year after taxes</b>		<b>(8,117)</b>	<b>(4,613)</b>	<b>(3,656)</b>

<b>APPROPRIATION ACCOUNT</b>		<b>Year ended December 31</b>		
	<i>Thousands of Euro (€)</i>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>A. Loss to be appropriated</b>				
A1. Loss for the period available for appropriation		(8,117)	(4,613)	(3,656)
A2. Loss to be carried forward		(13,407)	(8,794)	(5,138)
<b>B. Transfer from capital and reserves</b>				
B1. From capital and share premium account				
<b>D. Result to be carried forward</b>				
D2. Loss to be carried forward		21,524	13,407	8,794

### 7.3.2. Statutory balance sheet 2004-2006

STATUTORY BALANCE SHEET AFTER APPROPRIATIONS <i>Thousands of Euro (€)</i>	Year ended December 31		
	2006	2005	2004
<b>FIXED ASSETS</b>	<b>1,492</b>	<b>1,351</b>	<b>720</b>
<b>I. Formation expenses</b>	<b>643</b>	<b>838</b>	<b>312</b>
<b>II. Intangible fixed assets</b>	<b>380</b>	<b>106</b>	<b>30</b>
<b>III. Tangible fixed assets</b>	<b>437</b>	<b>374</b>	<b>345</b>
B. Plant, machinery and equipment	247	153	135
C. Furniture and vehicles	169	196	201
D. Leasing and other similar rights	13	18	0
E. Other tangible assets	8	7	9
<b>IV. Financial fixed assets</b>	<b>32</b>	<b>34</b>	<b>33</b>
A. Affiliated enterprises	0	0	0
A1. Investments	0	0	0
A2. Amounts receivable	0	0	0
C. Other financial assets	32	34	33
C2. Amounts received and cash guarantee	32	34	33
<b>CURRENT ASSETS</b>	<b>8,354</b>	<b>15,368</b>	<b>3,046</b>
<b>V. Amounts receivable after one year</b>	<b>78</b>		
<b>VI. Stocks and contracts in progress</b>			
<b>VII. Amounts receivable within one year</b>	<b>444</b>	<b>337</b>	<b>237</b>
A. Trade debtors	184	184	87
B. Other amounts receivable	260	153	150
<b>VIII. Investments</b>			
<b>IX. Cash at bank and in hand</b>	<b>7,714</b>	<b>14,899</b>	<b>2,796</b>
<b>X. Deferred charges and accrued income</b>	<b>118</b>	<b>132</b>	<b>13</b>
<b>TOTAL ASSETS</b>	<b>9,846</b>	<b>16,719</b>	<b>3,766</b>

	Thousands of Euro (€)		Year ended December 31
<b>STATUTORY BALANCE SHEET AFTER APPROPRIATIONS</b>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>CAPITAL AND RESERVES</b>	<b>7,926</b>	<b>15,618</b>	<b>2,927</b>
<b>I. Capital</b>	<b>14,115</b>	<b>13,713</b>	<b>8,706</b>
<b>A. Issued capital</b>	<b>14,115</b>	<b>13,713</b>	<b>8,706</b>
<b>II. Share premium account</b>	<b>15,335</b>	<b>15,312</b>	<b>3,014</b>
<b>III. Revaluation surpluses</b>			
<b>IV. Reserves</b>			
<b>V. Accumulated profit/(loss)</b>	<b>(21,524)</b>	<b>(13,407)</b>	<b>(8,794)</b>
<b>VI. Investment grants</b>			
<b>VII. Provisions and postponed taxes</b>	<b>0</b>	<b>0</b>	<b>0</b>
A. Provisions for liabilities and charges	0	0	0
A4. Other liabilities & charges			
<b>AMOUNTS PAYABLE</b>	<b>1,920</b>	<b>1,100</b>	<b>839</b>
<b>VIII. Debts payable after 1 year</b>	<b>400</b>	<b>13</b>	<b>0</b>
A. Financial debts	399	13	0
A1. Subordinated loans	391		
A3. Leasing and other similar rights	9	13	
A4. Credit institutions			
<b>IX. Debts payable within 1 year</b>	<b>1,293</b>	<b>1,012</b>	<b>678</b>
A. Current portion of debts after one year	4	4	
B. Financial debts	0	0	0
B1. Credit institutions			
C. Trade debts	906	775	540
C1. Suppliers	906	775	540
E. Taxes, remuneration & social security	383	233	138
E1. Taxes	75	41	36
E2. Remuneration & social security	308	192	102
F. Other amounts payables			
<b>X. Accrued charges and deferred income</b>	<b>227</b>	<b>75</b>	<b>161</b>
<b>TOTAL LIABILITIES</b>	<b>9,846</b>	<b>16,719</b>	<b>3,766</b>

### 7.3.3. Accounting Policies (Belgian GAAP)

The valuation rules have been prepared in accordance with the provisions of Chapter II of the Belgian Royal Decree of January 30, 2001 relating to the implementation of the Belgian Company Code (*Koninklijk besluit tot uitvoering van het wetboek van vennootschappen / Arrêté royal portant exécution du code des sociétés*). All amortisations and depreciations are done on a pro rata basis in the year of purchase.

#### 7.3.3.1. Formation expenses and costs relating to capital increases

These expenses, included the issuance costs, are recognised as assets and are amortised by 20% annually.

### **7.3.3.2. Intangible fixed assets**

#### **Research and development costs**

Research and development costs are expensed directly in the income statement.

#### **Patents, licenses and similar rights**

The costs relating to the request of these rights are expensed directly in the income statement. Costs relating to the maintenance of these assets are capitalised at purchase price or, if lower, at their useful value. Patents are depreciated on a straight-line basis over a period of 5 years and software rights and development costs are depreciated on a straight-line basis over a period of 3 years.

### **7.3.3.3. Tangible fixed assets**

These assets are capitalised and depreciated on a straight-line basis:

- IT equipment : over a period of 3 years
- Installations and equipment : over a period of 5 years
- Furniture : over a period of 5 years
- Laboratory equipment : over a period of 5 year
- Leasehold improvements : over a period of 5 year
- Leasing : over a period of 4 year

In the event where the accounting value exceeds the useful value (or the realised value for the assets that are no longer used), the Company should perform additional or exceptional depreciations.

### **7.3.3.4. Financial fixed assets**

These assets are capitalised at purchase price excluding any miscellaneous fees.

The shares and participations are reduced in value in case of depreciation or lasting reduction in value, as a result of the situation, the profitability or perspective of the company in which the shares or the participations are held.

Reductions in value of amounts receivable included in the financial fixed assets are recorded when the payment thereof or part thereof at their due date is uncertain or has become compromised.

### **7.3.3.5. Amounts receivable (after one year – within one year)**

The amounts receivable do not carry any interest and are capitalised at their nominal value.

#### **7.3.3.6. Treasury placements and available cash**

Placements with financial institutions are capitalised at their nominal value. The titles are capitalised at purchase cost excluding miscellaneous fees.

Reductions in value are recorded in the event where the realisation value at the date of the closing of the financial year is below the purchase cost.

#### **7.3.3.7. Provisions for risks and charges**

The provisions for risks and charges are individualised taking into account the corresponding risks and charges they are intended to cover.

The provisions for risks and charges can only be maintained provided that they exceed, as per the date of the closing of the financial year, an actual appreciation of depreciations, charges and risks for which they have been established.

#### **7.3.3.8. Debts (payable after one year - payable within one year)**

All debts are capitalised at their nominal value at the date of the closing of the financial year.

The valuation rules applicable to amounts receivable are also applicable for debts, with the difference however that the implicit *pro rata* interests are recorded in the regularisation accounts on the assets side.

At the date of the closing of the financial year, all charges to be paid in relation to the financial year concerned and the previous financial years are taken into account.

#### **7.3.3.9. Regularisation accounts**

##### **Regularisation accounts on the assets side**

These accounts include:

- The *pro rata* parts of the charges incurred during the financial year or during a previous financial year but that are related to one or more subsequent financial years.
- The *pro rata* parts of the proceeds that will only be received during a subsequent financial year but that relate to a previous financial year.

##### **Regularisation accounts on the liabilities side**

These accounts include:

- The *pro rata* parts of the charges that will only be paid during a subsequent financial year but that relate to a previous financial year.
- The *pro rata* parts of the proceeds received during the financial year or a previous financial year but that relate to one or more subsequent financial years.



### 7.3.3.10. Currencies

The amounts receivable and debts in currencies are converted at the applicable exchange rate at the date of the closing of the financial year.

Currency losses are recorded in the statement of results.

Unrealised currency gains are reported as proceeds to be recorded on the regularisation accounts on the liabilities side.

## 7.4. INDEPENDENT AUDITOR'S REPORT ON THE STATUTORY ANNUAL ACCOUNTS AS PER DECEMBER 31, 2006

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On February 9, 2007 the Company's independent auditor's issued the following report with respect to the statutory annual accounts as per December 31, 2006:

*"In accordance with legal and statutory requirements, we are pleased to report on the performance of the audit mandate which you have entrusted to us. We report on the fair view of the financial statements and the required additional disclosures (and information).*

### UNQUALIFIED AUDIT OPINION ON THE FINANCIAL STATEMENTS

*We have audited the financial statements for the year ended December 31, 2006, prepared in accordance with accounting principles generally accepted in Belgium, which show a balance sheet total of 9.848 KEUR and a loss of 8.117 KEUR.*

*The preparation of the financial statements is the responsibility of the board of directors. This includes, among other things, the implementation and maintenance of internal control procedures related to the preparation and the fair presentation of the financial statements free from material misstatement resulting from fraud or error; the application of adequate accounting principles and sound accounting estimates.*

*It is our responsibility to form an opinion on the financial statements and to report our opinion to you. We conducted our audit in accordance with Belgian legal requirements and auditing standards, as issued by the Institut des Réviseurs d'Entreprises/Instituut der Bedrijfsrevisoren. We planned and performed our work so as to obtain sufficient evidence to give reasonable assurance that the financial statements are free from material misstatements as a result of fraud or error.*

*In accordance with those standards, we considered the company's administrative and accounting organisation as well as its internal control procedures. Company officials have clearly responded to our requests for explanations and information. An audit includes examining, on a test basis, evidence supporting the amounts disclosed in the financial statements.*

*We have assessed the accounting principles used and significant accounting estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.*

*In our opinion, taking into account the accounting principles generally accepted in Belgium, the financial statements give a true and fair view of the company's net assets, financial position as of December 31, 2006 and the results of its operations for the year then ended.*

### ADDITIONAL DISCLOSURES (AND INFORMATION)

*The preparation of the annual report as well as the compliance by the company with the Company Code and the Company's bylaws are the responsibility of the board of directors.*

*It is our responsibility to include in our report the following additional disclosures and information which do not modify our audit opinion on the financial statements.*

- The directors' report includes the information required by law and is consistent with the financial statements. We are, however, unable to comment on the description of the principal risks and uncertainties which the company is facing, and of its situation, its foreseeable evolution or the significant influence of certain facts on its future development. We can nevertheless confirm that the matters disclosed do not present any obvious contradictions with the information of which we became aware during our audit.*
- Without prejudice to certain formal aspects of minor importance, the accounting records are maintained and the annual accounts have been prepared in accordance with the legal and regulatory requirements applicable in Belgium.*
- No transactions have been undertaken or decisions taken in violation of the company's articles of association or company law which we would have to report to you. The appropriation of the result proposed to the Annual General Meeting complies with the legal and statutory provisions.*
- In conformity with article 523 of the Company laws we report on the following transactions:*

*Decision of the board meeting held on 20 October 2003*

*On the meeting of the board of directors held 20 October 2003, it was decided to approve the "remuneration" proposal relating to Gil Beyen BVBA. Gil Beyen BVBA declares that, due to an oblivion, the said board meeting failed to expressly apply the conflict of interest procedure of article 523 of the Companies code although Gil Beyen BVBA had an interest which was conflicting with this decision. The conflicting interest consisted of the fact that Gil Beyen BVBA financially benefited from the decision, which resulted in a cost (payment of a remuneration) for the Company. The financial consequences for the Company remain limited to the amount of this remuneration.*

*The board notes that this conflicting interest is justified on the basis of the nature and the scope of the management services rendered by Gil Beyen BVBA to the Company and on the basis that the remuneration granted for these services is in conformity with market practice.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

*Decision of the board meeting held on 6 September 2004*

*On the meeting of the board of directors held on 6 September 2004, it was acknowledged that a director's liability insurance had been entered into with AIG Europe. The directors already in office at that time (i.e. all current directors except Sogam NV) declare that, due to an oblivion, the said board meeting failed to expressly apply the conflict of interest procedure of article 523 of the Companies code although they potentially had an interest which was conflicting with this decision. The conflicting interest consisted of the fact that the directors are covered by the insurance policy in case of director's liability, which resulted in a premium to be paid by the Company. The financial consequences for the Company remain limited to the amount of this premium.*

*The board notes that this potential conflicting interest is justified on the basis of the fact that it is a necessity and custom in similar companies to enter into such insurance contracts in order to be able to attract and keep directors that dispose of the necessary experience and qualities.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

*Decision of the board meeting held on 6 February 2006*

*On the meeting of the board of directors held on 6 February 2006, it was decided to approve the proposal by the remuneration committee relating to the remuneration of the members of the management team. Gil Beyen BVBA declares that, due to an oblivion, the said board meeting failed to expressly apply the conflict of interest procedure of article 523 of the Companies code although Gil Beyen BVBA had an interest which was conflicting with this decision. The conflicting interest consisted of the fact that Gil Beyen BVBA financially benefited from the decision, which resulted in a cost (payment of a remuneration) for the Company. The financial consequences for the Company remain limited to the amount of this remuneration.*

*The board notes that this conflicting interest is justified on the basis of the nature and the scope of the management services rendered by Gil Beyen BVBA to the Company and on the basis that the remuneration granted for these services is in conformity with market practice.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

#### Decision of the board meeting held on 24 March 2006

*On the meeting of the board of directors held on 24 March 2006, it was decided to increase the coverage of the aforementioned director's liability insurance. The directors declare that, due to an oblivion, the said board meeting failed to expressly apply the conflict of interest procedure of article 523 of the Companies code although they potentially had an interest which was conflicting with this decision. The conflicting interest consisted of the fact that the directors will benefit from an extended coverage in case of director's liability, which resulted in a higher cost (payment of higher premiums) for the Company. The financial consequences for the Company remain limited to the amount of this increased premium.*

*The board notes that this conflicting interest is justified on the basis of the fact that it is a necessity and custom in similar companies to enter into a director's liability insurance contract which is as good as possible in order to be able to attract and keep directors that dispose of the necessary experience and qualities.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

#### Decision of the board meeting held on 31 October 2006

*On the meeting of the board of directors held on 31 October 2006, it was decided to accept the proposal of the IPO committee to further negotiate with ING België NV (Corporate Finance division) and Piper Jaffray Ltd. as joint lead managers and book runners and Petercam NV as (active) co-lead manager to assist the Company with the possible IPO. ING België NV, director of the Company, declares that, due to an oblivion, the said board meeting failed to expressly apply the conflict of interest procedure of article 523 of the Companies code although it potentially had an interest which was conflicting with this decision. The conflicting interest consisted of the fact that the decision possibly financially benefits ING België NV, which resulted in a cost (payment of a remuneration for the performance of the task as joint lead manager) for the Company. The financial consequences for the Company remain limited to the amount of this remuneration.*

*The board notes that this conflicting interest is justified on the basis of the fact that ING België NV, both as shareholder and as underwriter of the 2005 private placement, has acquired an extensive knowledge on the Company which can be of a great use for assisting the Company with the possible IPO and on the basis that the remuneration stipulated for by ING België NV is in conformity with market practice.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

*Decision of the board meeting held on 6 February 2006*

*On 6 February 2006, a number of warrants were granted to, among others, Frank Luyten, Gil Beyen BVBA, Mrs. Marie-Hélène Plais and Mr. Sven Andréasson. For these directors, this transaction could be considered as a conflict of interest, as defined in Article 523 of the Companies Code.*

*The Board of Directors decided that this transaction contributes to the motivation of key people of the company and is in the company's interest, and therefore, approved the plan.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

*Decision of the board meeting held on 19 January 2007*

*On the meeting of the board of directors held on 19 January 2007, it was decided to approve the bonus proposal by the remuneration committee relating to Gil Beyen BVBA. Gil Beyen BVBA declares that, due to an oblivion, the said board meeting failed to expressly apply the conflict of interest procedure of article 523 of the Companies code although Gil Beyen BVBA had an interest which was conflicting with this decision. The conflicting interest consisted of the fact that Gil Beyen BVBA financially benefited from the decision, which resulted in a cost (payment of a bonus remuneration) for the Company. The financial consequences for the Company remain limited to the amount of this bonus remuneration.*

*The board notes that this conflicting interest is justified on the basis of the nature and the scope of the management services rendered by Gil Beyen BVBA to the Company and on the basis that the remuneration bonus granted for these services is in conformity with market practice.*

*We have reviewed the circumstances and justification of this decision and confirm that the financial consequences are fairly stated.*

*Zaventem, February 9, 2007*

*BDO Atrio Réviseurs d'Entreprises Soc. Civ. SCRL  
Statutory Auditor  
Represented by L. Annick"*

## 8. GLOSSARY

### 8.1. FINANCIAL GLOSSARY

<b>Articles of association</b>	The articles of association of TiGenix.
<b>Belgian GAAP</b>	Generally accepted accounting principles in Belgium
<b>CBFA</b>	Banking, Finance and Insurance Commission in Belgium (Commissie voor het Bank-, Financie- en Assurantiewezen / Commission Bancaire, Financière et des Assurances).
<b>CET</b>	Central European Time
<b>CIK</b>	The Inter-professional Securities Depositing Trust in Belgium (Interprofessionele Effectendeposito- en Girokas / Caisse Interprofessionnelle de Dépôts et de Virements de Titres).
<b>€ or Euro</b>	Euro, the legal currency of the European Monetary Union, of which Belgium is one of the members.
<b>Euronext Brussels</b>	Euronext Brussels SA/NV, located in Brussels, Belgium.
<b>Gearing ratio</b>	The gearing ratio expresses, in percentages, how the total financial debt relates to the total equity.
<b>VVPR</b>	Reduced withholding tax (Verminderde Voorheffing / Précompte Réduit)

### 8.2. BUSINESS GLOSSARY

<b>Arthroscopy</b>	Arthroscopy is a minimally invasive surgical procedure to visualize, diagnose and treat problems inside a joint. In an arthroscopic examination, an orthopaedic surgeon makes a small incision in the patient's skin and then inserts pencil-sized instruments that contain a small lens and lighting system to magnify and illuminate the structures inside the joint. By attaching the arthroscope to a miniature television camera, the surgeon is able to see the interior of the joint through this very small incision rather than a large incision needed for surgery.
<b>Articular</b>	Of or pertaining to a joint. Articular cartilage is the cartilage that covers the ends of bones in joints and enables the bones to move smoothly over one another.
<b>Allogeneic</b>	Produced from another person's tissues or derived from the body of another person, such as an organ taken from one person and implanted into another person.
<b>Autologous</b>	Produced from the subject's own tissues or derived from the subject's own body, such as skin taken from one part of the body and grafted to another part.
<b>Bone</b>	The dense connective tissue that makes up the majority of the skeleton of most vertebrates, consisting of a mineralised matrix surrounding living osteocytes.

<b>Cartilage (stable)</b>	<p>A dense connective tissue consisting of chondrocytes and extracellular matrix containing collagen type II and large amounts of proteoglycans. Cartilage is more flexible and compressible than bone and often serves as an early skeletal framework, becoming mineralised or replaced by bone as the animal ages.</p> <p>Stable cartilage is cartilage that remains intact over time and that will never undergo mineralisation nor be replaced by bone.</p>
<b>CBER</b>	Center for Biologics Evaluation and Research, a division of FDA that regulates biological products in the United States.
<b>CEF</b>	Cell Expansion Facility, production facility where the cells taken from the patient's biopsy are expanded according to specific culture methods in order to obtain a sufficient number of cells for re-implantation into the cartilage defect
<b>Chondrocyte</b>	Differentiated cell responsible for secretion of extra-cellular matrix of cartilage.
<b>Collagen</b>	A gelatinous protein present in all multi-cellular organisms, particularly in the connective tissue, to which it gives strength and flexibility.
<b>Culture media</b>	Any liquid or solid preparation made specifically for the growth, storage, or transport of micro-organisms or cells/tissues. The variety of media that exist (such as differential media, selective media, test media, and defined media) allow for the culturing of specific micro-organisms and cell types. Solid media consist of liquid media that have been solidified with an agent such as agar or gelatine.
<b>Embryonic</b>	Pertaining to the earliest stage of development of an organism.
<b>EMA</b>	European Medicines Agency, regulatory authorities in Europe responsible for medicinal products, public and animal health.
<b>FDA</b>	Food and Drug Administration, regulatory authorities in the United States responsible for food and medicinal products.
<b>Fibrous tissue</b>	Tissue consisting mainly of fibres or fibre-containing materials, such as fibrous connective tissue.
<b>GCP</b>	Good Clinical Practice, international regulations that must be observed to ensure high quality clinical studies and admissible data.
<b>GMP</b>	Good Manufacturing Practice, industry standards according to which a production facility should be operated in order to be allowed for production of medicinal products.
<b>Growth factors</b>	<p>A complex family of polypeptide hormones or secreted proteins that are produced by the body to control growth, division and maturation of cells. These factors occur naturally but some can be synthesised using molecular biology and are used in a variety of clinical indications. Examples include epidermal growth factor, platelet-derived growth factor and fibroblast growth factor. Perturbation of growth factor production or of the response to growth factor may be important in neoplastic transformation.</p>



<b>Histomorphometry</b>	The quantitative measurement and characterization of microscopical images using a computer; manual or automated digital image analysis typically involves measurements and comparisons of selected geometric areas, perimeters, length angle of orientation, form factors, centre of gravity coordinates, as well as image enhancement.
<b>Homeostasis</b>	In medicine and biology, this term is applied to the inherent tendency in an organism toward maintenance of physiological and psychological stability.
<b>Hyaline cartilage</b>	A type of cartilage that appears translucent, bluish-white in the fresh condition and predominantly consists of a type II collagen network and large amounts of highly sulphated, high molecular weight proteoglycan aggregates.
<b>Hyaluronic acid; hyaluronan</b>	A mucopolysaccharide, forming a gelatinous material in the tissue spaces and acting as a lubricant and shock absorbent generally throughout the body
<b>ICH</b>	The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.
<b>ICRS</b>	International Cartilage Repair Society.
<b>Immunogeneic</b>	Having the ability to provoke an immune response; having the properties of an antigen or any substance that may trigger a particular immune reaction, such as the production of antibodies.
<b>IND</b>	Acronym for Investigational New Drug Application. An IND is an application filed (usually by the sponsor) with the FDA that includes a detailed description of the planned clinical investigation.
<b>Joint surface</b>	The (cartilage) layer covering the ends of bones in the joint.
<b>Joint surface defect</b>	Defect of the cartilage and often also of the underlying bone in the joint.
<b>Ligament</b>	A type of white fibrous connective tissue that connects bones or cartilage, serving to support and strengthen joints.
<b>Medicinal product</b>	Pharmaceutical product.
<b>Meniscus</b>	An intra-articular structure of fibrocartilaginous tissue.
<b>Microfracture</b>	Perforation of the subchondral bone plate to create a blood clot which, mixed with bone marrow stem cells, tends to form a scar-like fibro-cartilaginous repair tissue.
<b>Musculoskeletal</b>	Referring to the muscles, tendons, ligaments, cartilage, bones, joints, and spinal discs.
<b>Osteoarthritis or OA</b>	Joint disorder associated with the degeneration of the joints including the bone and cartilage.
<b>Osteocyte</b>	A mature bone cell.
<b>Periosteum</b>	The membrane of fibrous connective tissue which closely surrounds all bones except at the articular surfaces, and has bone-forming potentialities.



<b>Progenitor cell</b>	Undifferentiated cells whose lineal descendants differentiate along the appropriate pathway to produce a fully differentiated phenotype.
<b>Proteoglycans</b>	Proteoglycans represent a special class of glycoproteins that are heavily glycosylated. They consist of a core protein with one or more covalently attached glycosaminoglycan chain(s). These glycosaminoglycan (GAG) chains are long, linear carbohydrate polymers that are negatively charged under physiological conditions, due to the occurrence of sulphate and uronic acid groups. Proteoglycans are a major component of the extracellular matrix, the 'filler' substance existing between cells in an organism.
<b>Regenerative Medicine</b>	Regenerative medicine refers to technologies that repair, replace, or regenerate diseased or defective tissues or organs. The main types of regenerative medicine utilize products naturally occurring in the body, such as genes and proteins (antibodies, growth factors, hormones); cells and tissues; embryonic stem cells, and biomaterials.
<b>Stem cell</b>	Cell that gives rise to distinct daughter cells, one a replica of the stem cell, one a cell that will further proliferate and differentiate into a mature cell. "Pluripotent" stem cells can give rise to different lineages, "Committed" stem cells only to some.
<b>Synovial membrane</b>	The synovium or synovial membrane is a thin, weak layer of tissue which lines the non-cartilaginous surfaces within the joint space, sealing it from the surrounding tissue. The membrane contains a fibrous outer layer, as well as an inner layer that is responsible for the production of specific components of synovial fluid, which nourishes and lubricates the joint. The membrane is also responsible for the removal of undesirable substances from the synovial fluid.
<b>Tissue</b>	An integrated group of cells with a common structure and function.
<b>Vascularisation</b>	The growth of blood vessels into a tissue to improve the oxygenation and nutrient supply.
<b>Xenograft</b>	A surgical graft of tissue from one species onto or into individuals of unlike species, genus or family. Also known as a heteroplastic graft.

## APPENDIX 1: PRESS RELEASES 2005-2006

Below is a summary of the press releases issued by TiGenix in 2005 and 2006. For further information relating to the contents of these press releases, referral is made to the Company's website [www.tigenix.com](http://www.tigenix.com).

<b>January 10, 2005</b>	TiGenix completes recruitment of multinational Phase III clinical trial for cartilage repair
<b>January 28, 2005</b>	TiGenix' Core Patents Granted in Europe
<b>June 10, 2005</b>	TiGenix Files IND for ChondroCelect
<b>June 15, 2005</b>	TiGenix and ProStrakan enter into OsteoArthritis research collaboration
<b>January 5, 2006</b>	TiGenix closes 16 million Series B financing round and expands shareholder base worldwide
<b>March 28, 2006</b>	TiGenix establishes US presence
<b>September 18, 2006</b>	Orthopaedic surgeons rate restoration of stable hyaline cartilage and good long term clinical outcome as ultimate goals in the treatment of knee cartilage defects. Publication of the results of a global web-based survey
<b>January 11, 2007</b>	TiGenix expands management team
<b>January 24, 2007</b>	TiGenix and Fidia Advanced Biopolymers enter into strategic partnership
<b>February 19, 2007</b>	TiGenix announces positive phase III results and plans listing on Euronext Brussels



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## APPENDIX 3: APPLICATION FORM





Limited Liability Company  
(naamloze vennootschap /société anonyme)  
Technologielaan 3  
3001 Leuven (Heverlee), Belgium

Registered with the Register of Legal Entities (Leuven) under company number 0471.340.123

OFFERING FOR SUBSCRIPTION OF UP TO €40 MILLION IN NEW SHARES  
**APPLICATION FORM** (to be completed in duplicate)

The undersigned (first name and last name) .....  
Residing at ....., street, n° .....  
Having had the opportunity to read the prospectus, declares to subscribe for the offered shares:

☐ **In the institutional tranche**

Number of shares <sup>1</sup>	At a price below (in €)
.....	.....
.....	.....
.....	.....

☐ **In the retail tranche: open to all investors**

..... shares<sup>2</sup> at the price published in the press on or about March 24, 2007 as follows

The offering price that will be determined through a book building procedure with international investors within the price range but which will, for retail investors, never exceed the upper end of the initial price range published on or about March 10, 2007 must be debited from my account N° ....., on the payment date expected to be on March 29, 2007.

I would like these offered shares:

- ☐ to be delivered to me as BEARER shares<sup>3</sup>  
☐ to be REGISTERED IN MY NAME in the Company's share register  
☐ to be deposited in my securities account N° ..... with .....

Done in duplicate, at ....., on March ....., 2007

The financial institution

The subscriber

<sup>1</sup> Fill out the number of offered shares requested

<sup>2</sup> Fill out the number of offered shares requested

<sup>3</sup> The cost for physical delivery is mentioned in section 2.12.4 "Tax on the physical delivery of bearer securities".

☐ Tick where appropriate





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Residing at ....., street, n° .....  
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Number of shares <sup>1</sup>	At a price below (in €)
.....	.....
.....	.....
.....	.....

☐ **In the retail tranche: open to all investors**

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☐ to be REGISTERED IN MY NAME in the Company's share register  
☐ to be deposited in my securities account N° ..... with .....

Done in duplicate, at ....., on March ....., 2007

The financial institution

The subscriber

<sup>1</sup> Fill out the number of offered shares requested

<sup>2</sup> Fill out the number of offered shares requested

<sup>3</sup> The cost for physical delivery is mentioned in section 2.12.4 "Tax on the physical delivery of bearer securities".

☐ Tick where appropriate



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