



November 2011

# SUMMARY

**please read, this is NOT a disclaimer !**

The idea of an open fund investing in European listed Biotechnology companies is a challenging one. But this is exactly what the Belsize Fund is aiming at. Beyond the obvious difficulties, I believe there are reasons to be confident. The first one is also the most publicly talked about: the inescapable need for big pharma to **bridge the patent cliff** (p.5) and find outside of their own downscaled labs their future drug candidates. In December 2011, Lipitor, the world's biggest selling drug with a peak turnover north of USD 12bn, starts facing generic competition in the US. There is a flip side to this story though, as **big pharma** are not only scouting the market in order to licence-in new compounds, they are also **cutting down development costs** in an unprecedented way, which means that deals are delayed to ever later stages. Combined with the difficult financing environment in general, biotechnology companies have been finding themselves between a rock and a hard place for several quarters now. But this is **reflected in the valuation** (p.6) and this is indeed the second reason to be confident. Valuations are depressed on a global basis, and non US biotechnology companies offer an additional discount as they lack any institutional attention. Finally , the last and arguably the most important reason to be positive is that for all the above mentioned gloom, there are extraordinary news to be expected in the near future from companies you have never heard of as their **pipelines reach an inflexion point** (p .8) True, the completion of the Human Genome Project , 10 years ago, has not been the game changer many expected but rather a sobering moment and the stepping stone for yet a bigger challenge, the deciphering of the proteome. These insights though, together with advances in bio informatics and technologies like the PCR made it possible that new targets could be identified and drug candidates virtually designed and optimised at lower costs. Take a look at **Algeta** (p.13). There will be more success stories like this one, I believe **Epigenomics AG** will be one (p.14). I shall finish off with a little puzzle: what is the performance of a portfolio of 10 stocks, equally weighted on day 1, and with only 5 stocks left at the end of the reference period, because 5 are bankrupt, 4 are unchanged and 1 is a „ten bagger“ ? (answer page 10)

# Investment objective

- The Belsize Fund aims to achieve significant capital appreciation over the long term, by investing selectively in European listed biotechnology and life sciences companies.
- Approximately 250 companies, listed in Europe in the biotechnology or related sectors.

# Why biotechs ? Why now ?

- The patent cliff
- The valuation gap
- The underresearched/underinvested sector
- The maturing pipelines
- The personalised medicine boost

# The patent cliff

## Top 15 best selling prescription drugs worldwide

Drug	Indication	Company	Sales 2007 (USD million)	Patent expiry
Lipitor	Cardiovascular diseases	Pfizer	12,900	2010
Seretide	Asthma	GlaxoSmithKline	7,070	2010
Plavix	Cardiovascular diseases	BMS/Sanofi	5,900	2011
Nexium	Heartburn	AstraZeneca	5,700	2014
Enbrel *)	Rheumatoid Arthritis	Amgen	5,263	na
Diovan	Hypertension	Novartis	5,012	2012
Zyprexa	Schizophrenia	Eli Lilly	4,760	2011
Rituxan *)	Cancer/Rheumatoid Arthritis	Genentech/Biogen IDEC	4,603	na
Singulair	Asthma	Merck	4,266	2012
Herceptin *)	Cancer	Genentech	4,047	na
Seroquel	Anti psychotic	AstraZeneca	4,027	2011
Risperdal	Anti psychotic	Eli Lilly	4,000	2008
Aranesp *)	Anemia	Amgen	3,716	na
Cozaar	Cardiovascular diseases	Merck	3,350	2010
Norvasc **	Hypertension	Pfizer	3,000	Expired
Total			77,614m	

# The Valuation Gap

- In the US, major and early successes include: Genentech, Amgen, Genzyme, Gilead, Celgene, Biogen IDEC which boast a combined \$200 bn market capitalisation.
- These major successes have lead to a much broader, well financed and well-researched US listed biotechnology sector.
- Valuation gap between US and European biotechs can be expressed in whole multiples not just double digit percentage point !

# The Niche

- The Street, both buy-side and sell-side, does have the scientific background to be successful in the sector, but the small size of biotech companies relative to pharma keeps them out.
- Dedicated small cap investors are generalist by definition and keep clear of the biotech sector, according to the principle of only investing in what one understands.
- Some powerful individual backers in mainly national players, but none has a diversified portfolio approach (Strüngmann and Hopp in Germany, Braathen in Norway, Rassjö in Sweden, Fernandez Sousa-Faro in Spain, Mulliez in France).
- About 15 biotech funds available in Europe, but assets heavily skewed towards US companies (75% to 95%).
- Venture Capital (VC) funds are rational investors during the initial investment phase, but very often manage the exit mechanically, as forced sellers, if no value inflexion point has materialised during the typical 10 years of the life of a fund.

# Maturing pipelines

- The Humane Genome was deciphered in 2001 ...
  - ... the hype is long gone, but much has happened since:
- Enabling technologies like bio-informatics and PCR (Polymerase Chain Reaction)
  - +
- Efficiency gains in the production of biologics up to 1000%
  - +
- Systematic exploration of pathways leads to a better understanding of mode of action of drug candidates
- Monoclonal antibodies are leading the targeted cell therapy in oncology
  - ... but also
- 2010: first therapeutic cancer vaccine is authorised by the FDA, PROVENGE (prostate cancer vaccine by Dendreon)
- 2010: first new treatment for Lupus in 50 years, Benlysta (Humane Genome Science)
- 2010: first stem-cell derived treatment for reconstructive medicine, ChondroCelect (Tigenix)
- 2011: first ADC (antibody drug conjugate) in Hodgkin lymphoma, Adcetris (Seattle Genetics)
- 2011: first approval of a personalized drug + test pair: Ventana's HER2 test with Herceptin.
  - ... Jury still out
- 2011: first gene therapy was expected to be approved in Europe (AMT), but experienced a last minute set back by EMA in a controversial decision.

# Personalised medicine

- Personalised medicine describes the combination of a drug and a test, specific for this drug.
- Stratification of patient groups increase chances to establish medical benefits and reduce failures.
- Boosts productivity of R&D, addressing big pharma's main concern.
- Gives patients access to treatments which might otherwise be shelved.
- Lowers the hurdle for reimbursement.

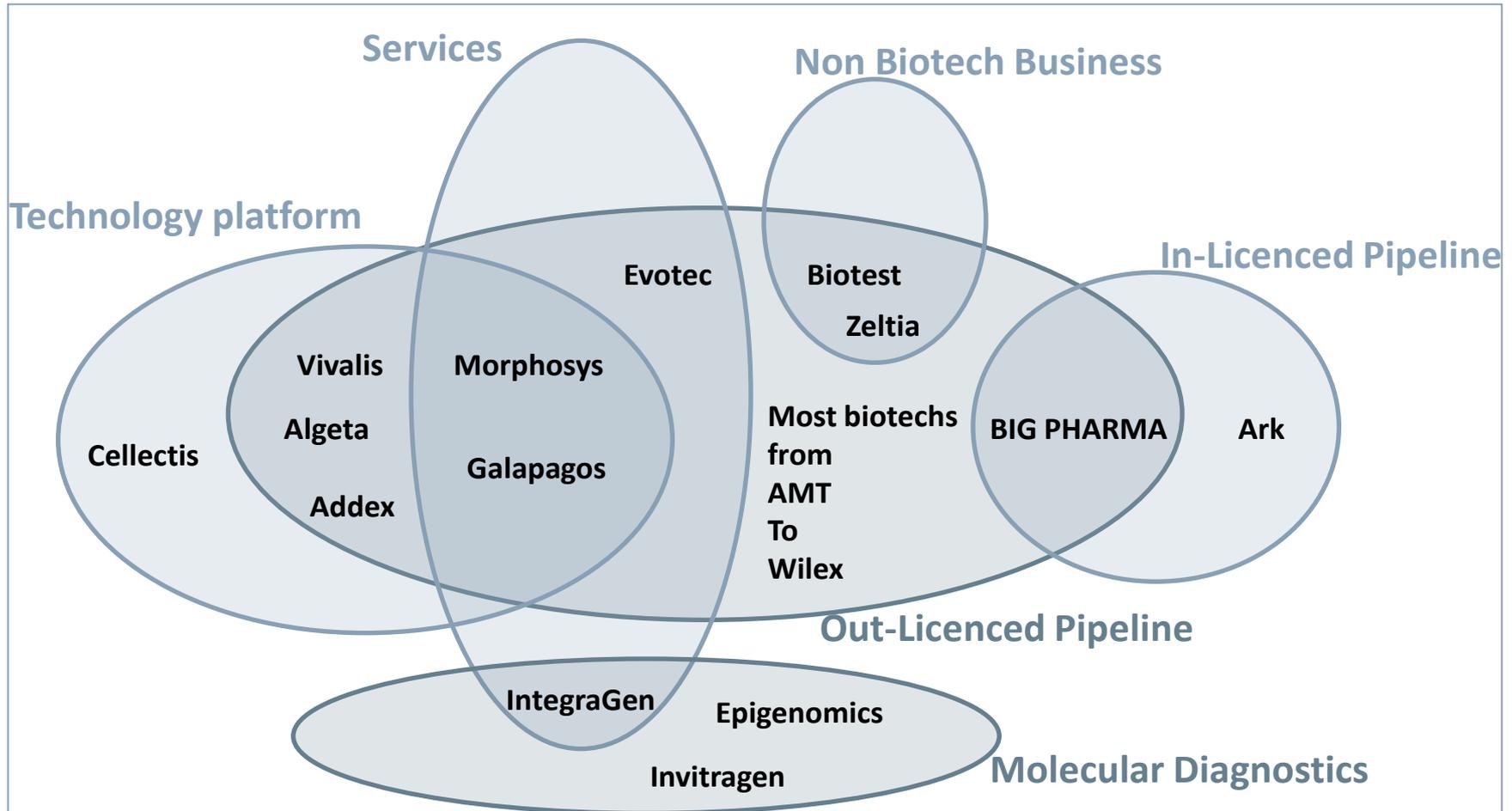
# Why should we be successful ?

- Managing a biotech fund obviously requires scientific knowledge but it also requires investment management skills, as any other fund.
- The answer to the puzzle in the introduction is +40%, and the really difficult part is not to find the potential „10 bagger“ but to stick to it when it is already a „3 or a 5 bagger“ ! A PhD in molecular biology won't help you do that !
- 20 years experience in European equity markets, concentrating exclusively on biotechnology in the last 2 years.
- I dedicate most of my time on the underlying science and draw on external experts on a case by case basis.
- I concentrate on the risks, try and evaluate each one of them. The ultimate criteria to invest is a risk/reward assessment.

# Sector and company Risks

- **The binary outcome risk:** n°1 risk, typical, almost specific to biotech companies
- **The financing risk:** cash burn rate and cash reach are the variables to watch
- **The strategic risk:** prioritizing projects in the pipeline, negotiating deals with potential partners.
- **The competitive risk:** always a risk in highly innovative businesses
- **The litigation risk:** always a risk in highly innovative businesses
- **The governance risk:** not only accounting but also scientific data can be „skewed“
- **The regulatory risk:** regulators can toughen rules, delay reviews, be overcautious with new classes of drugs
- **The contractual risk:** partnership/licencing deals can be called off
- **The share liquidity risk:** not specific, inherent to all small cap companies
- **The share overhang risk:** in particular the „Venture Capital Exit“ syndrome.
- **The valuation risk:** long term risk-weighted discounted cash flows are more of an art than a science !
- **The macro risk:** mostly uncorrelated to the business cycle, but financial „big picture“ has some influence.

# European Biotechnology Landscape



# Algeta: never as dark as before the dawn



# Epigenomics AG: how long before dawn ?

- Has developed and markets a blood-based screening test for colorectal cancer (CRC).
- Potential much higher than the HPV test market (USD 500m).
- The second generation of the test (improved performance, standardised components, highly scalable) awaits results of pivotal data any day. There is a body of evidence suggesting that the test should detect about ¾ of all cancer cases and about 2/3 of early stages, curable cases.
- The time to US market is about 12 months: filing for a PMA with the FDA before year end, then waiting and working on the approval for about a year. In parallel guidelines inclusion and reimbursement negotiations are taking place.
- Why is the market so sceptical ?
  - the free-float (German retail) has very limited knowledge. Legacy issues and the recent misguided attempt to market the first version of the test in Europe supersedes any positive outlook in the much more important US market.
  - major historical institutional investors (US and CH) have been continuous sellers for 18 months, for reasons of their own, not related to the operational development of Epigenomics
  - It is a typical case of David vs Goliath: the rhetoric is pro diagnostics, both from health care payers and big pharma. In reality, early detection means upfront costs for the former and potential threat to therapeutic drug margins to the latter. Add to the picture gastro-enterologists defending their golden goose colonoscopy business and a cosy US investors community, sticking its gun to the Exact Science management and its proven deal-making track-record.
  - Take-over can be ruled out for some time as big diagnostic players only buy products well established in the market
- What is the target price? What are the risks ? The target price is EUR 80 (vs 4 now) in 3 years time, and the main risk is a delayed FDA clearance making another very dilutive rights issue unavoidable. Even this risk and some other ones like pricing leave substantial potential, .... not to mention the prospect of a quantum leap in CRC early detection and medical outcome !

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# The Portfolio

- 4SC (Germany)
- Addex (Switzerland)
- AeternaZentaris (Germany/Nasdaq)
- AMT (Netherland)
- Bavarian Nordic (Denmark)
- BioInvent (Sweden)
- Cellectis (France)
- Epigenomics (Germany)
- Galapagos (Belgium)
- Genfit (France)
- Intercell (Austria)
- Innate Pharma (France)
- Medivir (Sweden)
- Mologen (Germany)
- NeuroSearch (Denmark)
- Paion (Germany)
- Pharming (Belgium)
- Tigenix (Belgium)
- Veloxis (Denmark)
- Vivalis (France)

# SIF limits and opportunities

- SIF = Specialised Investment Fund (Luxembourg Law of Feb. 2007)
- Qualified investors (EUR 125k minimum initial investment)
- No asset class restriction
- CSSF supervision (Luxembourg financial regulator)
- Luxembourg custodian (ING Luxembourg)
- Further reference  
[http://www.kpmg.lu/Download/Brochures/2007/ENG\\_NewLawonSIF.pdf](http://www.kpmg.lu/Download/Brochures/2007/ENG_NewLawonSIF.pdf)
- Belsize Total Return Fund
  - ISIN : LU0448281385
  - Fees : 1,25% pa management, 10% performance fee (high watermark)
  - Liquidity : weekly
  - Tax status: tax transparent according to German „Investmentsteuergesetz“

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