Article

Venture Capitalists as Gatekeepers for Biotechnological Innovation

Kenneth Fernald
is a PhD candidate in Economics at the Department of Applied Economics, the Erasmus School of Economics (ESE) with business development experience in life sciences. His educational background is in medical biology and business management in health & life sciences.

Ruud Hoeben
is a graduate student (MSc.) Management and Entrepreneurship in health & life sciences at the VU University, with an educational background in biomedical sciences.

Eric Claassen
is a board certified Immunologist and a professor of Knowledge Valorisation in Life Sciences at Erasmus Medical Centre Rotterdam (since 1994) he is also professor of entrepreneurship in the life sciences at the VU in Amsterdam. In addition, he holds several scientific-advisory-board and non-executive board positions in pharma and biotech companies.

ABSTRACT

Venture capitalists (VCs) aim at trade sales as a preferred exit-strategy for biotechnology companies they invest in. Therefore, VCs pay close attention to the wishes of larger (bio)pharmaceutical acquirers. In this paper we explore VCs' behavior and strategies by analyzing the technology fields and therapeutic areas in which they are invested most and which yield the highest relative returns by means of trade sales. The data show that VCs are by far most invested in oncology and this is also an area in which relatively high returns are realized. Regarding other areas, VCs could balance their average investment valuations more in correspondence with what acquirers are willing to pay. In addition, VCs have predictive insight in the types of technologies that do well and they seem to employ a strategy focused on both short-term and long-term success. They are investing most in small molecule drugs and protein/peptide therapeutics, which both yield high returns, followed by DNA/RNA technologies which underlie the possibilities of personalized medicine. We conclude that VCs act as technological gatekeepers because they are predicting long-term cure and care macro-trends.

Journal of Commercial Biotechnology (2015) 21(3), 32–41. doi: 10.5912/jcb704
Keywords: venture capital; biotechnology; trade sales; innovation

INTRODUCTION

Venture Capital (VC) is the primary source of funding for biotechnology ventures, with annual VC financing of biotechnology quadrupling in ten years from $2 billion in 1999 to $8 billion in 2008.[1,2] Since this 2008 high, annual VC financing has been relatively stable at $5.5 billion.[2]

From an investor's perspective biotechnology startups are considered to be high-risk investments.[3] On the flipside, VC firms can reap returns of five to ten times their initial investment when portfolio companies are successful, as measured by an initial public offering (IPO) or a trade sale (i.e. acquisition).[4] In light of recent merger and acquisition (M&A) trends in the (bio)pharmaceutical industry related to innovation deficits and the productivity paradox,[5,6] most biotechnology companies are currently built with a trade sale in mind as a preferred exit.[7] Not surprisingly, venture capitalists (VCs) pay close attention to the wants and needs of larger (bio)pharmaceutical firms.[7] However, the taste of big pharma can change over time – even within the average three to five years between investment and exit. For this reason, when it comes to investment decisions and valuations, VCs rely on their own intuition and market intelligence, in addition to the declared wants and needs of big pharma.

Correspondence:
Kenneth Fernald, Erasmus School of Economics, Erasmus University, Netherlands. Email: kenneth.fernald@gmail.com

In a sense VCs are the drivers for technological change within a given industry, and the biotechnology industry in particular. They act as "technological gatekeepers, accelerating the process of technological change".[8] By their investment decision-making, VCs set the tone for the entire life sciences market, essentially generating the supply of innovation to big pharma and the market in general. Considering multiple factors influencing investment decisions, it is imperative for both investors and bio-entrepreneurs to gain insight in global biotechnology investment strategies. Not only for deciding whether or not to get involved in new life sciences opportunities, but also to use this information in negotiating company valuations, business planning and raising capital.

Therefore, this paper aims to distill global investment strategies of VCs by analyzing the distribution and extent of investments with respect to therapeutic areas and technology fields. Furthermore, these areas and fields are analyzed in terms of exit potential and relative returns on investment (ROI), which are based on trade sale multiples.

The aim is to explore the therapeutic areas and technology fields in which VCs are invested most and whether that corresponds to where they realize the highest relative returns. Therefore, a total of 2,639 life sciences companies receiving VC backing between 1999 and 2013 are analyzed to identify the most popular areas and fields for investment and acquisition. In addition, the average investment amounts and average trade sale transaction values are analyzed by technology field and therapeutic area of the lead product(s) to gain insights in investments and show what acquirers are willing to pay for different types of companies. Finally, the average trade sale multiples are calculated in order to evaluate relative success rates of VC investments per technology field and therapeutic area. From the results an overall investment strategy is interpreted that is useful to investors and entrepreneurs in considering their engagement in new life sciences opportunities.

METHODOLOGY

An initial dataset was developed, containing early-stage investments in life sciences ventures between 1999 and 2013 based on data extracted from ThomsonReuters' SDC Platinum VentureXpert database (official database of the National Venture Capital Association; NVCA). A total of 2,639 dataset entries were analyzed individually to determine the companies' main technology field and therapeutic area focus. Subsequently, medical technology/devices (medtech) companies and service-oriented companies were excluded from the dataset, resulting in a total of 1,217 small molecule and biotechnology ventures that received their first investment round between 1999 and 2013. Of those 212 companies were acquired later on and for these, additional data on transaction details have been gathered from the ThomsonReuters' SDC Platinum VentureXpert M&A database and news reports, to calculate the average trade sale values and multiples.

Biotechnology fields

Based on 21 exploratory interviews with VCs and literature,[9,10] a classification of technology fields is used. The categorization of individual companies is based on in-database and online company descriptions as well as companies' lead products in development. In addition, the Cooperative Patent Classification (CPC) codes were analyzed, if available and as provided by Espacenet (worldwide.espacenet.com), of respective companies' patents to verify our categorization. First medical technology (devices), small molecule drugs, and biotechnology are separated. Medical technology companies are excluded from further analysis and Biotechnology is further categorized in biotechnology fields (DNA/RNA; Proteins/peptides; Cell/tissue engineering; Gene/RNA vectors; Targeting/delivery; Bioinformatics; Nanobiotechnology; and Glycobiotechnology), depending on the technology used for the respective company's lead product(s) (Table 1). Note that some companies may focus on combinations of technologies, so the illustrated data will add up to more than 100% of actual funding.

Therapeutic areas

Based on the WHO ICD-10, literature,[7] and declared investment interests in 21 exploratory interviews with VCs, a full range of therapeutic areas is used for analysis. Again the classification of backed companies was based on their lead product(s) in development. Ultimately the 15 most invested areas are included in the analysis. Note that some companies may focus on different indications and therapeutic areas simultaneously, so the illustrated data will add up to more than 100% of actual funding.

Limitations

While our analysis aimed to be a systematic, bias-free, review of life sciences VC investments and average trade sale multiples, several limitations apply. First, our dataset is in essence a data sample as we are unable to ensure that the collection of relevant data is 100% complete. While we are confident that the large majority of early stage life sciences investments is included in our dataset, we

Table 1: Overview of Biotechnology fields

Biotechnology Field	Biotechnology Subfield
DNA/RNA Technologies	
	Genomics/pharmacogenomics
	Gene probes/DNA markers
	Genetic engineering
	DNA/RNA sequencing/ synthesis/ amplification
	RNAi/siRNA (inhibiting gene function)
	Gene expression profiling/Antisense technology
Proteins/peptides and other large molecules	
	Engineering of proteins and peptides/ recombinant proteins
	Proteomics
	(Monoclonal) Antibodies
	Subunit/VLP vaccines
	Protein isolation and purification
	Peptide/protein sequencing/ synthesis
	Signalling Analysis (of cytokines, chemokines, transcription factors, cell cycle proteins, and neurotransmitters)
Cell and tissue engineering technologies	
	Cell therapy (including Immunotherapy)
	Tissue engineering (including tissue scaffolds and biomedical engineering)
	Cellular fusion
	Embryo manipulation
Gene and RNA vector technologies	
	Gene therapy
	DNA vaccines
	Viral vectors
Drug targeting/delivery technologies	
	Proteins
	Liposomes
	Micelles/dendrimers
	Inorganic/biodegradable
	Nanostructures
Bioinformatics (ICT applications in life sciences)	
	Construction of databases on genomes
	Modelling complex biological processes (including systems biology)
Nanobiotechnology	
Glycobiotechnology	

Based on 21 exploratory interviews with venture capitalists and literature. [9,10]

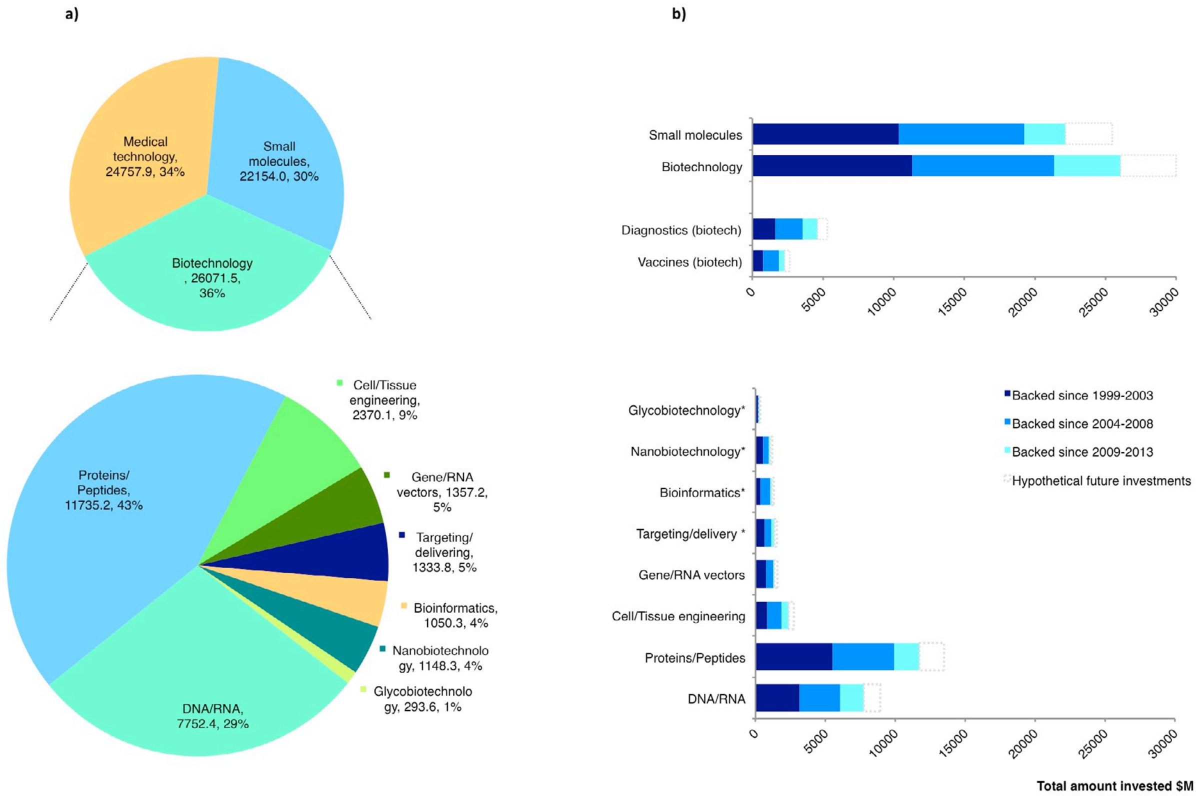

Figure 1: VC investments ($M) per technology field and per biotechnology subfield (a); and VC investments ($M) per technology field and date of first round

Note: Hypothetical future investments are included, as a subset of companies backed since 2009–2013 will most likely receive later-stage financing in the near future. For illustration purposes, an estimated 15% is added. This percentage is based on average later-stage funding of companies initially backed in previous periods.

Source: ThomsonReuters' SDC Platinum VentureXpert Database, company websites, worldwide.espacenet.com

cannot claim a 100% coverage of all deals, as the search criteria might have excluded deals that should have been included or the ThomsonReuters SDC Platinum VentureXpert database, which is based on self-reported data, might not include all existing deals. Second, the categorization process was conducted using several indicators to assess technology fields and therapeutic areas, namely lead products and programs, company websites and profiles, and CPC codes. Although two researchers conducted this process separately, some cases are still open to interpretation and for others limited information was available. Nevertheless, we are confident that most VC backed companies were categorized correctly. Third, of approximately 37% of trade sales, transaction values were not disclosed. Therefore, the average trade sale valuations as used for the analysis are also based on a sample of trade sales and we do not claim to cover 100% of all existing data. Fourth, the dataset included global data, and differences between geographic regions were not analyzed. Such differences may provide additional insights and could be an avenue of further research. Finally, this study does not aim at uncovering absolute returns for VCs in biotechnology as we focus on trade sales as successful exits and do not include losses or other gains VCs have made with their investments. Further research may attempt to reveal general results of VC investments in biotechnology. However, this paper aims at comparing general VC investments in technology fields and therapeutic areas with realized trade sale multiples in those fields and areas.

RESULTS

The majority of backed companies concerned medtech companies (965) followed by biotechnology companies (813) and small molecule drug companies (456). VC financing, however, is almost equally distributed

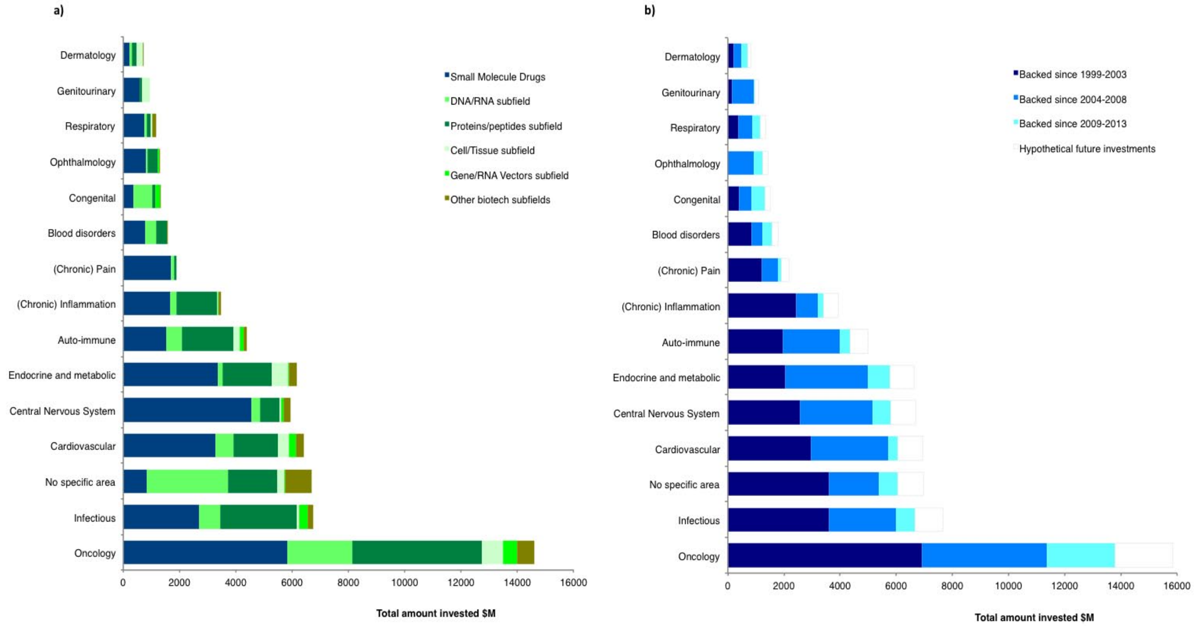

Figure 2: VC investments ($M) per therapeutic area and technology field (a); and VC investments ($M) per therapeutic area and date of first round (b)
Note: Hypothetical future investments are included, as a subset of companies backed since 2009–2013 will most likely receive later-stage financing in the near future. For illustration purposes, an estimated 15% is added. This percentage is based on average later-stage funding of companies initially backed in previous periods.
Source: ThomsonReuters' SDC Platinum VentureXpert Database, company websites

over these three fields of technology, with biotechnology taking the upper hand (36%). Thus, small molecule drug companies receive the highest average investment per company ($48.6 million), followed by biotechnology companies ($32 million) and medtech companies ($25.7 million). The total amount of $26 billion invested in biotechnology is distributed among several biotechnology fields as specified in Table 1.

Technology fields

As shown in Figure 1, almost half (43%) of VC investments in biotechnology has been invested in companies focusing on proteins/peptides, which include products and technologies such as recombinant proteins, monoclonal antibodies, recombinant subunit and virus like particle (VLP) vaccines, peptide therapeutics, engineered enzymes, and proteomics. Subsequently, 29% has been invested in DNA/RNA technologies mainly involving genomics and pharmacogenomics; gene probes and DNA markers; sequencing, synthesis and amplification of DNA/RNA, RNAi and siRNA gene regulation therapeutics; and gene profiling and antisense technology. Following these two subfields, which are undoubtedly most popular, 9% of VC financing of biotechnology companies involved cell/tissue engineering technologies, which include (stem) cell therapy (immunotherapy); tissue engineering; cellular fusion and embryo manipulation. Thereafter, 5% concerned gene/RNA vector technologies, involving gene therapy; vector vaccines and DNA vaccines. Another 5% has been invested in drug targeting and delivery (encapsulation) technologies using proteins; liposomes; micelles/dendrimers; inorganic, biodegradable structures; and nanostructures. As such there is overlap with nanobiotechnology, in which 4% of VC biotechnology funds has been invested. The remaining 5% was invested in bioinformatics (4%), involving IT as a basis for new diagnostics and therapeutics; and glycobiotechnology (1%), which involves the synthesis of glycolipids and glycoproteins. Moreover, 21% of backed biotechnology companies focused on molecular diagnostics technologies, mostly within the subfield of DNA/RNA. In total $4,6 billion has been invested in biotechnology related diagnostics companies (Figure 1).

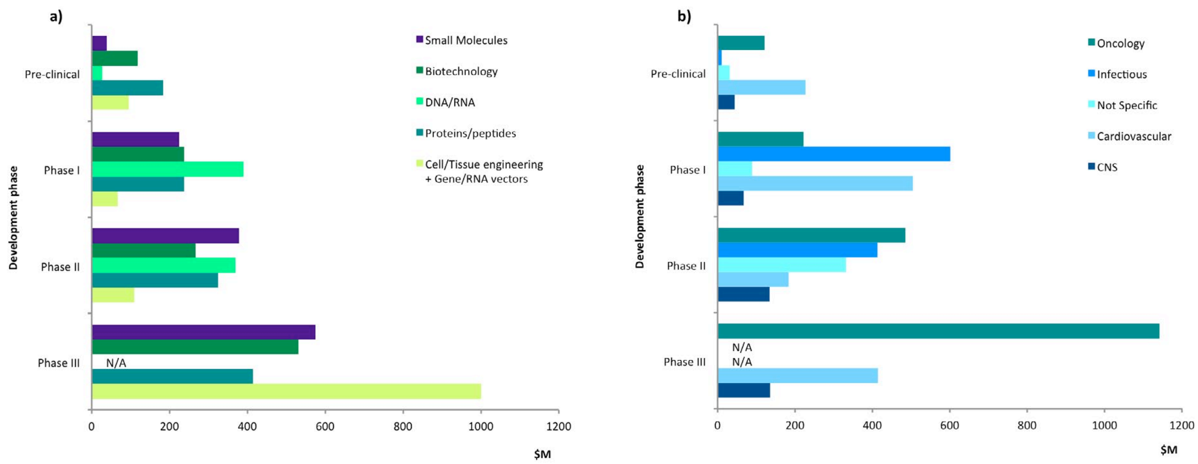

Figure 3: Average trade sale prices ($M) per therapeutic area (a) and per technology field (b), for each phase in clinical development
Source: ThomsonReuters' SDC Platinum VentureXpert and M&A Databases, company websites, clinicaltrials.gov

Therapeutic areas

Figure 2 shows that 29% ($13.8 billion) of all small molecule and biotechnology investments have been in companies that focused on oncology, making it by far the most invested therapeutic area (Figure 2). The following five most invested areas are infectious diseases ($6.7 billion), platform technologies, defined as 'no specific area' ($6 billion), cardiovascular diseases ($6 billion), central nervous system (CNS) indications ($5.8 billion), and endocrine and metabolic diseases ($5.8 billion).

Not surprisingly, small molecule drugs are mostly invested in when targeted on a specific disease area and not often when developed as platforms (Figure 2a). They are mostly focused on CNS, pain, oncology, endocrine and metabolic diseases, and cardiovascular diseases. However, it seems that different biotechnology subfields are used for a wide variety of therapeutic areas (Figure 2a). Proteins/peptides are developed mostly for treating oncology, infectious diseases, inflammation, auto-immune diseases, and endocrine and metabolic diseases, while DNA/RNA includes many discovery and diagnostics technologies, which seem to be mainly developed for oncology, platforms, and for congenital diseases. Furthermore, cell therapy and cell/tissue engineering is used most for oncology and endocrine and metabolic diseases, while gene therapy and vectors are mainly focused on oncology, infectious diseases, cardiovascular diseases, and auto-immune diseases. This data seem quite accurate considering advances such as immune cell modifications (cell therapy/immunotherapy) to treat cancer and the use of vector- and DNA vaccines for infectious diseases.[11, 12, 13]

Trade Sales

As IPOs and more so trade sales are the most important denominators for success from an investor's perspective the dataset includes which companies went public and which ones have been acquired. Of the 1,217 small molecule and biotechnology companies backed between 1999 and 2013, 212 have been acquired and 132 went public. Of those that were acquired, subsequent data was collected on the transaction values, if disclosed, and the clinical development phase of the respective company's lead product. This data was collected from ThomsonReuters' SDC Platinum M&A database (thomsonreuters.com/sdc-platinum), clinicaltrials.gov, company websites and additional webscraping of business websites (e.g. businessweek.com). Average trade sale transaction values are plotted per development phase for different therapeutic areas and technology fields (Figure 3).

The average trade sale valuations of companies in different development phases vary amongst therapeutic areas and technology fields, suggesting different risk profiles. Strikingly, trade sale valuations of oncology focused companies increase substantially with each development phase, whereas those of cardiovascular diseases or CNS show different patterns. In figure 3b, the complexity of newer technology fields (e.g. cell therapy and gene therapy) is represented by relatively low trade sale valuations of such companies up until phase III clinical trials. Yet, when phase III is reached, the value of such companies increases substantially, illustrated by the acquisition of Biovex by Amgen in 2011. Small molecule drugs, however, as a more classical technology field, show a more predictable and stable path as average trade sale

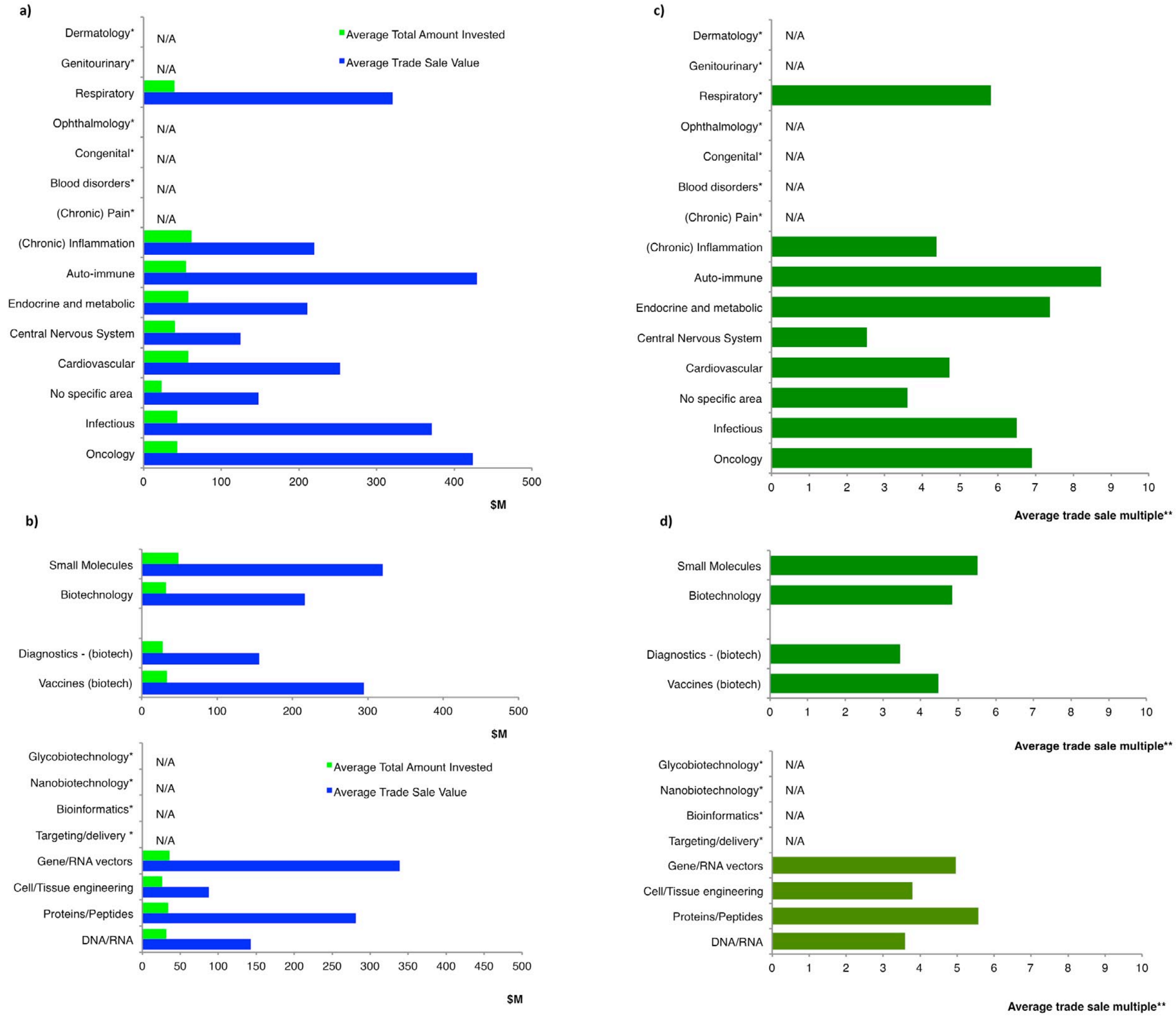

Figure 4: Average trade sale price ($M) and average total investment amount ($M) per therapeutic area (a) and per technology field (b); and average trade sale multiples per therapeutic area (c) and per technology field (d)
** Too few or no trade sales to calculate appropriate average (N/A).*
*** Trade sale multiple = (Trade sale value)/(Total amount invested in acquired company).*
Source: ThomsonReuters' SDC Platinum VentureXpert and M&A Databases

valuations of small molecule drug companies increase more gradually with each development phase. The same holds true for proteins/peptides.

Deal values and Multiples

Arguably, there are various ways to evaluate the success of individual investments and of investments over categories. In order to review patterns between where VCs invest the most and where they earn the most, the average trade sale values and the average total amounts invested in companies are evaluated per therapeutic area (Figure 4a) and technology field (Figure 4b). In addition, for the VC backed companies in our dataset that have been acquired, the trade sale multiple was calculated for each individual acquisition to determine the average trade sale multiples, again per therapeutic area (Figure 4c) and technology field (Figure 4d).

As shown in Figure 4a, average trade sale transaction values are highest for auto-immune diseases ($430 million) and oncology ($424 million), followed by infectious diseases ($371 million). Interestingly, this top three of therapeutic areas for acquirers is different from the top three areas based on average VC investment values. Per company VCs have invested most, on average, in (chronic) inflammation ($62 million), endocrine and metabolic diseases ($58 million), and cardiovascular diseases ($58 million). Auto-immune diseases comes fourth for VCs with an average total investment amount per company of $55 million, while it seems to be the first area for acquirers. Moreover, average trade sale transaction values for different therapeutic areas seem to have a much wider range (from $125 million to $430 million) than the average total VC investments per therapeutic area ($40 million for CNS to $62 million for inflammation).

The average multiples, however, are highest for auto-immune diseases (8.7), endocrine and metabolic diseases (7.4), oncology (6.9), and infectious diseases (6.5). Of these the first two are also in the top four of areas that receive the highest average investments from VCs. The second highest multiple has been realized in endocrine and metabolic diseases, while the difference between average VC investment and average trade sale value for this area is not very large ($58 million versus $211 million). This suggests that the successful exits have come from relatively lower investments in this area. For all other areas, the average trade sale multiples are quite consistent with the average trade sale values, confirming little differentiation of average VC investments with regards to therapeutic areas.

For the technology fields, an overall difference in average VC investments is shown between biotechnology ($32 million) and small molecule drugs ($49 million). The biotechnology subfields subsequently range between $26 million for cell/tissue engineering to $36 million for gene/RNA vectors, with $32 million for DNA/RNA and $34 million for proteins/peptides in between. This suggests that VCs undoubtedly expect most from the technology field of small molecule drugs, especially when also considering the total amount invested in this field (30% of all funds; Figure 1). Although high expectations for this field are justified by the corresponding average trade sale value ($320 million) and multiple (5.5), similar trade sale multiples have been realized for the biotechnology subfields proteins/peptides ($282 million; 5.6) and gene/RNA vectors ($339 million; 5.0). The average trade sale values for the subfields DNA/RNA and cell/tissue engineering are much lower ($143 million and $87 million respectively). However, the average multiples for these fields are relatively close (3.6 and 3.8), suggesting that the successful trade sales resulted from relatively lower investments in these fields. This is especially true for the DNA/RNA subfield, considering the average VC investments in this field ($32 million), which is the same as the average for the entire biotechnology field. Moreover, the total amount invested in DNA/RNA technologies is high (29% of all biotechnology investments) relative to what big pharma is willing to pay for these technologies. This suggests a notable interest of VCs in the DNA/RNA technology subfield.

The average multiples in the technology fields as shown in Figure 4d show less variation (4–6) than those in the therapeutic areas (3–9; Figure 4c). VCs, thus, seem to be better at anticipating returns within technology fields and adjusting their investment allocation accordingly, than doing the same for the various therapeutic areas.

CONCLUSIONS

We conclude that VCs act as technological gatekeepers because they are predicting long-term cure and care macro-trends. They have predictive insight in the types of technologies that do well. However, in terms of therapeutic areas, VCs can balance their average investment valuations more in correspondence with what big pharma is willing to pay. We set out to distill global investment strategies of VCs by analyzing the distribution and extent of investments with respect to technology fields and therapeutic areas. It seems that VCs employ a strategy focused on both short-term and long-term success. On the one hand they play it safe, minimizing risk by investing most in small molecules and proteins. On the other hand, they are investing heavily in DNA/RNA technologies, which as a field seem to be underperforming (Figure 4b, 4d). As VCs and bio-entrepreneurs build for big pharma, the blockbuster business model directly affects new venture financing by VCs for the short term. However, VCs are also rebelliously investing for long-term cure and care macro-trends, as they invest in biotechnologies that underlie the possibilities of personalized medicine.

For therapeutic areas, a discrepancy between variation in average VC investment amounts and variation of average trade sale transaction values is illustrated by an imbalance in average multiples (3–9). Acquirers seem to attach greater importance to differentiating between therapeutic areas than VCs do, resulting in unnecessary overinvestment in one area versus potential underinvestment in another. As VCs are essentially building for big pharma,[7] they, their investors and bio-entrepreneurs would benefit from a portfolio balanced more in correspondence with what pharma is willing to pay. Doing this can in turn lead to more predictability and consistency of average multiples over the therapeutic areas. However, success ratios between therapeutic areas may be more susceptible to rapid changes than technology fields, making prediction difficult. Many VCs might therefore be investing quite opportunistically with less distinction per therapeutic area.

With regards to technology fields, there seems to be a macro investment strategy that appears to focus both on short-term and long-term success. For the short-term, VCs are investing heavily in small molecule drug companies with a relatively higher average investment valuation. In addition, within biotechnology they are investing most in the proteins/peptides subfield (43% of all biotechnology investments), while keeping their average investments relatively low. This conservative risk-averse strategy corresponds with pharma's blockbuster business model as small molecules and proteins/peptides are the only type of products that can become blockbusters (in the form of new molecular entities and biologicals).[14] This strategy has resulted in average multiples of around 5.5 for both these technology fields. However, VCs have invested less in the gene/RNA vectors field, while there have been some tremendous recent successes in this field.

In addition to the conservative investment strategy tailored to pharma's business model, VCs have also invested a large proportion (29%) of biotechnology funds in the DNA/RNA technology field. The DNA/RNA field includes the technologies required for realizing the potential of personalized medicine, which has been claimed to be the future of medicine, promising to significantly increase the quality of healthcare.[15,16,17] Here, we find evidence that despite the low average multiple and average trade sale valuation for this field, VCs are embracing their role as technological gatekeepers.[8] They are investing in this field and thereby the future, while a proven business model for personalized medicine that could be equally lucrative as the blockbuster model is still lacking now.

For other investors and VCs with less experience investing in life sciences, a similar investment strategy is recommended. Moreover, we believe it to be wise to evaluate the therapeutic areas new ventures are focusing on, with respect to both an appropriate match with technology types and relative ROI rates. It is however noteworthy that VCs evaluate companies on a case-by-case basis and employ strict criteria for their investments (e.g. competition, regulations, reimbursement, management team, financials) irrespective of therapeutic areas or technology fields. Notwithstanding, oncology, infectious diseases and auto-immune diseases seem to be the most interesting therapeutic areas to invest in, considering investment amounts, average trade sale valuations and average multiples.

In the current investment climate, bio-entrepreneurs can increase chances of being funded by combining a focus on radical innovation within technology fields with blockbuster potential with a focus on therapeutic areas where investors can realize relatively high multiples. When developing technologies underlying personalized medicine and diagnostics, where the blockbuster model is not applicable, it is imperative that entrepreneurs focus on business models for generating income during (early) development stages, ensuring survival whilst cure and care macro-trends continue towards a personalized and patient-centered approach.

REFERENCES

1. Bradford, T. C. (2003) Evolving symbiosis—venture capital and biotechnology. *Nature Biotechnology* 21(9): 983–984.
2. EY (2013) Beyond Borders; Matters of evidence. Biotechnology Industry. http://www.ey.com/Publication/vwLUAssets/Beyond_borders/$FILE/Beyond_borders.pdf
3. Stewart, J. J., Allison, P. N., & Johnson, R. S. (2001) Putting a price on biotechnology. *Nature biotechnology* 19(9): 813–818.
4. Lee, D. P., & Dibner, M. D. (2005) The rise of venture capital and biotechnology in the US and Europe. *Nature biotechnology* 23(6): 672–676.
5. Malik, N. N. (2009) Biotech acquisitions by big pharma: why and what is next. *Drug discovery today* 14(17): 818–821.
6. Fernald, K. D. S., Pennings, H. P. G., & Claassen, E. (2015) Biotechnology Commercialization Strategies: Risk and Return in Interfirm Cooperation. *Journal of Product Innovation Management* 32(6): in press.
7. Giniatullina, A., Boorsma, M., Mulder, G. J., & van Deventer, S. (2013) Building for big pharma. *Nature biotechnology* 31(4): 284–287.
8. Florida, R. L., & Kenney, M. (1988) Venture capital-financed innovation and technological change in the USA. *Research Policy* 17(3): 119–137.
9. OECD (2005) A Framework for Biotechnology Statistics. http://www.oecd.org/science/inno/34935605.pdf.
10. Van der Valk, T., Moors, E. H. M., & Meeus, M. T. H. (2009) Conceptualizing patterns in the dynamics of emerging technologies: The case of biotechnology developments in the Netherlands. *Technovation* 29(4): 247–264.
11. Kalos, M., & June, C. H. (2013) Adoptive T cell transfer for cancer immunotherapy in the era of synthetic biology. *Immunity* 39(1): 49–60.
12. Barouch, D. H., & Picker, L. J. (2014) Novel vaccine vectors for HIV-1. *Nature Reviews Microbiology* 12: 765–771.
13. Mairhofer, J., & Lara, A. R. (2014) Advances in Host and Vector Development for the Production of Plasmid DNA Vaccines. Cancer Vaccines. Springer: New York, pp. 505–514.
14. Fernald, K. D. S., Weenen, T. C., Sibley, K. J., & Claassen, E. (2013) Limits of biotechnological innovation. *Technology and Investment* 4, 168–178.

15. Davis, J. C., Furstenthal, L., Desai, A. A., Norris, T., Sutaria, S., Fleming, E., & Ma, P. (2009) The microeconomics of personalized medicine: today's challenge and tomorrow's promise. *Nature reviews Drug discovery* 8(4): 279–286.

16. Sander, C. (2000) Genomic medicine and the future of health care. *Science* 287(5460): 1977–1978.

17. Schilsky, R. L. (2010) Personalized medicine in oncology: the future is now. *Nature reviews Drug discovery* 9(5): 363–366.