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EARLY-LATE COMPANIES: THE NEW SWEET SPOT FOR EUROPEAN BIOTECH VENTURE CAPITALISTS?

By Dr. Holger Reithinger, Principal, Global Life Science Ventures

In the complex and ever-shifting landscape of the biotechnology industry, the challenge for venture capitalists to target companies that promise attractive returns on investment is as great as ever. The traditional model, based on more than 20 years of VC experience in the US, is straightforward: invest early, obtain a major share of the company, obtain external validation of the concept through a partnership with a leading pharma company, build up a steep valuation curve, and exit by IPO. But with the large majority of biotech companies still unprofitable, a temperamental IPO market, cash-hungry clinical trials and a history of many money-losing investments, VCs have become wary of throwing money at concepts which are interesting from a scientific point of view but unproven. The current trend is for VCs to focus on late stage biotech companies where the risk is greatly reduced.[1] This trend is visible in recent successful fundraisings by funds focusing on rather later stages, such as BB Biotech, whose founding team surprisingly came from traditional early stage VCs.

And yet, investing at the end of the value creation chain is, in a sense, contradictory to the VC philosophy of assuming a significant but calculated risk in the anticipation of achieving high potential returns. An additional consequence of reduced interest in early stage companies is that fewer late stage companies are emerging. With large pools of venture capital chasing relatively few remaining late stage opportunities, these financing rounds have also become increasingly expensive, and at the same time often uninteresting as the result of companies' tendency to in-license late stage products with a questionable product profile or unknown history. The question then is: how can VCs realise the returns expected of them while keeping the risks under control?

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Global Life Science Ventures (GLSV) sees the solution in targeting relatively young companies at a specific stage in their development and assuming a highly active role in the value creation process. The strategy is to enter at a point where a maximum impact can be effected while keeping cash burn to a minimum, and where it can be ascertained in a relatively short period of time whether the investment is delivering the expected results. This means being able clearly to formulate important risk reducing, technical milestones, with the money tranched against achievement of those results. About a year before a lead product is scheduled to enter phase I trials, a biotech company is still considered too early for many investors, but it is precisely at this point where there is a great potential for impact and a maximum upside.

Using the investment for company building, increasing the headcount and growing the internal structure might not always be the optimal use of resources, as it can lead to a sharp increase in the cash burn rate without adding significant value. In fact, as has been argued by Hal Broderson in his discussion of virtual biotechs[2], outsourcing to a network of contracted experts can take a company to critical decision-making points at a far lower cost than with the fully integrated model. The capital should best be used to invest in projects that create maximum value, and which can be evaluated within 12 months for their validity.

Another important aspect is the VCs' influence on the strategy of the company. In GLSV's model, the investors, together with the CEO, formulate a very focused strategy leading rather to a well-managed project than an operational business. For this model to be successful it ideally needs a specific type of CEO, typically not the general manager-type of personality but rather a narrowly focused project leader with strong execution-oriented leadership, who can live and act in a virtual organisation.

This approach does not in itself remove the inherent risk that a pre-clinical drug candidate will fail to meet clinical expectations. However, in addition to understanding the underlying science and complexity of the platform or technology, VCs can make a difference by providing an optimal strategy and financing scheme for the validation of such novel concepts. Due to the early stage of the investment, this approach also provides the possibility to capture a 25% to 30% share of the company at a particularly advantageous point in the value-creation curve, and direct the use of limited invested capital in an optimally efficient manner. In favourable cases, the result can be a rapid transition from an early stage to late stage company, with attractive exit opportunities. As was observed by Arthur Klausner[3] with respect to

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exiting via an IPO, it is often about providing public stock buyers, "with the types of companies/products that they desire while investing the smallest amount of money for the least amount of time." Two recent investments carried out by GLSV are examples of the investment model described above.

The first case is Vienna-based Fibrex Medical. The company was founded on the basis of a new mode of action in the inflammation process and the identification of a first compound, but was still considered much too early for nearly all investors. The lack of an experienced management team was another reason for many investors not to initiate any serious due diligence on the basic science. However, GLSV recognised early on the potential of the lead product candidate, for which most results had been generated at the University of Vienna. With a due diligence package, GLSV attracted an industry-experienced CEO for this early venture and closed a significant financing round of US$10m together with Atlas Ventures and two smaller funds in early 2005.

The investment strategy at the time was to fund the final pre-clinical development programme and subsequent clinical phase I and IIa trials for the lead product candidate in reperfusion injury, an indication for which all previous product candidates had failed. In addition, non-dilutive funding was used to generate enough data in a second indication. The size of the company was kept at a ceiling of about seven people to keep the operational burn rate very low and maintain flexibility in the use of the funds. Within a time frame of less than one year, Fibrex transformed itself from an early stage venture to a later stage clinical product company, and not surprisingly it became attractive to the majority of funds looking for first clinical data. However, the existing investors are prepared to fund the company further until proof-of-concept in humans, which is an important factor in the game. With a second indication following closely behind and a potential third on the horizon, with an underlying technology based on a new mode of action, and with strong entrepreneurial management and a flexible structure, Fibrex has changed completely within just 12 months after financing.

The early-late concept is also illustrated in the financing of Neuraxo Biopharmaceuticals, a pre-clinical company that received more than €12m in September 2005, in a financing round led by GLSV and Biomed Invest. Neuraxo's area of expertise is nerve regeneration, an area of huge interest, and its first challenge is to test a new concept and compound in acute spinal cord injury (SCI), another indication where every past attempt has so far failed for various reasons. Based on excellent pre-clinical and proof-of-concept data, Neuraxo's lead candidate will be in the clinic less than nine months after financing, with the possibility of showing preliminary results to investors within a 15 month time frame. Although the compound targets the niche indication acute SCI, GLSV sees the prospects as very encouraging, with the compound's orphan drug status providing further protection and the huge chronic SCI market on the horizon. Again, the company is led by an experienced management team not afraid to work for a small organisation in a project management-like role. It cannot be excluded that they will need to look for a new job in a short time frame if the novel concept of nerve regeneration does not prove itself in humans. However, if it does work out as hoped, they will participate integrally in the sharp increase in value of the company.

These examples illustrate some of the ideas GLSV has had in order to cope with the early stage dilemma of the last years. Of course, an experienced VC cannot build a portfolio solely with companies like Fibrex and Neuraxo. Both companies will have to face the same cold wind

Dr. Holger Reithinger

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of clinical development as any other biotech company, and later stage investors are looking for more balanced pipelines and more strongly financed companies. Even with the business model GLSV is pursuing, the firm continues to look for diversity. These companies are nonetheless a key strategic element in GLSV's portfolio.

GLSV's recent trade sale of the pre-clinical company GlycArt to Roche confirmed that there is an attractive market for small, early stage ventures, as long as the underlying IP position is solid and the concept promises a future competitive advantage. In fact, big pharma is showing increased interest in identifying promising drug candidates relatively early on in their development, as late stage deals become rarer. Without predicting a new trend in the industry, some international pharma companies have already directly approached VCs with the idea of obtaining access to their early stage portfolio companies. Maybe we will return to where the industry started: the novel concepts created in universities will be pursued commercially in small biotech companies financed by VCs, and the more regulated part of the development and later marketing will be done by pharma, as proposed decades ago by Jürgen Drews[4]. Eric Schmid, senior analyst at Cowen & Co, recently expressed the view that smaller companies with late stage products will be able to command a higher price to be acquired[5]. By translating early ventures very quickly and creatively into later stage branding, GLSV is building attractive assets for further VC investments or possible acquisitions, as well as IPOs.

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