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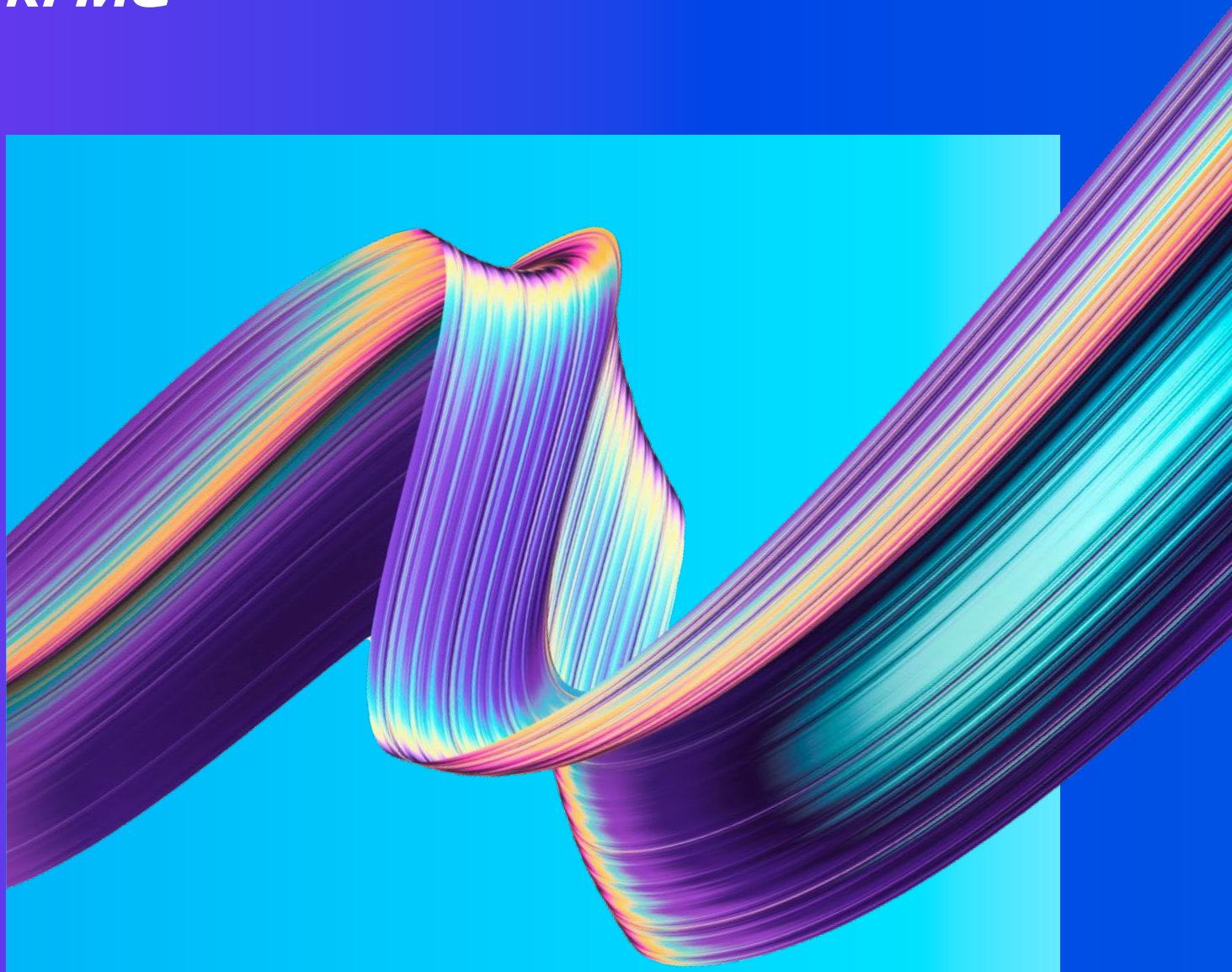


Data, strategy and team

The three pillars to secure series A financing and long-term success

In the tech industry, network effects create a reinforcing positive feedback loop, leading to monopoly-like situations, as seen with Alphabet in search, or Meta in social networks. In biopharma the situation is different, and the network itself develops the drug. Academic research, investors, incubators, pharma companies and biotech startups work together like a finely tuned orchestra to discover, develop and commercialize novel medicines. Seminal discoveries made in academia form the basis of new biotech companies, which themselves often emerge from incubators. The biotech companies then further develop the discoveries up to – or beyond – clinical proof-of-concept studies in humans. Later, the companies are often picked up – either via a licensing deal or an acquisition – by a global pharma company. Fueling this network is a combination of innovation in science and technology, paired with experience and money.

Recent years have seen a massive influx of capital into the ecosystem.

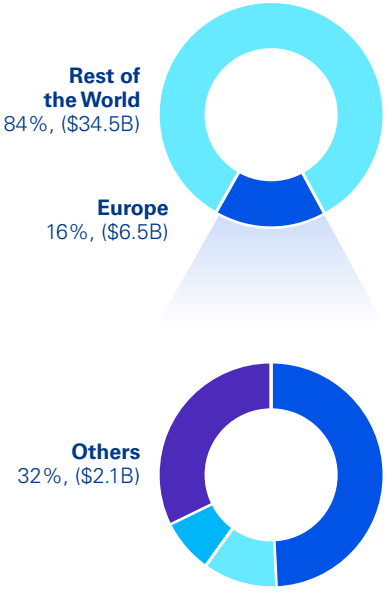
In 2021 global venture capital investments into biotech reached an all-time high of $41B[1]. The US still accounts for the largest share with $25.6B, while European biotech companies raised roughly $6.5B last year. We can expect a cool-off in 2022 due to the difficult global economic situation. However, over the last few years, many venture funds have raised large sums that they need to deploy – and are currently still seeking opportunities to do so.

In Europe, the UK is leading in regard to biotech venture capital (VC) investments in 2021, with $3.3B[2] raised ($1.8B in 2020[4]). The country is followed by France in second place with $700M[2] ($800M in 2020[4]) and Switzerland in third with $500M[2] ($1.2B in 2020[4])[2] – or second with roughly $900M according to the Swiss Biotech report. In terms of IPO proceeds, Switzerland is leading the pack in Europe in 2021, with roughly $1.9B (CHF 2.2B) raised. Nature biotech's recent report assessing the biotech competitiveness of countries globally also placed Switzerland in the top spot[3].

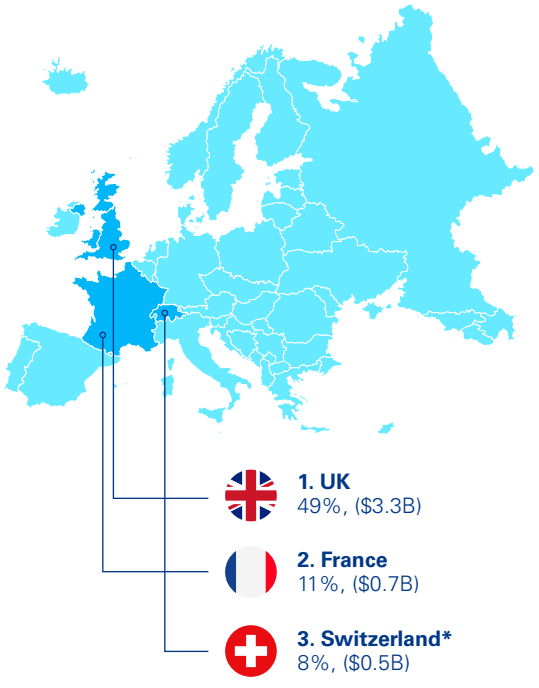
Within Switzerland, the Basel area is the clear leader, with more than half of all VC investments being raised by Basel-based companies[5].

[1] 2021: a breakthrough year for Healthtech & Biotech | Dealroom.co
[2] UK biotech financing in 2021 | BIA (bioindustry.org)
[3] The Worldview national ranking of health biotech sectors
[4] The science of success: UK biotech financing in 2020
[5] Swiss Biotech Report 2022

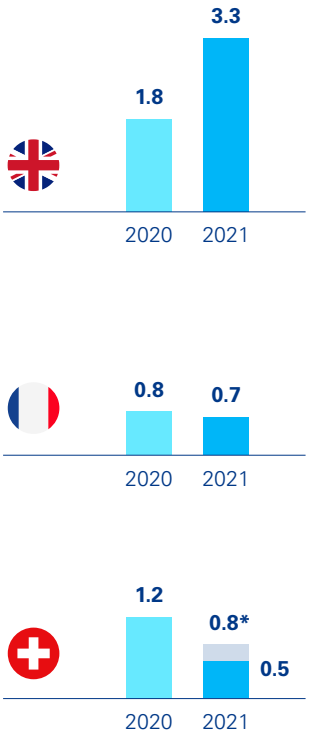
Global venture capital investments into biotech, 2021 = **$41 billion**



European venture capital investments into biotech, 2021, **top 3 countries**



Amount raised (in billion $) **2020 and 2021**



* according to the Swiss Venture Capital reports, Switzerland is second with $0.8 billion.
** Exchange rates april 2022: GPD – Dollar = 1.3 / CHF – Dollar = 1.1

Raising the first venture capital round

Three components are critical for successfully raising venture capital financing: a compelling scientific data package, the strategic business relevance, and a team that can deliver.

The data package

The foundational science and novel technologies form the basis of the company. Ideally, a company should get to the stage where it can raise significant venture financing within two years. The inability to attract financing within this time frame may be lethal to a biotech startup, and founders should ensure they have generated material translational data before they start the company.

The specifics of the scientific data package are very individual to each company with their own technology and scientific basis. It is hard to generalize, but three high level points apply:

1. **Efficacy:** Generating proof of concept data in in vitro and in vivo models – that are wisely chosen in term of translatability – demonstrating efficacy
2. **Safety:** A first set of preliminary – and relevant – (non-GLP) toxicology studies
3. **External data:** While the efficacy studies can be run in house, the toxicology package should be generated by contract research organizations (CROs). In addition, at least some of the key proof-of-concept data should be outsourced to a CRO.

Importantly, a convincing scientific data package can usually be generated with a relatively limited investment of a few hundred thousand dollars.

Defining a solid company strategy around the first program

In terms of the business aspects, there are a few important points to get right from the get-go. The most crucial ones include crafting a well thought through licensing deal for the foundational IP; building a coherent company strategy in regard to positioning; and assembling the right team. Much has been written on what is important for licensing deals, and we will not recapitulate this here. We focus instead on the strategic aspects, which should initially concentrate on defining the therapeutic areas and indications to pursue (first), and the team.

Finding the (first) therapeutic area and indication to develop the lead program

This is key. The scientific data package discussed above will be used to convince venture funds to invest and will largely dictate the fundraising success. But it will also define the long-term development trajectory – and hence the overall financing strategy – and ties into business development considerations beyond the scope of this paper.

Selecting the lead indication

Translatability of preclinical data
Translatability of preclinical results to humans is crucial. Choose an indication with animal models that translate well into the human setting where possible.

Development and regulatory aspects
Select an indication that can quickly prove the biology and/or the technology of the approach in clinic in a patient population with a clear unmet medical need. An orphan indication will benefit from the favorable regulatory environment. Patient stratification via biomarkers and straightforward clinical endpoints will streamline development.

Commercial rollout strategy
The first proof of concept should ideally also open up the approach for larger, commercially more interesting areas that might come later.

Ability to compete with the current standard of care
Make sure that the drug has the chance to be better than the current standard of care and demonstrate superiority against other drugs in development for the same indications.

In some cases, the science, biology and technology of the company make a certain indication the obvious choice. But it is more likely that a company's approach could address many potential indications or even therapeutic areas. A typical example would be oncology-related discoveries, which very often intersect with immunology-driven diseases. In such cases, it is not trivial to define where to focus the lead program. Broadly speaking, there are three areas that should be considered when selecting the first program to pursue. And these have to be balanced against each other:

Translatability of preclinical data: Selecting an indication where there are good and well accepted animal models – such as mice, other rodents, monkeys etc. – that can recapitulate important aspects of the human disease can greatly de-risk projects. Animal studies can offer a first indirect signal as to whether the hypothesis is correct, and this can be especially powerful in monogenetic disease settings. Unfortunately, most animal models of human disease are only approximations so this aspect should be ideally combined with ex-vivo data of human samples – such as experiments in human blood extracts or similar. In the last few years, much progress has been made in 3D human cell cultures modulating certain important aspects, and these can give a lot of valuable information. Ideally, different approaches should be combined to get the most complete data package.

Development and regulatory aspects: Typically, it is an indication that can rather quickly (from the clinical standpoint) prove the hypothesis of approach in a relatively small patient population with a clear unmet medical need. Orphan indications benefit additionally from both the favorable regulatory environment for drug development and from the easier path to reimbursement. But importantly, this first proof in humans should also inform the second and third – often larger and commercially more relevant – indications that the company wants to pursue. Ideally, patient stratification via biomarkers is feasible, while the clinical endpoints are straightforward to assess.

Commercial aspects and competition: The market size of the first indication does not necessarily have to be the most commercially interesting. As mentioned above, the first indication will ideally be chosen for the ease and feasibility of development and in order to provide a quick proof of hypothesis while opening up the path for larger, more commercially interesting areas for further expansion. Also important is that a company's own approach is superior to the current standard of care as well as compared to other drugs currently under development for the same area. The possibility to compare head-to-head is ideal, but could be challenging for some modalities such as cell therapy. In such settings, superiority over the competition has to be very strong in efficacy, the toxicology profile, or the durability of the treatment. A more traditional approach, e.g., small molecule-based, will be much cheaper, as it is much easier to manufacture and deliver to patients, and hence will have a lower hurdle to clear when negotiating with market access stakeholders.

The process of deciding upon the first indication to pursue is iterative and should be constantly informed based on new scientific insights generated. It also requires access to key opinion leaders in the field, physicians and additional deep domain experts such as partners with knowhow in drug development, market access and commercial experience to exchange ideas on these topics. Feedback from touchpoints with pharma companies, investors and regulators should also always be taken into account. Finally, business development perspectives excluded here for sake of brevity will also play a role.

A team that can deliver

As discussed above, going from bench to beside requires experience often lacking among academic founders. This comes from many years of hands-on roles in the biopharma industry, in areas as drug discovery and development, business development or related functions. This depth and breadth of experience cannot simply be "learned" by attending workshops, so it is crucial to team up early on with people who have the relevant backgrounds. Connections such as mentoring and coffee catch-ups can be helpful. But what early companies really need are people with skin in the game and a vested interest seeing the company succeed. Ideally, they should come in the form of board members or C-level executives that closely work alongside the founders and have an actual say rather than "just" providing advice. Of note, a well-balanced team of academic founders and experienced executives can also completely change the dynamics of interactions with venture funds and pharma companies.

In reality, early startups can rarely afford to offer industry-standard salaries. So ideally, incoming people will join or co-found the company, become founding shareholders. In the case of substantial equity (such as when someone joins as an early CEO), this can be structured such that some of the equity is received upfront and some of it when certain company milestones are reached (for instance a venture financing round). Generally, the equity positions should vest over time and not be received all upfront. As people will sometimes part ways again, for various reasons, it can be detrimental for an early biotech company to have people with substantial equity but no active role in the company anymore. So a well thought-through shareholder agreement between the founders should be put in place right from the beginning. This should, of course, also cover the academic founders as they can decide to leave the company as well.

Conclusions

The three components outlined above – asset, strategy and team – are crucial for the success of a biotech startup. However, we need to come back to the notion that the biotech industry at large is operating as a fine-tuned network of companies, universities and collaborations, and an individual startup can only succeed within a network that can provide scientific excellence, biopharma and commercial experience, and money. All are essential, and as an academic founder, it is important to work with entities that can tap into this network to assemble all necessary ingredients to put an early company on a solid basis and on the right path for future growth.

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