



Feature

Global or local: The future of biotech

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Biotech start-ups often begin as domestic companies relying on local resources and talent, but this approach might not be effective in achieving rapid growth and long-term success, particularly for developing new therapeutics that require significant resources and extensive commitment. Here, we argue that born-global biotechs are better equipped to tackle major industry challenges, such as innovation, resource constraints, and limited talent diversity, especially in current challenging times. We also highlight the importance of capital efficiency in maximizing the benefits of being a born-global biotech, and provide an operational framework, based on the FlyWheel concept, for becoming a successful born-global biotech.

Keywords: startup; biotechnology; born global; open innovation; social capital; global network; organizational diversity; capital efficiency; FlyWheel

Introduction

Born-global companies are business organizations that seek to operate internationally at their founding to leverage their unique set of innovation, capabilities, network, and knowledge [1,2]. By contrast, a domestic firm might passively evolve to become a multinational enterprise, but internationalization is never a core growth strategy. To execute a born-global strategy effectively, biotech start-ups must actively pursue international market-oriented opportunities [3].

Given that the development of novel drugs is a long and highly resource intensive process, requiring a median development cost of US\$1.1 billion per product [4], we advocate that biotech companies

focusing on therapeutics are best positioned as born global. Here, we explore the advantages and challenges of launching a born-global biotech compared with a domestic one, and share the journey of one such born-global biotech, HiFiBiO Therapeutics. To enhance the success of this born-global approach, we propose to apply optimized capital efficiency for maximizing these global advantages and provide an operational framework adapted from Jim Collin's FlyWheel concept to translate these key benefits into building a sustainable born-global biotech [5].

Advantages of a born-global biotech

Therapeutic companies require deep scientific knowledge and technological exper-

tise beyond any geographical limitations to address unmet medical needs. This is particularly relevant for innovative therapeutics, given their long development time and complex mechanisms of action compared with generics [6]. As start-ups face tremendous obstacles to succeed, an approach that provides extensive innovative scientific networks, large amounts of capital, and high-quality talent would be most promising for the biotech industry. With their expanded geographical presence, born-global biotechs might be better positioned to capture these resources compared with domestic companies. Historically, start-ups have remained local because of their lower operational cost and organizational simplicity [7].

In addition, different policies and standards from health regulatory agencies, such as the US Food and Drug Administration (FDA), European Medicines Authority (EMA) and National Medical Products Administration (NMPA) make a multiregional presence challenging. We summarize the advantages and challenges of global versus local profiles in [Table 1](#). When evaluating the choice between staying local or going global, various factors must be considered. Here, we highlight crucial factors to ensure the success of a therapeutic biotech, which requires scientific innovation and sufficient resources to drive projects, as well as top talents to deliver value to patients.

Open innovation

The quality of scientific innovation is fundamental to the success of biotechnology. The exchange of scientific knowledge among biotechs, pharmaceutical companies, and academic research institutions through open innovation has become common practice and is crucial for ensuring access to the most advanced scientific discoveries [8]. Breakthrough discoveries through open innovation are characterized by the synergy of scientific and technological contributions combined with

best practices from partners to enhance the overall probability of success [9]. Therefore, a biotech can gain unique advantages from building a global network to foster open innovation and access cutting-edge science and technology beyond borders. For domestic firms, cross-border collaborations can become difficult because of a variety of factors, including language, time zones, culture, and material sharing [10]. Having physical offices in different locations enables a more effective exchange of knowledge and materials with collaborators directly [11].

Open innovation runs through the DNA of HiFiBio Therapeutics; its proprietary single cell technology was born out of an interdisciplinary collaboration among professors at ESPCI Paris, the Broad Institute in Cambridge MA, and Harvard University in Boston. Upon the launch of therapeutic efforts in 2017, the company quickly expanded to sites in China. It has partnered with institutions, hospitals, biotechs, and pharmaceutical companies globally, such as Curie, ESPCI, and Gustave Roussy in France, Harvard, Broad, Kite, and FibroGen in the USA, Nankai University and Xinhua Hospital in China, as well as multinational companies,

including Pfizer and Takeda. These partnerships have yielded vast benefits to the innovative single cell technology platform of the company and to the progression of its novel therapeutic programs, several of which have since entered the clinic or been out-licensed.

Social capital

Social capital is defined as the ‘stock’ that is created when a group of organizations develop the ability to work together for mutual productive gain [12]. Biotechs, which are often early-stage research and development (R&D) powerhouses, can build social capital through establishing both upstream collaborations with academic institutions for novel technology or scientific discovery and downstream partnerships with pharmaceutical companies for product commercialization [13]. An international presence enables the expansion of these types of global collaboration and enhances partnership success. In addition, global social capital can be leveraged to access different patient populations for clinical trials, and partnerships with international hospitals and patient groups can help global biotechs achieve increased patient diversity, lower costs, and speed up recruitment in trials as well as to better understand local unmet needs [14].

Social capital can also facilitate international funding when the financial strategy aligns with the vision and mission of the company. This funding can be nondilutive, such as tax rebates, grants, and loans, and often requires the recipient to have a local presence. Direct government R&D investment in South Korea for biotech small-medium enterprises (SMEs) and the biotech cluster strategy in Singapore through foreign direct investment are examples of these funding opportunities [15,16]. Such funding can help offset the operational and administrative cost of running international offices.

Dilutive funding can come from both international and regional investors across multiple institutions, such as venture capital, hedge funds, and pharma. One study revealed that foreign and domestic capital inflows could be driven by distinct factors, with location-specific factors having a greater impact on foreign inflows [17]. Therefore, it is possible that a born-global biotech can take advantage of both domes-

TABLE 1

Comparison of the advantages and disadvantages of a global versus local biotech.^a

Global biotech	Local biotech
Advantages	
- Broad access to world-leading science and technology platforms with extensive network for open innovation	- Focused regulatory requirements and business practice
- Wide coverage of global markets to address local unmet need	- Effective local collaborations and resource access
- Maximized opportunities to leverage international social capital towards investments, grants, loans, etc.	- Deep understanding of local landscape and market
- Diverse talent pools with unique expertise and training from different countries	- Straightforward internal communications and collaborations
- Enhanced operational efficiency with effective resource sharing across sites	- Streamlined talent recruiting process and corporate culture building
Challenges	
- Comprehensive knowledge of international regulation and business practices	- Narrower exposure to foreign science and technology
- Complexity to ensure effective internal communication and collaborations	- Limited social capital access, such as investments, grants, partnerships, etc.
- Cohesive global corporate culture while maintaining local uniqueness	- Smaller, less diverse, talent pools

^a Global biotech gains unique access to resources, such as innovative science and technology, funding sources, and diverse talent pools, compared with local-only biotechs. However, there are known challenges around regulatory and business practices, operational costs, internal coordination, and culture that global biotechs must successfully navigate before extracting benefits from a born-global strategy. Conversely, local-only biotechs have the advantage of operating under the laws and regulations of a single country, significantly simplifying operations, but miss out on opportunities to obtain innovative science, investments, and talent.

tic and foreign capital inflows and access broader international investors from different institutions to gain wider funding opportunities, whereas a local firm might not benefit from such access.

The global footprint of HiFiBiO Therapeutics has facilitated numerous funding opportunities from US and Asia-based international investors, as well as nondilutive funding from multiple government grants and tax rebates in the USA, France, and China. The global social capital of the company built over the years in biotech clusters in the three countries has further elevated its capability to secure additional long-term funding and partnerships.

Organizational diversity

Another advantage of a global footprint is greater access to international talent pools, increasing the likelihood of recruiting individuals from diverse backgrounds and experiences. This diversity has been shown to benefit both financial and nonfinancial areas. In a study of biotech SMEs that completed an initial public offering (IPO) between 1989 to 2009, those with more diverse management teams benefited with larger IPO raises [18]. Additionally, multicultural teams with deep-level diversity (perspectives, values, and cognitive frameworks) are positively correlated with creativity and innovation when given complex, interdependent tasks. By contrast, surface-level diversity (nationality, cultural, and ethnicity) might not necessarily lead to significant benefits [19]. We can assert then that, unlike surface level diversity, which can be achieved in a domestic setting, building deep-level diversity requires finding individuals who differ in upbringing, education, and beliefs, a task more conducive in a global setting.

HiFiBiO Therapeutics has gone beyond surface-level diversity to embrace deep-level diversity by building teams across three continents of individuals from different upbringings, educational backgrounds, and perspectives. The company has created a shared company culture called SOAR (Supportive, Optimistic, Adaptable, Responsible) that promotes cross-site collaboration and communication to ensure that opinions are heard and valued. In addition, each country has unique talent to fill gaps faced by other sites. As a result,

the company grew to over 80 people in 3 years with integrated R&D capabilities and an integrated platform to accelerate drug development from target to patients.

Challenges of being a global biotech

Although the benefits of a born-global biotech are prominent, it is necessary to address the challenges associated with a global operation. Being global, a biotech must invest in international offices and teams while complying with local regulatory and business practices. Fortunately, certain centralized functions, such as finance, communication, and IT, can be built at the global level. This frees up capital for R&D talent. Although costs such as rent and utilities cannot be avoided, they can be mitigated through local subsidies and shared incubator facilities. As an added benefit, these spaces can help a biotech improve its visibility to local partnership and funding networks [20]. Having a strong understanding of the intellectual property (IP) laws of each country is also crucial for ensuring proper protection before conducting business internationally. In terms of organizational diversity, there are social costs associated with having employees in different countries who must collaborate with different business etiquettes, communication styles, and decision-making processes. Cultural insensitivity can lead to miscommunication, inefficient performance, and creation of an ‘us versus them’ mentality [21]. When integrating diverse employees across international sites, it is important to maintain the local uniqueness of each site, while aligning on global cultural values. Therefore, a strong corporate culture is necessary to bind everyone to a set of shared principles and facilitate the benefits of having deep-level diversity for increased innovation and commercial success.

HiFiBiO Therapeutics has been able to overcome these challenges by minimizing redundancies across sites to keep costs low while intersite collaboration is maximized to fully leverage the diversified capabilities of the company. The emphasis on company vision, mission, and strategy across different sites has a crucial role in rallying international employees together to work as one organization. Moreover, the globally shared SOAR culture promotes a sense of community facilitated through company-wide initiatives, such as newslet-

ters, awards, Townhalls, and hot topic presentations.

Maximizing the value of global advantages

Despite the challenges discussed, we assert that biotech start-ups should adopt a born-global model when the values generated outweigh the costs. Capital efficiency has been previously used to measure the effectiveness of various funding options for biotech R&D [22]. It is also the mantra of venture capitalist Bruce Booth, who defines capital efficiency as the value generated per unit of dollar invested [23]. To ensure that a company can maximize the value of born global, we propose to monitor capital efficiency at the site level.

We define the capital efficiency (E_L) of a local company as its net value, V_{NetL} , divided by its operational cost, C_L , whereas the capital efficiency of a global biotech, E_G , equals the sum of the net value (V_N) generated in each country (1,2,3... N) divided by the total operational cost (C_N) (Figure 1a). V_N and C_N can be significantly impacted by the factors discussed, such as social capital and organizational diversity. However, given the challenge of independently measuring their effects, we advocate a simpler approach for calculating capital efficiency globally optimized average (E_{GO}), whereby each country N must independently maximize its capital efficiency. With this simplified approach, as long as a company can increase E_{GO} by entering a new country, it is advantageous to do so. However, if the capital efficiency of a new country lowers the average E_{GO} , it is better to invest in improving the capital efficiency of existing locations first.

Following this principle, biotech start-ups should consider launching first in a country where the capital efficiency is the greatest for its founder(s). For example, John Oyler, cofounder and CEO of BeiGene, recognized that the China pharmaceutical market was rapidly evolving with favorable talent growth, reimbursement policies, and clinical trial costs [24]. These advantages were significant drivers that made China more capital efficient for Mr Oyler to launch a biotech in than his home country, the USA. His bet paid off and, since BeiGene’s inception in 2010, the company has grown to 9,000 employees across 40 offices and five continents,

(a)

V = value generated from business activities; C = costs spent to date

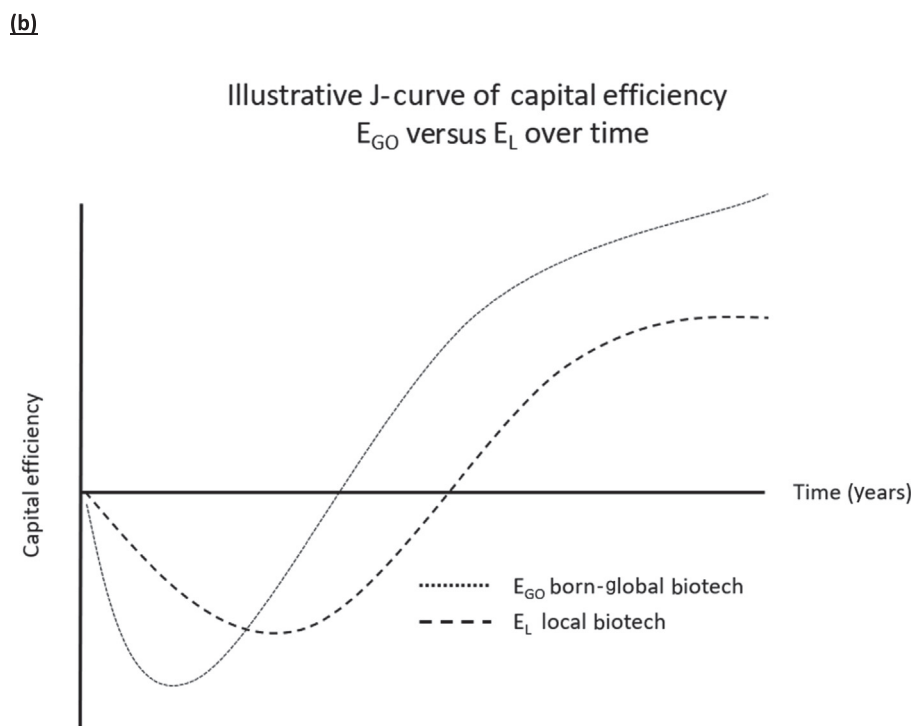
$V_{Net} = V - C$; L = local country; $1, 2, 3, \dots, N$ = each country of a born-global biotech

Local biotech capital efficiency Global biotech capital efficiency

$$E_L = \frac{V_{NetL}}{C_L}$$

$$E_G = \frac{V_{Net1} + V_{Net2} + V_{Net3} + \dots + V_{NetN}}{C_1 + C_2 + C_3 + \dots + C_N}$$

$$E_{GO} = \left(\frac{V_{Net1}}{C_1} + \frac{V_{Net2}}{C_2} + \frac{V_{Net3}}{C_3} + \dots + \frac{V_{NetN}}{C_N} \right) / N = (E_1 + E_2 + E_3 + \dots + E_N) / N$$



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FIGURE 1

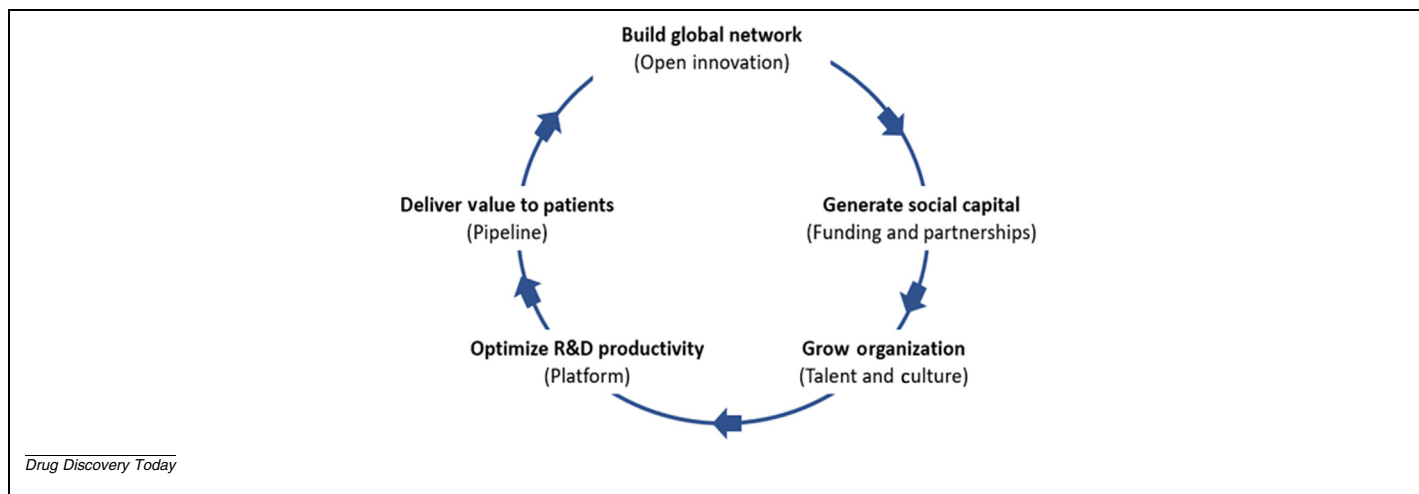
A capital efficiency model to maximize value generation when going global **(a)** Capital efficiency model for a born-global strategy. V equates to the value generated from business activities [research and development (R&D) milestones, partnerships, grants, investments, etc.]. C represents all the internal (operational, R&D, talent, etc.) and external costs (CROs, consultants, legal, etc.) associated with running a biotech. V_{Net} represents the net value ($V - C$) generated from business activities within the local country, L , or international sites ($1, 2, 3, \dots, N$). Capital efficiency, E_L or E_G , for a local or global biotech, respectively is defined as the net value generated, V_{Net} , divided by the sum of the costs C . In a global biotech, this equates to the sum of all the net value generated at each site divided by the sum of the total cost. E_{GO} represents the capital efficiency of a global biotech optimized and can be calculated using the average of the individual capital efficiency of each site. **(b)** Illustrative J-curve measuring capital efficiency over time for born-global and local biotechs. Capital efficiency, E , is expected to be negative for both born-global and local start-up biotechs because net value, V_{Net} , typically starts out negative (costs are higher than value generated). Born-global biotechs might experience a more negative initial capital efficiency because more resources (higher costs) are dedicated to international expansion. However, the effective use of expanded resources in the global market accelerates the increase in capital efficiency over time. Peak capital efficiency is higher for born-global firms because they have more opportunities to obtain and deploy capital for value-generating work while also distributing costs to more favourable markets.

generating over US\$1 billion in product revenue [25].

Whether starting internationally or expanding globally, it is crucial for start-up biotechs to continuously increase their

capital efficiency as operations mature. This increase over time can be modeled using a J-curve as often used by investors to track start-up returns [26]. We adopt this curve to track capital efficiency over

time as an indicator of value creation when comparing local versus born-global biotechs (Figure 1b). In the first few years after inception, we expect negative V_{Net} (resulting in negative capital efficiency) as

**FIGURE 2**

FlyWheel framework for building a successful born-global biotech. This framework highlights the cyclical nature of building a successful born-global biotech, which starts with open innovation through a global network. This provides access to cutting-edge scientific and technological discoveries with extensive partnerships. This global presence facilitates the accumulation of social capital, which can be leveraged at the international level. The funding allows for accelerated organizational growth and strengthening of a core global culture. The talent recruited worldwide can further advance novel scientific findings and enhance research and development (R&D) productivity with a robust pipeline of therapeutics. All these key aspects working together in the flywheel ensure the delivery of critical value to patients globally, which further strengthens the ability to practice open innovation in new countries and therapeutic areas, repeating the cycle.

both local and global biotechs invest in infrastructure, equipment and services before generating revenue streams. Depending on the extent of internationalization, the capital efficiency of born-global biotechs might be more negatively impacted compared with that of local firms, but it can accelerate faster in generating positive capital efficiency as the global biotechs deploy their resources to build revenue streams. Conversely, local firms have fewer operational complexities to navigate, but also fewer resources to access, leading to a slower climb to peak capital efficiency. Born-global biotechs have a higher capital efficiency ceiling, because either costs can be optimized among global sites or more value-generating opportunities become available with global partners.

Applying this capital efficiency model to HiFiBiO Therapeutics, the company has successfully maximized E_{GO} through actively maximizing the capital efficacy of each site. In the USA, the company gained investors, grants, and partnerships as well as translational and clinical expertise. In France, collaborations, tax rebates, grants, and single cell platform advancement enable its positive capital efficiency. Its China presence enables access to Asian investors as well as tax rebates and partnerships with hospitals and academia. By

maximizing value generation and reducing costs in each country, HiFiBiO Therapeutics is continuously increasing its capital efficiency, E_{GO} , over time.

Path for a born-global biotech

To build a sustainable born-global company, we propose an operational framework (Figure 2) based on the FlyWheel concept introduced by Jim Collins to fully leverage open innovation, social capital, and organizational growth [5]. This concept proposes that no successful business transformation can be achieved through a short burst of effort. Instead, it takes the continuous turning of a giant flywheel to achieve a sustained momentum of breakthroughs. The first stage of the flywheel involves building a global network to facilitate open innovation opportunities for scientific exchange. Once ample differentiation and technological novelty are created, social capital is generated to attract further funding and partnerships. With a global network and funding, the organization will grow with new capabilities and a diverse culture. This results in higher R&D productivity, often through innovative platform technology advancement and rapid progression of therapeutic pipelines. The profit generated is reinvested back into the company, creating a

virtuous cycle of continued international growth and success.

The journey of HiFiBiO Therapeutics as a born-global biotech is reflected in this FlyWheel framework, highlighting how intentional early global expansion can accelerate value generation. The company initially launched two global sites in Cambridge, MA and Paris, France. Although this approach incurred higher costs, the international social capital facilitated partnerships with major pharma companies, such as Pfizer, Takeda, and Kite, and the acquisition of an antibody generation platform from the Paris-based H-Immune. Shortly afterward, the company launched operations in China, rapidly expanding the research team and closing a US\$37.5 million Series B led by several Asia-based investors. Fast forward to 2023, the company has generated an additional US\$200+ million in both diluted and undiluted funding from global investors and partnerships, operationalized a powerful single cell and data intelligence platform (DISTM), advanced a series of potential first-in-class and best-in-class therapeutics into the clinic, and grown a globally shared SOAR culture.

Concluding remarks

We assert that creating a born-global biotech provides a potential solution for over-

coming the current tough environment of 'biotech winter' characterized by competition for top talent, fewer deals, depressed stock prices, and tightening investor funding [27]. Even under favorable macroeconomic conditions, having a global presence presents biotechs with more options compared with local firms to secure the talent, funding, and innovation needed to rapidly advance their development. We underline the advantages of going global, such as the increased opportunity for open innovation, social capital generation, and organizational growth and diversity, which, when executed correctly, outweigh the costs of running a global operation. We propose a strategy to optimize the value of a born-global biotech and suggest to drive capital efficiency at each site to achieve maximum E_{GO} . Furthermore, we map a path for a born-global biotech based on the FlyWheel concept to ensure all key advantages of an international presence can be built into the business framework.

Conflict of Interest Statement

The authors whose names are listed immediately below report the following details of affiliation or involvement in an organization or entity with a financial or non-financial interest in the subject matter or materials discussed in this manuscript.

Vincent Tse, MBA, is employed full time as Senior Director of Staff and Strategy at HiFiBiO Therapeutics. Liang Schweizer, PhD, is employed full time as the Founder, Chairperson, and CEO of HiFiBiO Therapeutics.

Data availability

No data was used for the research described in the article.

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