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Abstract: Whether it is a government research institution, a public-private partnership, or a private enterprise, the South African biotechnology industry requires funding for the biotechnology industry. Our goal with this research is to look into the role of venture capital (VC) in financing biotech enterprises and demonstrate how VC finance could aid in the development of diagnostic kits and vaccines for Covid-19 or future pandemics in South Africa.

Moreover, the study aims to provide policymakers with a clear image of the importance of funding the biotechnology sector as recognized by the industry's key players. We employed a questionnaire and an interview survey with the key agencies in biotechnology eco-system to understand the role of biotechnology funding, notably during the Covid-19 pandemic.

Overall, participants believe that South Africa's biotechnology lags behind that of other developing countries, but that it has the potential to grow greatly with enablers. It is also regarded immature, fragmented, and fractured due to a lack of financing and a committed organization to organize operations. The South African biotechnology venture capital business is in its infancy stage, risk-averse, conservative in its investment power. In addition, the response time to the pandemic, financial coordination for Covid-19 research, a lack of communication between authorities, and several labs out of operation owing to full-lockdowns have all been noted as problems.

Keywords – Covid-19, Venture capital (VC), financing, biotechnology industry, South Africa

1. Introduction

Biotechnology is defined as the application of science and technology to living organisms and parts, products, and models thereof to alter living or non-living materials for the production of knowledge, goods, and services (OECD, 2001, p. 1). According to this definition, biotechnology encompasses a broad range of technologies and a wide range of applications and products such as health care, agriculture, food, and the environment, among others (Uctu and Jafta, 2018). As a result, biotechnology has enabled countries to address the challenges they face and contribute to faster economic growth, progress, and human welfare (Haar, 2017).

Biotechnology is currently one of the fastest-growing industries in the world (Ang, 2006; Blanco-García, 2020), with global revenues of US$188 billion in 2017 and 316 commercially approved products in the US and Europe by mid-2018 (Blanco-García, 2020). One of the hurdles in the biotechnology industry is the dependence on financing, starting from the idea phase to drug approval, clinical trials, and finally bringing a product to the market. To get started, new biotechnology companies may need millions of dollars (Lee & Dibner, 2005); the biotech product cycle, unlike the ICT sector, lasts 10 to 12 years and requires investments ranging from US$650 million to US$1.8 billion.

Whether it is a government research agency, a public-private corporation, or a private enterprise, the South African biotechnology sector needs funding to develop pharmaceutical products. During the Covid-19 pandemic, it was clear that developing countries struggled to get Covid-19 related pharmaceutical products from developed countries, particularly during vaccine roll-outs, since developed countries prioritized their citizens.

This research aims to examine the role of financing in the South African biotech industry and demonstrate the importance in the development of diagnostic kits and vaccines for the Covid-19 or future pandemics. An exploratory study was undertaken using a questionnaire and an interview survey to better understand the importance of biotechnology finance, particularly during the Covid-19 pandemic.

The article begins with a brief background of the Covid-19 pandemic, followed by an overview of innovation ecosystems in biotechnology and the role of venture capital investments. Then the paper presents our questionnaire and survey results. The last section summarises and considers areas for further research.

2. Covid-19 Pandemic

In recent decades, several viral epidemics have emerged, including the Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV identified in 2002/2003), Swine Flu (H1N1 influenza identified in 2009), and the Middle East Respiratory Syndrome Corona Virus (MERS-CoV identified in 2012) (Behera *et al.*, 2021). The latest outbreak of a coronavirus known as the Covid-19 pandemic has been labeled as the global health crisis of the century and one of the biggest challenges humankind faced since World War II (WWII). The COVID-19 is a novel virus (SARS-CoV-2) that belongs to the same virus family as SARS and some common colds (Goris *et al.*, 2020; Rezaei, 2020;

Behera *et al.*, 2021; www.who.int, 2021a; www.undp.org, 2021). It was identified for the first time in Wuhan, China, in December 2019, and the World Health Organisation (WHO) announced it as a Public Health Emergency for International Concern in January 2020, and as a pandemic in March 2020 (www.euro.who.int, 2021). At the time the article was written, as of 25 October 2021, over 240 million cases (244,539,045) were reported, with over 4.9 million (4,966,180) confirmed deaths (www.worldometers.info, 2021). UNDP (2021) defined the pandemic as a global health crisis and a socio-economic crisis. According to the UNDP, 400 million people will lose their jobs, and remittances will drop by US$110 billion this year, leaving 800 million people unable to meet their basic needs (www.undp.org, 2021).

The virus's emergence has prompted several scientists worldwide, including biotechnologists, immunologists, epidemiologists, mathematicians, physicists, and engineers, to shift their primary research emphasis to find solutions to the COVID-19 pandemic (Goris *et al.,* 2020) by creating potential vaccines, diagnostic tests, and other community-driven responses to SARS-CoV-2 (Nicola *et al.*, 2020). Furthermore, many researchers also looked into the social and economic impacts of the pandemic (Nicola *et al.,* 2020). Such a pandemic is a complex issue that requires multidisciplinary research with a global focus and borderless approach needed to combat COVID-19 (Rezaei, 2020). Therefore, governments, research institutions, universities, biotech and pharmaceutical firms, and non-governmental organisations (NGOs) had to collaborate to develop diagnostic tools, drugs, and vaccines to combat the pandemic. The current pandemic also deepens the understanding of infectious diseases and prepares the world for future potential outbreaks (Joshi, 2021).

Vaccine development typically takes more than ten years due to the complexity of developing a safe and effective vaccine. In response to the pandemic, several companies began developing COVID-19 vaccines in early 2020, and it is being prioritized for clinical evaluation for safety and effectiveness, funding, and preparation to produce billions of doses and potential global deployment and equal access to vaccines for developed and developing countries (https://sacoronavirus.co.za, 2021). As of 16 April 2021, there are 272 COVID-19 vaccines in development worldwide, with 88 in the clinical trials, 184 in pre-clinical development, and six of them approved for emergency or full use by at least one WHO-recognized stringent regulatory authority (Oxford–AstraZeneca, Pfizer-BioNTech, Sinopharm-BBIBP, Moderna, Sinovac, and Johnson & Johnson) (www.who.int, 2021b).

2.1. Covid-19 Pandemic and South Africa: Recent Developments

The COVID-19 pandemic had a devastating effect on countries globally. South Africa had more than 2.9 million (2,919,632) known cases and more than 88 thousand (88,925) official covid related deaths as of 25 October 2021 (www.worldometers.info, 2021). The availability of COVID-19 vaccines in developing countries, including South Africa, has been a major concern from many perspectives. It disrupted the delivery of routine healthcare globally and is likely to do so in South Africa. For instance, the delivery of routine healthcare for tuberculosis (TB), human immunodeficiency virus (HIV), and HIV/TB co-infection, is already a significant burden for the South African health care system where the majority of the population depends on an under-resourced and poorly managed public healthcare system. South Africa has a two-tiered healthcare system where the

public sector provides healthcare to 84 percent, and the private sector covers only 16 percent of the population (Staunton *et al.*, 2020). Government support for COVID-19 requires huge financial input in light of small healthcare budgets and the burden of diseases in South Africa. For example, the cost of South Africa's vaccine roll-out programme is expected to be 20.6 billion South African rands (ZAR), roughly equivalent to US$ 1.4 billion (www.gavi.org, 2021). Since COVID-19 is a global pandemic, international assistance for new COVID-19 drugs and vaccines is likely to be scarce as well (Bangalee and Suleman, 2020).

One of the critical questions raised could be potentially focusing on how to have a better biotechnology ecosystem, where South Africa could better finance its biotechnology industry to develop its own vaccines and diagnostic kits. The below research identified the recent developments in healthcare during the Covid-19 pandemic.

Recent Developments

- The Vaccines and Infectious Diseases Analytics (VIDA) Research Unit of the University of the Witwatersrand (Wits VIDA) trains clinical scientists and researches vaccine-preventable diseases. In collaboration with Oxford University, Wits performed COVID-19 vaccine trials for the Oxford vaccine candidate in the African region in 2020 (www.wits.ac.za, 2021). The South African Medical Research Council is co-funding the project with ZAR10 million ($666,666[1]) together with other philanthropic funders such as the Bill and Melinda Gates Foundation. (www.samrc.ac.za, 2021). Wits VIDA is also performing trials for the US-based Novavax vaccine (phase 3).
- Two South African companies (Biovac and Aspen) upgraded their facilities to produce COVID-19 vaccines using active pharmaceutical ingredients from vaccine developers and manufacturers outside South Africa. The ability to formulate, fill, and finish vaccines locally reduces the trade balance, provides high-skilled jobs, and, in the long run, ensures vaccine supply stability.

  Biovac is a specialist vaccine company (one of four vaccine manufacturers operating in Sub-Saharan Africa), with product development, formulation, and filling capabilities tailored to vaccines. It has the right to formulate, fill, bag, and mark vaccines under its license. Biovac was established as a Public-Private Partnership in collaboration with the South African government. It currently supplies about 70% of South Africa's vaccine needs and was expanding its manufacturing capabilities prior to the pandemic. Biovac's current activities include bacterial vaccine development, sterile formulation and filling, labeling, packaging, and cold chain distribution (www.sacoronavirus.co.za, 2021). Biovac recently announced a local manufacturing agreement with ImmunityBio, a US-based immunotherapy firm, to develop Biovac's second-generation Covid-19 vaccine in South Africa. Currently, 'ImmunityBio's vaccine is in Phase 1 clinical trials at the University of Cape Town (UCT) (www.moneyweb.co.za, 2021).

[1] 1$= 15 Rand, 11 March 2021

Aspen is a multinational pharmaceutical company headquartered in Port Elizabeth. It recently improved its sterile capability, specifically for small molecules. Aspen and Johnson & Johnson (J&J) have announced that Aspen will devote some of its vaccine manufacturing (fill-finish) resources to the J&J's COVID-19 candidate. This provides the country with increased fill-finish capability and vaccine access (www.sacoronavirus.co.za, 2021).

- Cape Bio Pharms, founded by researchers from the UCT Biopharming Research Unit (BRU), has received approximately ZAR900 million ($62 million) grant from the European Investment Bank (EIB) and the Foundation for Innovative New Diagnostics (FIND), a global non-profit organization to accelerate the development of low-cost plant-based rapid diagnostic COVID-19 test kits.

  The grant will be used to build Cape Biologix Technologies, a new subsidiary of Cape Bio Pharms in Mauritius. The facility will commercialize the efficient production of plant-based recombinant proteins by scaling up advanced innovative plant-based manufacturing (www.uct.ac.za, 2021).
- Quro Medical, a Johannesburg-based startup, was founded in 2018 to provide affordable healthcare solutions in South Africa. Compared to traditional healthcare methods, they focus on reducing healthcare delivery costs by using real-time and data-driven clinical interventions. The company's programs, such as remote patient monitoring (including monitoring Covid-19 patients remotely), and healthcare delivery (including hospital at home), would undoubtedly be critical components of a long-term solution. Quro Medical has received seed funding from Enza Capital (based in Kenia) and South African-based Mohau Equity Partners (www.ventureburn.com, 2021).

South Africa has excellent clinical and laboratory research expertise, which served as the foundation for developing a broad research agenda for COVID-19, including vaccine production. (www.sacoronavirus.co.za, 2021). The government has allocated ZAR95 million ($6.3 million) to develop COVID-19 vaccines, treatments, therapeutics, and diagnostics. The South African Medical Research Council is in charge of financing research programs to evaluate possible COVID-19 vaccines in clinical trials (www.sacoronavirus.co.za, 2021).

Yet, looking at the recent developments, it is either a collaboration in vaccine clinical trials for other companies or a license agreement to manufacture vaccines of other companies, with the exception of Cape Bio Pharms, which aims to develop diagnostic test kits for Covid-19. According to WHO (2021b), of the 272 vaccine candidates, only five candidates in pre-clinical trials are from the African continent, of which four are from the National Research Centre in Egypt and one from Helix Biogen Consult in Nigeria. Officially, there are no vaccine candidates in pre-clinical or clinical trials from South Africa yet (as of April 16, 2021).

During vaccine roll-outs, it was apparent that developing countries struggled to get vaccines from developed countries since priority was given to citizens from the latter nations. South Africa was no different, as the South African government opted to channel its resources towards procuring vaccines from developed countries rather than investing in the local biotechnology industry to develop its own vaccines.

In the rest of the article, we investigate the role of venture capital (VC) firms in financing biotech firms in South Africa and discuss its potential role in developing diagnostic kits and vaccines for the Covid-19 or future pandemics.

3. Innovation Ecosystems in Biotechnology: The Role of Venture Capital Investments

Most scholars believe that the innovation ecosystem comprises of interconnected and interdependent network actors (core companies, consumers, suppliers, complementary innovators, and regulatory agencies), all of whom are reliant on the system environment (Huang *et al.,* 2020). According to Granstrand and Holgersson (2020, 3), "*an innovation ecosystem is the evolving set of actors, activities, and artifacts, and the institutions and relations, including complementary and substitute relations that are important for the innovative performance of an actor or a population of actors*." In a similar vein, Kagami (2019, 19) refers to the "*innovation ecosystem"* as *"…a network of people, services, and physical environments that enable Innovation Driven Enterprises (IDEs) to start, develop, and scale."*

Biotechnology has been identified as one of the innovation-driven industries, and the emergence of biotechnology ecosystems facilitated collaborations between cross-sectoral institutions and businesses. According to the Economist magazine (bio.org, 2017, 1), "*Creating new drugs through biotechnology is at the risky end of a business in which superhuman stamina and bottomless pockets are minimum requirements*". Talents and specialists from various fields and institutions are needed to transform a scientific breakthrough into a life-changing product. These include government institutions, universities, private firms, venture capitalists, pre-clinical and clinical research and development, regulatory, biotech lawyers, intellectual property law firms, business development, commercial and financial experts (Warneck, 2018). It is challenging to create and sustain such ecosystems, but in order to succeed, biotech startups need ecosystems that compete for talent and investment in their efforts to advance bio-economic development (Hiller, 2019).

Sainsbury (1999), identified ten critical factors grouped into three sets that encourage the development of biotechnology. These factors include exploitation of the research base (covering a solid science base and entrepreneurial culture), company development (covering the ability to attract key staff, supportive physical and logistics infrastructure, availability of finance, business support services, and large companies in related sectors, and a skilled workforce) and government support (effective networks, and government support). In this research, our focus is to investigate the role venture capital (sufficient funding/availability of finance) plays in biotechnology development. Schoemaker and Schoemaker, 1998; Meyers and Hurley 2008; Malazgirt, 2011; Uctu and Jafta 2018, summarise the above in three structural elements, or the "three pillars," needed for a biotechnology startup to succeed, namely efficient management, access to cutting-edge technology that leads to new products and adequate funding.

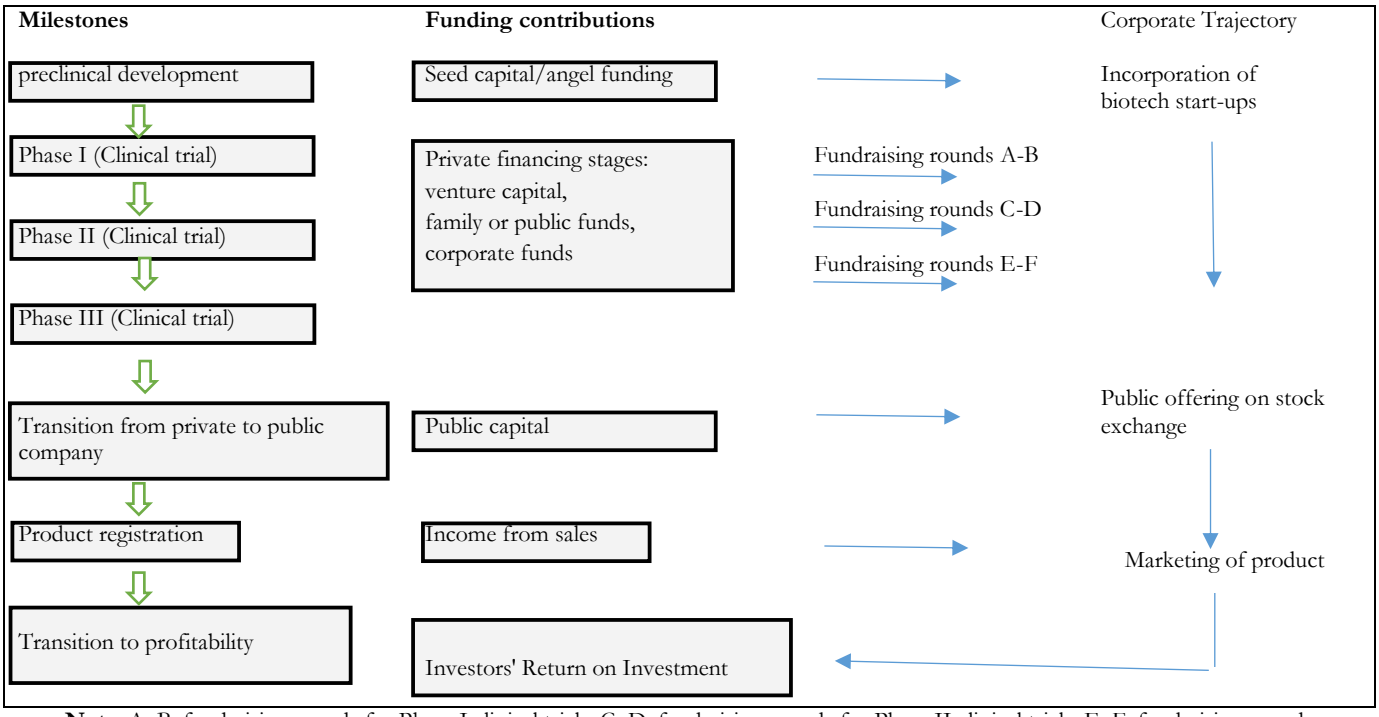
Biotechnology is a long and expensive journey from discovery to commercialization and is different from other technology startups due to the investment taking longer to show return on investment, as well as the amount of funding required from (private) investors such as venture capital firms (Ang, 2006; Lebret, 2018).

Many academic papers focused on VC firms due to their active role in forming new businesses (Jeong *et al.,* 2020). Venture capital has been a primary source of funding for startups and growth companies (Ford and Nelsen, 2014) and is characterized as an independent, professionally managed, dedicated pool of capital that focus on equity or equity-linked investments in privately held, high growth companies (Lerner, 2009, 146 cited by Rossi *et al.,* 2011, 357; Scheela and Chua, 2011). Venture capitalists maintain a fund, which was raised from institutions, mutual funds, private investors, etc. with the aim to make substantial long-term capital gains (Scheela and Chua, 2011). There are two approaches to venture capital; venture capital as a financial asset and venture capital to assist emerging technology-based businesses. Rossi *et al.,* (2011) believed that VC plays a catalytic role in innovation by enabling translation of research and development (R&D) activities into commercial outcomes. Jeong *et al.* (2020) sites another perspective, highlighting that VC companies have important intangible assets and capital investments, based on their expertise and networks. This aspect of VC investment is essential, as young businesses often lack financial and intangible resources, such as prior experience and expertise, which are required to grow their businesses. The mature market VC typically invests in high-risk enterprises with a high rate of return if they succeed, especially in early-stage companies with high capital requirements for developing new products. Biotechnology is one of the most common such businesses (Ang, 2006; Bains *et al*., 2014). The VC firm receives substantial equity positions in young, high-risk companies in exchange for its investment and has the ability to realize significant returns on its investment until these companies begin selling stock on public markets or are acquired (Lee & Dibner, 2005).

Due to the limited government support, young entrepreneurs were driven to seek alternative sources of finance, setting the framework for a new paradigm in which venture capital investors covered the rising costs of clinical product development. Figure 1 depicts biotech capital sources based on the stage of production of each R&D project (Blanco-García, 2020). According to Ford and Nelsen, the primary sources of biotechnology capital include family and friends, angels, foundations and patient groups, government agencies, family funds, corporate venture capital and venture capitalists (Ford and Nelsen, 2014; Blanco-García, 2020).

A survey by BioAbility (Lee and Dibner, 2005) reveals that biotechnology VC funds in the United States and Europe are heavily diversified into companies involved in therapeutics, diagnostics, medical devices, or platform production. These areas are thought to have both appealing consumer potential and long-term significance. Biotechnology VC funds are invested to a minor degree in agriculture, engineering, and chemicals in both the United States and Europe, and a comparatively limited amount is invested in contract research organizations compared to other fields of biotech investment.

Figure 1: Sources of biotechnology capital, by R&D project development phase



Note: A–B: fundraising rounds for Phase I clinical trials; C–D: fundraising rounds for Phase II clinical trials; E–F: fundraising rounds for Phase III clinical trials
Source: adapted from Blanco-García, 2020

3.1. Biotechnology Venture Capital Investments in South Africa

Obtaining sufficient capital and availability of funding are a continuous struggle for South African biotechnology companies. As mentioned in the previous section, biotechnology is a capital-intensive sector and needs many years of research and development and vast amounts of capital, more so for early-stage companies. According to Konde (2011), cited in Uctu and Jafta (2018), early-stage biotechnology investment is a resource-intensive industry in which entrepreneurs must establish close relationships with local and global investors, companies, and government agencies. In India, similarly to South Africa, early-stage funding is typically led by the government, not by private investors. Private equity (PE) and venture capital (VC) funds are the primary sources of later-stage funding for Indian biotech companies. The decline in early-stage funding has left Indian startup biotech companies vulnerable in recent years. The main explanation is that, due to a lack of private funds to invest in innovative and risky ventures, investors are shifting to later-stage investment strategies (Konde, 2011; bio.org, 2014). Financing for early-stage biotechnology firms in South Africa is also strongly government-led through the Medical Research Council (MRC), the Technology Innovation Agency (TIA), the Industrial Development Corporation (IDC), and the Support Programme for Industrial Innovation (SPII), an initiative of the Department of Trade, Industry and Competition (the DTIC). Table 1 shows the global VC Investments in the biotechnology sector. In comparison, Africa and South Africa are far behind in financing the biotechnology sector.

Table 1: Global Biotech Venture Capital Investment (amount raised, million dollars)

	2016	2017	2018	2019	2020
Americas	9,309	14,229	17,198	16,237	22,591
Europe	2,817	2,222	3,712	3,537	4,937
Asia-Pacific	2,460	2,575	5,506	4,822	6,201

Source: DeFrancesco, 2021

Private funding for biotechnology, including the VC market, is underdeveloped and severely limited in South Africa (Sherwin, 2007). As was mentioned by Sherwin, 2007; Uctu and Pillay, 2012; Pillay and Uctu, 2013; Uctu and Jafta, 2014; Uctu and Jafta, 2018; Uctu and Essop, 2020, inadequate funding from the public and private sector for seed and startup capital is consistently described as a barrier to the South African biotechnology sector's development, even though it is a promising sector for the economy. According to Sherwin (2007), the issue in South Africa is that the majority of funds are going to replacement capital, such as management buy-outs and black economic empowerment transactions.

In recent years, South African biotech firms only have two local, biotech focused VC companies to consider, namely BioVentures and OneBio Seed Investment Fund.

BioVentures

Until 2018, the only biotechnology-focused venture capital company in South Africa was BioVentures which was launched in 2000. However, the Fund was closed in 2010 due to investing its total capital capacity. It was a fixed period fund, and the company had reached the end of its life and de-registered the Fund (which was established as a Trust). In 2001, the BioVentures company raised approximately 12 million dollars or ZAR80 million (the current exchange rate is 5.3 million dollars[2]) from the South African IDC and the International Finance Corporation (Washington, DC). By May 2010, the company invested R76 million in total in 8 private equity/venture capital investments, and in 2012, the portfolio size dropped to three companies (table 2 shows the current status of the investments made[3]) (Masum and Singer, 2010; Masum et al. 2010; Pillay and Uctu, 2013; Uctu and Jafta, 2018). Currently, only two companies are still active. It was seen as a modest financial success as it was the only biotechnology venture capital in South Africa. Yet, because the small-size funding company could not have a return on investment in the investments made, the company gave up equity to raise additional funds and sell healthy assets earlier than required. (Masum and Singer, 2010). Table 2 shows the current status of the BioVentures investments.

[2] 1$= 15 Rand, 11 March 2021

[3] To update, we contacted the founder of Bioventures, 23 April 2021

Table 2: Current status of BioVentures Investments

Company name	Summary	Active/Non-exist
Amandla Water Systems	Wastewater bioremediation technology worked, but the business model failed from extended infrastructure tendering cycles and reliance on large water companies.	no longer exist
Electric Genetics	University of the Western Cape spin-offs in Bioinformatics. The sector as a whole did poorly.	no longer exist
Mbuyu Biotech	Joint venture with Council for Scientific and Industrial Research to commercialize the Council's bioprocessing technologies.	no longer exist
Natural Carotenoids SA	Focuses on production and extraction of carotenoids from algae for food, cosmetics, and pharma industries. The business did not reach the commercialization stage.	no longer exist
Shimoda Biotech PlatCo Technologies	One drug licensed and on the market; 10 in various stages of development and trials; mostly enhanced generics. The company, with its subsidiary PlatCo Technologies which was set up to explore the potential for novel platinum-based anti-cancer compounds, sold to Abraxis Biotech in 2008 for $15 million. In 2010, Abraxis BioScience was acquired by Celgene Corporation. Based on Celgene's website, as of 2016, Abraxis no longer exists as a named division within Celgene.	no longer exist
Disa Vascular	Develops and produces stents for cardiac and other arteries to keep previously blocked arteries open. (Disa Medinotec, Disa Life Sciences)	active
Synexa Life Sciences	Proprietary bioprocessing technology for production of natural compounds and recombinant proteins (https://www.synexagroup.com)	active

Source: Authors' own construction, 2021 based on Masum and Singer, 2010

OneBio Seed Investment Fund

The government officially supports the biotech industry in South Africa, but government funds for the biotechnology industry are minute and can even be considered insignificant. The South African government has funded around R1 billion ($68 million)[4] from 2003 to 2011 in biotechnology start-ups (Semete-Makokotlela, 2014/2015). To improve this situation, OneBio was launched in 2018 by Michael Fichardt and Dr. Nick Walker and received R83.5 million Rand ($5.6 million[5]) from the South African SME Fund to provide venture capital to early-stage startup companies. To date[6], OneBio made its first and only investment in 2021 in a biotech startup in South Africa.[7]
This total funding is not enough to stimulate the sector, which could lead to the biotech sector remaining underdeveloped (see Al-bader *et al.,* 2009 and Uctu and Jafta, 2018).

3.2. Research Methodology

The study aims to look at the role of venture capital (VC) in South African biotech financing and show how it can equip the healthcare system to be better prepared for future pandemics.

First, a literature review was conducted to gain a better grasp of the basic concept and present difficulties surrounding the Covid-19 pandemic, as well as the necessity of venture capital investment for biotechnology. After then, an exploratory study was undertaken using a questionnaire and an interview survey to better understand the role of biotechnology finance, particularly during the Covid-19 pandemic. The survey was managed in two steps; first, we identified the key players in the biotech ecosystem. These are government organizations, higher education institutions, biotechnology venture capitals, biotech firms and startups, public and private biotech incubators and non-profit companies.

[4] $1= 14.66 Rand, 25 October 2021
[5] 1$= 15 Rand, 11 March 2021
[6] To update, we have contacted with the founders, 23 April 2021
[7] For more details (https://www.onebio.africa, 2021)

Participants in the study covered the most active regions[8] in biotechnology, including Western Cape, Gauteng, Kwazulu Natal, followed by the Eastern Cape and Free State.

In the second stage, a questionnaire was created for the ecosystem's major participants. The questionnaire was emailed to 20 participants from supporting agencies in April-May 2021. The questionnaire prompted important questions regarding the South African biotechnology ecosystem, South African biotechnology prospects globally followed by the significant characteristics and challenges relevant to the biotechnology venture capital industry, the reasons South Africa stayed behind in the global competition of Covid-19 vaccine development, and challenges identified during the pandemic in South Africa. Further, to garner support agencies' perspective in the ecosystem, we arranged and conducted interviews with some key players. The interviews provided a significant amount of data, which can be used by practitioners and policymakers to make better decisions.
Fourteen agencies responded to the questionnaire via email and were interviewed through virtual interviews later with a few selected participants. Since the interviews used the same questionnaire as a basis, we combined the data supplied by the participants with the data obtained from virtual conference calls. To protect the participants' privacy, we applied coding methods (see table 3).

Limitations of the study

Participants expressed their own opinion; therefore, no inferences to the institution/organization they affiliated with can be drawn from the primary data and its analysis. Furthermore, the data were collected remotely due to the Covid-19 pandemic, to minimize participant interactions.

Table 3: Participants affiliations

Affiliation		**Participants**
Government Organizations	GOVORG	GovOrg1, GovOrg2
Higher Education Institutions Technology Transfer Offices	HEI-TTOs	TTO1, TTO2, TTO3
Biotechnology Firms	BF	BF1, BF2
Biotechnology Startups	BS	BS1, BS2
Venture Capital Firms (incl. biotechnology, hardware)	VCF	VCF1, VCF2, VCF3
Others (biotechnology incubators, non-profit companies in the biotech space, etc.)	OTHERS	OTHERS1, OTHERS2

Source: Authors' own construction, 2021

4. Research Results and Discussions

In this section, the research evaluates the participants' perspectives regarding the South African biotechnology ecosystems.

4.1. Views on biotechnology ecosystems in South Africa

The biotechnology ecosystem in South Africa comprises of government, facilitators (includes R&D labs, incubators, accelerators, business organizations, NGOs), universities, funding agencies

[8] South Africa consists of 9 provinces: Western Cape, Eastern Cape, Northern Cape, North West, Free State, Kwazulu Natal, Gauteng, Limpopo and Mpumalanga.

(public and private), and biotechnology companies. In this section, participants were asked about the biotechnology ecosystems in South Africa. According to the participants, the sector is still far behind compared to other developing countries, yet South Africa has the potential to build an excellent biotechnology ecosystem. R&D universities, research institutions, hospitals, incubators and, technology transfer offices are listed as enablers. Nevertheless, the South African biotechnology sector is also seen as under-developed, fragmented, and fractured due to the lack of funding (including seed funding) and a dedicated organisation to coordinate the activities. Other comments included that more had to be done to develop young scientists' entrepreneurial skills, relaxation of high levels of taxation, and align macro policy to help develop the biotech industry. It was also mentioned that the whole biotech ecosystem is very reliant on government funding and has become highly politicised. Some participants argued that the depoliticising of the sector is required for a better biotechnology ecosystem.

The participants' views were grouped under each agency:

According to *the government institutions,* the South African biotechnology industry is conservative and needs greater risk tolerance. Additionally, the ecosystem should be more amendable and facilitate policy changes to relax taxation and align macro policy to implement change in the industry, moving away from heavy reliance on imports to local R&D and manufacturing. To achieve this, the government needs to eradicate corruption, cut ties with old unsustainable networks and change the landscape to be less politicised.

Moreover, participants argued that South Africa has excellent researchers in terms of publications and international collaborations but that the country also needs to invest more in younger talent and not only a few well-published project leaders.

Biotechnology is a long-term and expensive investment, especially phase 3 clinical trials. The country needs strong industry partners such as corporates to co-invest and develop the industry.
SA scientists were at the forefront of COVID identification, but the coordinated effort to capitalise on it was lacking. Opportunities exist, the scientific and technical skills are there, but not the skills to scale-up and commercialise products. To scale-up is a clear challenge, especially for large-scale trials and developing core skills in manufacturing and the production of scaled products and services. Participants felt that the latter should be a priority for the country.

According to *the Technology Transfer Offices,* South Africa lacks a strong local pharmaceutical manufacturing sector compared to other countries of similar socio and economic profile. There is no single publicly listed biotech firm in SA, which limits start-ups to aim for IPOs as an exit strategy and can easily deter prospective investors in this sector. Moreover, the ecosystem is decentralised and fragmented, and there is no single organisation to coordinate the sector, the people or the sector's activities.

The Technology Transfer Offices proposed the concentration of biotech companies in geographical areas to form biotech hubs or clusters with leading universities, research institutes, hospitals, and private companies to stimulate collaborative research and innovation. This will enhance the ecosystem and facilitate partnerships between government, academia, hospitals, and the private sector.

The participants have the opinion that South African biotechnology sector has enormous potential but needs more investment.

The Biotech Firms agree that the ecosystem is small and lags behind other developing countries but has great potential. In their opinion, the Western Cape performed the best on cluster formation, and several exciting biotech start-ups emerged in the last ten years.
In their opinion, it might be too late for the SA biotech ecosystem in the current pandemic, but efforts should be made to ensure that the sector is better prepared in the future when another major event happens.

The biotech start-ups have a more negative perception of the biotech ecosystem in South Africa and that there is currently no actual biotech ecosystem in South Africa, which is not conducive to innovation as innovation is not simply a product, but an environment.

The VC sector believes that the biotech sector is promising with some groundbreaking research, but very little of this is translated to commercial products as it is not a very entrepreneurial ecosystem. Although the system is fragmented, there are key elements which could contribute to a strong innovative ecosystem such as quality R&D labs at the universities, a country rich in biodiversity, disease profiles and a commitment from the Department of Science & Innovation. The key missing component is a commitment from the SA Government Treasury and Department of Trade, Industry and Competition to fully support the industry from a government perspective such as guaranteed off-take and long term contracts). There is also a significant lack of funding and other support through all phases from Seed onwards to almost no finance going into the sector to enable commersialisation of the products.

Globally, biotech has also thrived in an already established pharma sector, yet South Africa only has generics companies.

The other stakeholders confirm the previous opinion that the biotech sector is underdeveloped and fractured and does not have sufficient critical capacity/mass to compete at a global level.
However, it is still young with a lot of opportunities. Unfortunately, the ecosystem is not yet nearly connected or collaborative enough. These participants believed that there are some excellent ecosystem enablers, like BioCiTi, Launchlab, the CPGR, and university technology transfer offices, but that these enablers needed to work together more closely.

4.2. Views on biotechnology prospects

Governments worldwide are increasingly concerned about creating and developing knowledge and technology-focused businesses including IT, health and medical care, biotechnology, nanotechnology etc., which is seen as a key source of economic growth. Since biotechnology is regarded as a global source of possible development, respondents were asked about their thoughts on South Africa's biotechnology prospects.

According to the participants, South Africa is still far behind compared to other countries in biotechnology. Even though it was agreed that the potential exists with strong scientific activities and rich biodiversity, but funding/support is necessary to upgrade research facilities and to bring new technologies to the market.

The Government Institutions are confident in South African scientists' ability to produce quality scientific papers, services, and products, but believe that the ability to take products to the global market is lacking, partially due to SA not being a patent examining country and therefore losing out on opportunities. It believes that the IP law firms should step up and protect local intellectual property. It also mentioned that the world is moving towards the biotechnology age with the global biotech market steadily maturing alongside the information age with biotech data-driven technologies and precision medicine, but the SA biotech sector is not keeping up with global trends.

The Technology Transfer Offices are more optimistic regarding SA biotech prospect globally due to SA being one of the most biodiverse countries in the world. It can create substantial markets for new high-value products based on local flora and the untapped indigenous knowledge systems.
In addition, African people are the most genetically varied with unique genetic variants bringing huge opportunities for precision medicine and personalised medicine solutions for unmet medical needs. The tech transfer office representatives believe that South Africa can compete globally on technology and science, but funding is needed to upgrade research facilities, bring new technologies to the market and to increase the pace and scale to compete internationally.

Generally, the TTOs argue that South African R&D is held back by the lack of capable and able staff within the Department of Science and Innovation and the narrow perspective of the latter. It is further mentioned that the DSI platform managers use subjective criteria to assist people within their network, and only projects with direct links to platform managers or previously supported projects are funded. The support of the entire value chain is also lacking.

According to *the Biotech Firms,* some of the sectors in the SA Biotech Industry, such as agri-bio, have excellent prospects as per the example of the R900m European investment in Cape Bio Pharms recently, but the pharma and medical sectors are not performing that well.

The Biotech start-ups are less optimistic about the global prospects for SA biotech. In their opinion, without massive investment in the billions of rands, it has little hope of succeeding. In the few instances where local biotech competed successfully in the global market, the lack of support forced it to inevitably export the IP.

The VC firms are of the opinion that SA has a strong research base with a lot of potential, but the industry is weak and needs to create a more entrepreneurial culture. The COVID pandemic may turn this around and overcome the stigma of being 'from Africa', therefore not a good investment.

The Other stakeholders confirmed that the sector holds loads of promise, especially in niche areas with a competitive advantage. The participants reiterated that focusing on global collaboration for skills transfer and access to networks is vital for the younger, intelligent professionals keen on building businesses**.** Unfortunately, the government was identified as one of the factors compromising venture formation and development by not offering to procure at sustainable prices, forcing the biotech business to global markets and local markets losing out.

4.3. The major characteristics and challenges relevant to the biotechnology venture capital industry

Private VC investors have shown little interest in financing biotechnology in developing countries.

Furthermore, South African policymakers decided to change focus by moving from a regional biotech (i.e. Cape Biotech) model to national biotech (TIA) model. Given these two developments, limited funding and other political considerations, the TIA moved its focus to invest only in 'low hanging fruits' or in companies close to commercialization of their products. Some perceived it as a poor policy decision since, when it comes to investing in biotechnology companies, one should consider that growing the industry is dependent on investment in early-stage developments, as many companies cannot pass the "Death Valley" because of the lack of funding.

Interestingly, the respondents from the different areas of the biotech sector had similar views regarding the characteristics and challenges of the South African biotechnology venture capital industry, which can be summarized as follows:

1. The sector is small relative to any global peer comparison and can be considered t in its infancy stage. The small and young sector creates a gap in funding for applied research and concept development.
2. The VC sector in South Africa is risk-averse and long-term investments with young, untested firms are considered unattractive.
3. The background of VCs is not biotech-related. PE and VC do not have biotech experts consulting in their teams and therefore have a low appetite for biotech. Moreover, the VCs generally do not hold a long-term investment view, an essential aspect for the biotech industry.
4. Government agencies are the primary source of early funding. Given the small pool of government capital available, this is an apparent concern, especially given the government's focus on funding ready to commercialize products.
5. There are insufficient funds available for early-stage development and seed funding.
6. The absence of a centralized coordinating body that can run eco-system enabling programmes is hampering the development of the sector.
7. More needs to be done to establish effective networks where companies and people can learn in de-centralised networks.
8. If sufficient investment is made, biotech firms will be in a better position to obtain international investors for follow-on funding with a long investment period.
9. Generally, there is very little foreign funding in the South African biotech sector.

4.4. The reasons South Africa stayed behind in the global competition to develop a Covid-19 vaccine

Overall, participants felt that, there hasn't been enough research in this area due to a lack of investment in facilities, biotech firms, and skills development of young scientists. One participant beautifully summarized the problem as follows; "*The funding purse has been rather limited, but the system has seriously lacked supporting basic research ideas, and this comes to the fact that we still have the same old scientists being supported yearly and the number of new scientists supported are limited. In fact, funding for research and positions for young scientists in the scientific biotech space has dwindled. The job scope is low and this impacts all round. The number of vaccine/biological manufacturing companies is also almost non-existent and it's because we want to assume support of a single player and in doing this we are never going to make headway in all vaccine development formats and we are*

not creating a competitive environment. Biovac is a great company who can manufacture conjugate vaccines. They have no expertise in other vaccine technology. Supporting other players in developing or manufacturing, other vaccines may lead to healthy development of the industry but blocking players from entering the vaccine space is shortsighted. Therefore, the issues in the South African innovation system is endemic to all these underlying issues. We also seem to have a NSI that is hinged on the network and it makes one wonder -how open is the system to finding new gems and awarding opportunity to young enthusiastic graduates who will drive their ideas with passion? So I come back to the point that we need to ensure we fund in a holistic manner the people and the idea! Not farm other people's ideas by trying to create one giant – we will not meet with any success. In fact, we kill ideas before we can see the potential. Besides this, we not working with pharma companies in a strategic way to build the industry. We should be more open to big business as we don't have enough money to fund across the value chain due to limited funds, we don't have core skills developed in the manufacturing and vaccine development field. The connotations of being bias and collusion with business is stifling as it's a chicken and egg situation: you need to form a strong tie with perhaps a single industry partner to grow the space. The South African market is too small for it to create sustainable startups we need product sales in outside markets to become more sustainable so look at small economies like in the EU how they have developed or Singapore is a very good example. We need to employ more realistic strategies instead of politicizing everything".

Another participant (a venture capital firm) noted that it would be senseless to invest vast amounts for vaccine development in South Africa as the vaccine would likely not be successful outside of South Africa due to the existing, approved vaccines in the global market. A different participant (a biotech start-up firm) claimed that there is a pre-clinical stage vaccine candidate, but the firm in question is currently fundraising to take it to clinical trials (according to the WHO there are presently none from South Africa, as noted earlier).

Below are the reasons South Africa is lagging behind the rest of the world, as summarized by the participants.

In the opinion of the *Government Institutions*, funding has been one of the limiting factors but also the system has seriously lacked supporting basic innovative research ideas due to the same scientists being supported yearly, and the number of new scientists supported are limited and even dwindling.

In the past 20 years, SA has rather procured than develop its own products. During the apartheid years, with the sanctions, the SA government had to put money in its own resources, resulting in world-class science and technology from the SA scientists. Post-apartheid, however, the government has deemed procurement from other countries easier than investment in its own innovations.

The Technology Transfer Offices agreed with the government institutions that not enough has been done in this sector. South African has stayed behind in the vaccine race due to the speed of development, access to research funds, stage of readiness of local vaccine manufacturers and getting new pharmaceutical products registered for use in SA.

The Biotech Firms agree with the previous opinions that South Africa spends comparatively little on R&D. Even though South Africa has a dedicated vaccine manufacturer, it was not ready to develop and manufacture vaccines when needed. Early difficulties, a change in focus to packaging imported vaccines, manufacturing vaccines through tech transfer agreements, and limited capacity, were cited as some of the reasons.

The lack of communication on many levels between government, universities, and VCs contributed to the sector falling behind in the race towards vaccine development.

The biotech start-ups believe that the lack of vaccine development is reflective of the complete reliance most African countries have on foreign aid to fund their research activities over the past few decades. South Africa has stayed behind because there has been no significant investment into the biotech sector by the government or the local private sector for decades.

The VC firms agreed that too little early-stage investment was made previously in vaccine development, and it is still the case. It also echoed the previous opinions of Africa as relying almost entirely on hand-outs. The Biovac vaccine manufacturer (a Public-Private Partnership investment) has been talking for years about building vaccine development capacity, but a lack of sufficient long-term capital inputs to develop those capabilities were not made.

The Other stakeholders confirmed previous opinions that the SA government didn't invest effectively in the past, and the investments made (e.g. Biovac) are hampered by political interference. Other reasons cited are that the regulatory environment (SAPHRA) has been ineffective and that the government has been slow to act on the vaccine research strategy.

It was also mentioned that the research has very little commercialization activity, and university-private company partnerships are seldom found.

4.5. Funding Issues and challenges identified during the pandemic in South Africa

All participants agreed that funding the biotechnology sector is critical, now more than ever, whether it is because of Covid-19 or not. Below we summarized the participants' opinions about supporting the biotechnology industry.

In the opinion of the *Government Institutions,* SA should learn from the COVID pandemic. Investment in discovery, POC, and scale-up is required. Biotech companies in US and UK receive investment and funding and therefore produce vaccines, and its citizens receive preference for access to vaccinations. South Africa needs to invest in people with ideas instead of just ideas and fully support them across the commercialization value chain. The level of investment is also a factor to ensure success.

The other aspect of funding that must be considered is the supporting regulatory framework and incorporation of new local innovation into the procurement policies and economic policies of governments to support local products in the marketplace, with fewer tenders awarded to imported products.

Government funding is limited, and the South African Transformation policy inhibits access to financing for many innovators. The spreading of funds available should be on merit-based criteria to develop ideas that will give SA real economic return. Many ideas were conceptualized in SA, but due to lack of funding and support, the innovations were taken abroad and have become global successes e.g. Quantum DX[9] - resulting in a missed opportunity for South Africa.

[9] Quantum Dx is a medical technology firm dedicated to providing cutting-edge, high-quality molecular diagnostic solutions to customers all over the world (www.quantumdx.com, accessed on 20/11/2021). Quantum Dx was founded in Sussex in 2008 and spent some of its early years in South Africa, but it relocated to Newcastle in 2011 after being drawn to the Centre for Life's life sciences facilities (https://www.business-live.co.uk, accessed on 20/11/2021).

The Technology Transfer Offices have a positive view on the potential of the South African Biotech sector to address the triple challenge of SA, particularly in the fields of health (both human and animal), agriculture, food, and the broader industrial biotech category. Moreover, in times of a pandemic like now, the latest advances in biotech could be key in developing a whole range of novel therapeutics, but it is critical to building a robust funding platform for a functioning biotech industry to develop it further towards the market.

The Biotech Firms reiterated that even though biotechnology has been recognized as critical to SA to move to a more high-tech economy, and because the biotech industry is generally high profit and has the potential to create many jobs and stimulate investment, the availability of Covid-19 vaccines has highlighted the need for South Africa to be more self-sufficient too, and the need to put sufficient resources into the management of challenges experienced by the developing world.

The Biotech Start-Ups highlighted that more funding is vital, not just in relation to COVID, but also with generic molecules, cancer molecules and biosimilars, since licensing and clinical trials are extremely expensive.

The VC Firms agreed that it is a very opportune time to invest more in biotech, not just because of Covid-19. Biotech has recently developed the ability to positively affect so many people worldwide in industries including food, health, and industry.

South Africa also needs to be diagnostic, therapeutic, and vaccine secure, but the industry needs funding and development. In addition, the government needs to take more early-stage risks to allow private capital to follow these investments. Without the will and real impetus from the government departments, it will be a futile battle.

The Other stakeholders confirmed that government funding is declining, healthcare needs are increasing, and the country is at risk of falling far behind a fast-developing space.

A pandemic such as the Covid-19 pandemic created challenges on many levels. Below are the challenges participants identified in South Africa:

1. The biggest issue was the lack of communication between different role players - not everyone was aware of the funding support and who to contact in the scientific health biotech space which led to missed opportunities. The sector needs to align and create a unified network similar to the knowledge network created by the UK government who had similar issues.
2. Africa is not necessarily poor, but funds management is a problem due to corruption.
3. The focus was on the procurement of vaccines and minimal amounts allocated for the local development of vaccines. Procurement was easier than investment. It will cost South Africa in the future – not only to pay back the loans, but also the development that did not occur in comparison to other countries who focused their funding on development.
4. The challenges with getting pharmaceutical products registered in SA need to be addressed.
5. Research support infrastructure is a challenge, for example, why the National Research Foundation could not coordinate the funding of research for Covid-19 related solutions and innovation in the time that was required.

6. The other challenge encountered was the reaction time to the pandemic. The SA Technology Innovation Agency was slow to react, and when the scope of their call for applications was agreed upon, it was practically too late, and the turnaround time for feedback was also delayed.
7. The call for proposals from some funding agencies was haphazard and lacked a targeted approach. It included essential oils development for sanitizing applications; a call for partnership with Egyptian entities focusing on Covid-19 solutions, and call on AI & Health related to the pandemic. The abruptness of these calls made it very difficult to participate; secondly, these calls assumed that the technology areas that universities already have projects ready, are at the required Technology Readiness Levels (TRL).
8. The biotech sector should develop a targeted approach by using the investors' assessment tools to prepare for investment. The process should include a sit down with the top five healthcare firms– Discovery, NIH, Medscheme, Netcare, Life & MediClinic and secure the market upfront before development.
9. Government labs were out of operation for months during the pandemic, and researchers/scientists could not access labs even though they had equipment and resources needed at the time to develop Covid-19 related products for diagnostics and treatment. This caused delays of over four months which indicates an evident lack of good leadership in public biotech-related organisations.
10. The vast majority of senior managers at public biotech-related entities need to be replaced by more competent people.
11. Private investors require good (non-academic) scientific support and a platform by which scientific initiatives are screened. i.e. non-scientific financial persons who want to invest have no credible board of advisors who can help them differentiate between credible, non-credible and unicorn-type projects in the biotech sector. There is no system or support to translate bioscience into commerce. The IP laws are archaic which makes the situation even more difficult.
12. Recently many challenges have shown that SA needs to improve on the production of its commodities, diagnostics and vaccines. This will require a partnership between the government, donors, and the private sector.
13. There were significant cuts in funding to incubation programs and funding to early-stage businesses through the government entities such as TIA etc. The industry needs more funding flowing to seed funding through the TIA seed fund program but administered through implementing partners to ensure quick turnaround and effective incubation support.
14. There has been a lack of coordinated action by the government in this pandemic. The insistence implement testing and vaccination isn't reflected by the capacity in the public sector. The antagonistic relation between state and private sector will hamper and even unravel biotech development, including developing a more effective health care system.
15. South Africans are not good innovators in the biotech space. The research has very little commercialization activity. There is also lack of university and private company

partnerships, due to the universities not organized enough, or too greedy to give upside to a private partner, it will instead let research stop before being developed/commercialized by an external partner.

5. Conclusions and Policy Recommendations

South African policymakers see new growth areas, specifically knowledge-based industries like ICT, biotechnology, and nanotechnology, as essential means of contributing to the achievements as part of broader policy measures targeted at enhancing economic growth and creating jobs.

As a result, this study fills a critical gap by assessing key players' inputs on the South African biotechnology ecosystem and prospects globally, and the significant characteristics and challenges relevant to the biotechnology venture capital industry, as well as the reasons why South Africa has lagged in global competition of Covid-19 vaccine development, and challenges identified during the pandemic in South Africa. Secondly, it gives policymakers a clear picture of the necessity of funding the biotechnology sector, particularly during the Covid-19 period, as recognized by biotechnology's important actors.

The study's goal was to examine the role of venture capital (VC) in South African biotech finance and demonstrate how it may better prepare the healthcare system for future pandemics. We constructed the following results and policy recommendations based on the literature and data collected through surveys and interviews with government agencies, higher education institutions, biotechnology venture capital firms, biotech firms, biotech startups, public and private biotech incubators, and non-profit companies.

Overall, participants believe that South Africa's biotechnology is still lagging behind that of other developing countries but that it has the potential to grow significantly through enablers such as R&D universities, research institutions and hospitals, incubators, CPGR, and tech transfer offices. However, because of a lack of finance (specifically seed funding) and the lack of a committed organization to organize activities, it is also considered underdeveloped, fragmented, and fractured. In terms of the key characteristics associated with biotechnology venture capital investment, all participants agreed that there is no viable early-stage finance available for biotechnology firms in South Africa and that they prefer mature investments. Furthermore, respondents identified that the South African biotechnology venture capital industry is in its infancy stage, risk-averse, conservative in its investment power within this space, and the VCs' backgrounds are not biotech-related.

Participants agree that weak basic research concepts and inadequate investment in this sector, particularly early-stage investments, are possible reasons why South Africa would not develop Covid-19 vaccine in time. In addition, the reaction time to the pandemic, coordination of funding for Covid-19 research, lack of communications between the agencies, many labs out of service due to the full-lock downs, are further challenges identified.

Policymakers and other key actors, agencies, and institutions should evaluate a variety of concerns raised by the literature and this research, with the inputs of the participants, listed below while deciding how to move forward with the biotechnology sector's development:

1. Creating a meritocratic, fair, and unbiased method to funding would improve this field.
2. Create momentum and interest in the space, and attract more young people.

3. Because South Africa is dependent on imports in this industry, the government needs to relieve taxation on raw biotech industry materials and other substances. South Africa also needs a tiered plan to expand the industry with SA-made products and services first.
4. There is a lack of a strong biotechnology VC tradition in South Africa, compared to global VC funds, which generally invest in the early-stage start-ups with high growth prospects, whereas, in SA, VC funds typically invest in late-stage products and management teams with commercial experience.
5. There is a significant opportunity to invest in infrastructure, systematic testing and surveillance, additional research, investment attraction, and other areas, which will necessitate a strong inward-oriented investment pull, which will need to be backed up by creating a supportive ecosystem.

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