**PROJECT NARRATIVE**

The biggest challenge to fighting COVID-19 pandemic is the lack of a specific anti-SARS-CoV-2 drug that targets all the variants, has lesser side effects, high efficacy and reduced costs. Ayass Bioscience is developing novel AYA2012004_L aptamer that targets SARS-CoV-2 trimer S protein, offering a promising treatment strategy against current and emerging SARS-CoV-2 strains due to its versatility with broad reactivity across variants, ease of self-administration via inhalation, high stability and efficacy, low costs and high scalability given its ease of chemical synthesis, and lack of toxicity and immunogenicity.

## COMMERCIALIZATION PLAN

### Executive Summary

**Product description:** AYA2012004_L is a single-stranded DNA (ssDNA) aptamer used for the treatment against current and emerging SARS-CoV-2 strains in COVID-19. AYA2012004_L will be self-administered via inhalation route through handheld nebulizers.

**Value Proposition:** AYA2012004_L aptamer will offer a promising treatment strategy against current and emerging SARS-CoV-2 strains due to its versatility with broad reactivity across variants, self-administration via inhalation, high stability, low costs and high scalability given its ease of chemical synthesis, and lack of toxicity and immunogenicity. This will ultimately reduce the infection severity and hospitalization risks.

**Market size:** The COVID-19 infection market was valued at USD 18.69 billion in 2021 and is expected to reach USD 48.99 billion by 2029, registering a Compound Annual Growth Rate (CAGR) of 12.80% during the forecast period of 2022 to 2029. The global antiviral drugs market is expected to reach the value of USD 107 billion by 2030, with a CAGR of 5.5% during the forecast period[2].

**Users/Customers:** Ayass Biosciences' initial customers will be patients, followed by pharmaceutical companies that are interested in sublicensing AYA2012004_L aptamer, which will be prescribed by doctors. End-users will be patients with COVID-19 who can self-administer it through handheld nebulizers.

**Business Model & Commercialization:** Once systemic AYA2012004_L aptamer demonstrates initial safety and functional improvement in patients, Ayass Bioscience will project an integrated commercial model comprising direct-to-consumer online sales, channel distribution partnerships, and biopharma licensing agreements. Earlier revenues will fund late-stage clinical development activities. Ayass Bioscience will be marketed first in the U.S., followed by Europe and the rest of the higher-volume North American market before exploring additional global expansion opportunities.

**Company:** Ayass Bioscience LLC (the "Company"), a Limited Liability Company, based in Texas, USA was established in 2014. It is a biotechnology firm dedicated to advancing a platform centered around its innovative DNA aptamer technology.

**Key clinical investigators & partnerships secured:** Dr. Mohamad Ammar Ayass MD, a practicing physician specialized in pulmonary and critical care medicine (CEO and PI), Dr. Lina Abi Mosleh PhD, expert in molecular biology with cross-functional leadership skills (VP and Principal Scientist), Dr. Natalya Griko PhD, expert in the development of aptamers (Senior Scientist), Dr. Trivendra Tripathi PhD, expert in designing and validating clinical flow cytometry assays (Scientist), Dr. Victor Pashkov PhD, expert in molecular genetics and genotyping (Research Scientist) and Dr. Jin Zhang, MD, expert in clinical data analysis (Epidemiologist) are key clinical investigators in Ayass Biosciences' team who have successfully designed and validated AYA2012004_L aptamer as an inhaled therapeutic treatment against current and emerging SARS-CoV-2 strains. Ayass Bioscience has secured the interest and engagement of key opinion leaders including Dr. Xuebin Qin, Dr. Massoud Motamed and Dr. Jeremiah Gassensmith. It has also partnered with Texas Biomedical Research Institute, a contract research organization (CRO), for toxicology and efficacy studies in small and large mammals and InspectIR Systems, which is research, development & device company for the development of inhalation device for AYA2012004_L aptamer.

**Projected sales volume:** Assuming 1% treatment penetration targeting 25% of domestic infections and an average price of $500 per treatment course, we project that AYA2012004_L aptamer could achieve annual revenues of approximately $200M in full-price annual profit across online, pharmacy and royalties.

### A - VALUE OF THE PROJECT, EXPECTED OUTCOMES, AND IMPACT

***Value of the proposed project***

Coronavirus Disease 2019 (COVID-19) pandemic is a global outbreak of infectious Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). As of today, more than 6.98 million deaths have been attributed to COVID-19 worldwide with 1.13 million in the United States of America alone (https://data.who.int/dashboards/covid19/cases?n=c). Along with the mortality burden, the coronavirus outbreak is causing a global economic collapse. The economic toll of the COVID-19 pandemic in the USA is estimated to reach $14 trillion by the end of 2023[3]. Over three years have passed, but SARS-CoV-2 continues to strain healthcare systems due to daily reports of millions of new infections and global casualties[4]. Besides this, the burden of patients having 'Long-COVID-19' (the lingering or protracted illness that patients of COVID-19 continue to experience even in their post-recovery phase) is going to be huge and it is expected to produce another public health crisis on the heels of current pandemic[5]. Manifestations of end-organ damage can

include but are not limited to acute respiratory distress syndrome (ARDS), cardiac injuries (ventricular arrhythmias and hemodynamic instability), thrombotic manifestations, renal, hepatic, and gastrointestinal damage[6,7].

Challenges

**Problem #1:** **Inadequacy and side-effects of existing therapies**. The biggest challenge to fighting COVID-19 is the lack of specific anti-SARS-CoV-2 drugs that target different variants. The common strategy of current COVID-19 treatment is repurposed drugs - "old drug, new use". Most of these used therapeutics show adverse side effects such as cardiotoxic, hepatotoxic, nephrotoxic, and hematologic toxicity consequences[8]. Moreover, the administration of convalescent plasma and other antibody-based drugs through intravenous route is another pitfall that limits the accessibility.

**Problem #2:** **Limited reactivity and efficacy of current treatments.** Current COVID-19 therapies have decreased efficacy against specific variants of SARS-COV-2 due to limited reactivity and in some populations of immunocompromised individuals[9].

**Problem #3:** **The socio-economic burden impacting Quality of Life (QOL) of COVID-19 patients.** Besides having a direct impact on the physical health regardless of the time elapses since discharge or recovery[10], the SARS-CoV-2 poses a threat of great magnitude including mental health[11] and economic burden[12], overall, significantly decreasing the QOL of the patients.

**Ayass Bioscience** is proposing **AYA2012004_L aptamer** that offers a promising treatment strategy against current and emerging SARS-CoV-2 strains due to its versatility with broad reactivity across variants, ease of self-administration via inhalation, high stability and efficacy, low costs and high scalability given its ease of chemical synthesis, and lack of toxicity and immunogenicity. AYA2012004_L aptamer has the capability of preventing infections, curbing disease progression and reducing mortality in SARS-CoV-2 infected cases.

Value propositions

**Value #1:** **AYA2012004_L aptamer offers higher safety profile and ease of administration.** With a fully synthetic production scheme absent of any animal-derived components, the non-immunogenic AYA2012004_L DNA aptamer has exhibited no discernable adverse effects in pharmacokinetic analyses to date, providing a vital safety advantage over previous synthetic antibody modalities relying on shaky molecular scaffolds. Also, the ease of self-administration via inhalation though hand-held nebulizer provides an advantage over the current antibody-based therapies.

**Value #2:** **AYA2012004_L aptamer demonstrates broad coverage of variants.** *In vitro* testing has shown potent neutralization of all major SARS-CoV-2 variants including Delta, Delta plus, Alpha, Lambda, Mu, and Omicron strains, in contrast with substantial susceptibility gaps noted for authorized monoclonal antibodies. The DNA aptamer binds a highly conserved region of the spike protein to curb escape potential.

**Value #3:** **AYA2012004_L aptamer reduced burdens on society and increase QOL.** The stability, efficacy and ease of self-administration of AYA2012004_L aptamer aims to avoid undertreatment in minority and socially disadvantaged groups consistently demonstrating worse COVID outcomes. Enhanced practicality and lowered complexity promise to curb disparities by extending access to vulnerable communities repeatedly denied sophisticated biologic interventions reliant upon infusion networks absent in underserved neighborhoods. Also, *in vivo* cell culture experiments showed that AYA2012004_L aptamer produced a 95% decrease in viral infection rates. Furthermore, animal models document near full protection from lung viral infection and weight loss endpoints that serve as correlates for reduced infection severity and hospitalization risk.

## ***Impact of the project***

COVID-19 is a highly contagious infectious viral disease caused by SARS-CoV-2, which rapidly escalated to a global pandemic that led to a dramatic loss of human life worldwide. As of today, more than 6.98 million deaths have been attributed to COVID-19 worldwide with 1.13 million in the USA alone (https://covid19.who.int/). In addition to its devastating morbidity toll, COVID-19 also lead to significant financial costs for people needing treatment and for public and private payers. COVID-19 related hospital costs per adult hospitalization varied from $8,400 in a general ward to more than $50,000 in an intensive

care unit with a ventilator[13,14]. COVID-19 associated hospitalization continues to predominantly affect adults aged ≥65 years and represent a continued public health threat[15] (Fig. 1). Over three years have passed, but the daily reports of millions of new infections and global casualties and the lasting symptom burden of patients having 'Long-COVID-19' manifesting end-organ damage continue to strain healthcare systems[5]. Adding to that, COVID-19 still remains a paramount public concern presenting unprecedented challenge to every aspect of our livelihoods including health, environment, food systems, psychology, global socio-economy, education and what not, ultimately drastically reducing the QOL[16,17]. Along with this burden, the coronavirus outbreak is causing a global economic collapse which is estimated to reach $14 trillion by the end of 2023 for USA alone[3].

The current therapeutic treatments for COVID-19 listed in the National Institutes of Health (NIH) guidelines, are limited and are basically repurposed drugs such as RNA-dependent RNA polymerase inhibitors (e.g., Remdesivir, Favipiravir, Ribavirin and interferons), protease inhibitors (e.g., Lopinavir and Ritonavir), hydroxychloroquine, azithromycin, monoclonal antibody, or convalescent plasma[1]. Among these, Remdesivir and Paxlovid are the only FDA-approved drugs, and other treatments, such as, Molnupiravir, convalescent plasma, and monoclonal antibodies, are expensive and scarce. Intravenous administration requirements further limit their accessibility[18]. Therefore, with individuals still at risk and patients relying on supportive and nonspecific therapies, there is an unmet and urgent need for rapid, cost-effective, and equitable therapeutics with broad reactivity with the capability of preventing infections, curbing disease progression, reducing mortality, and ensuring accessibility across diverse regions[18]. Moreover, complicating matters including natural mutations of SARS-CoV-2 have spawned variants like Omicron, known for heightened transmissibility and resistance to existing treatments[19], necessitates innovative solutions.

Aligned with this need, Ayass Bioscience has developed novel aptamer technology for COVID-19 treatment. Aptamers have recently emerged as promising tools for targeted treatment of COVID-19 infection, particularly in the face of variant challenges[20,21]. Aptamers are short single-stranded (ss) oligonucleotides that consist of either RNA or DNA that have high specificity and affinity to their target molecules. They are generated by an artificial method known as Systematic Evolution of Ligands by Exponential Enrichment (SELEX). These nucleic acid-based modalities, known for their small size, stability, low immunogenicity, programmability, and versatility, hold potential for diagnosis, prophylaxis, and treatment[20–22].Our laboratory has developed a series of ssDNA aptamers specifically targeting the trimeric S proteins of the Wuhan original strain of SARS-CoV-2. These aptamers underwent a comprehensive evaluation to assess their efficacy and potential as therapeutic agents against COVID-19[23,24]. The most potent aptamer AYA2012004_L exhibits a remarkable ability not only to bind to the trimeric S protein of the Wuhan original strain but also to bind to multiple variants of trimeric S proteins, including Delta, Delta plus, Alpha, Lambda, Mu, and Omicron. Therefore, AYA2012004_L aptamer is a promising treatment strategy against current and emerging SARS-CoV-2 strains due to its versatility with broad reactivity across variants, self-administration via inhalation, high stability and efficacy, low costs and high scalability given its ease of chemical synthesis, and lack of toxicity and immunogenicity. The widespread acceptance of the AYA2012004_L aptamer in the market has the potential to mitigate the challenges presented by the prevalence of COVID-19. This could result in significant cost savings for the U.S. healthcare system by reducing the strain on hospitals. Additionally, it could contribute to maintaining good health, fostering a pleasant environment, ensuring uninterrupted education and job security, promoting a favorable socio-economic balance, and ultimately improving the overall QOL for patients.

## B - COMPANY OVERVIEW

***Company history and corporate objectives.***

Ayass Bioscience LLC (the "Company"), a Limited Liability Company, based in Texas, USA was established in 2014. It is a biotechnology firm dedicated to advancing a platform centered around its innovative DNA aptamer technology. As a pre-clinical-stage biopharmaceutical company, it envisions a broad range of applications for its innovative technology and aims to fulfill the vast therapeutic and diagnostic promise that antibodies have long aspired yet failed to actualize for the majority of patients in need. The company's initial focus on clinical validations in coagulation has expanded to encompass urgent and high-value therapy areas, including but not limited to COVID-19 and cancer immunotherapy. By enabling more affordable precision diagnostics and treatments, Ayass' pioneering technology platform and supporting capabilities seek to dramatically lower the average cost of healthcare by accelerating access to safer and more effective medicine. Ayass Bioscience is founded by Dr. Mohamad Ammar Ayass, a practicing physician specialized in pulmonary and critical care medicine. The company plans


**Fig. 2.** Company Logo

to raise funds to advance their aptamers into Phase I/II clinical trials starting with COVID-19 as the primary indication.

*Strategy and Vision*: Ayass Bioscience is dedicated to the development of AYA2012004_L aptamer as a novel therapy for COVID-19 infection. The proposed Project is expected to provide the necessary funding ($2.35M) to complete all of the pre-clinical and IND-enabling studies required to support clinical trials on AYA2012004_L aptamer. Once our aptamer has shown pre-clinical safety and efficacy and Ayass Bioscience is approaching IND filing (Q2 2027) for AYA2012004_L aptamer, we expect that Ayass Bioscience will be able to raise a significant institutional venture capital round to conduct a Phase I/II clinical trials. Because full commercialization will require at least $100-150M funding, Ayass Bioscience's strategy is to build a strong pipeline of therapy approaches through Phase II efficacy testing and then to partner with pharma companies to generate a continuous revenue stream in the form of milestone payments as well as royalty payments on sales.

***Company team***

Ayass Bioscience has an interdisciplinary management team of professional scientists and business experts with a strong track record for technology development in life sciences and healthcare.

**Management, Leadership and Scientific Team**

- ***Mohamad Ammar Ayass M.D., Founder and CEO.*** Dr. Ayass is a practicing physician specialized in pulmonary and critical care medicine and researcher with over 30 years of pulmonary, immunology thrombosis and molecular research experience. He received his medical doctor degree at Damascus University College of Medicine, then completed his post-doc training at the University of Michigan and University of Tennessee. He completed his board certification in internal medicine and pulmonary disease and opened his own pulmonary clinic in west Texas and the DFW area. He is the founder of Ayass Lung Clinic, PLLC, Ayass Laboratory, LLC, and Ayass Bioscience, LLC, Aptamer Diagnostic, LLC, Ayass Research Institute, LLC and Apsilon Financial Services, LLC. *Dr. Ayass is responsible for Ayass Bioscience's R&D as well as business development and financial operations.*
- ***Lina Abi Mosleh Ph.D., Principal Scientist and Vice President.*** Dr. Abi Mosleh is an accomplished research scientist and leader with over 10 years of experience spearheading innovative scientific programs and discoveries that improve patient outcomes. She combines her expertise in molecular biology with cross-functional leadership skills to build high performing research teams focused on transformative science and personalized medicine. She is very well equipped to lead research initiatives in an executive role that directly advance patient care and health. She received her Ph.D. in Molecular Genetics and Biochemistry at the University of Texas Southwestern Medical Center at Dallas in the laboratory of Nobel laureates Drs. Michael S. Brown and Joseph L Goldstein. *Dr. Abi Mosleh is responsible for Ayass Bioscience's R&D in addition to overseeing, managing, and leading daily operations of both the clinical and research aspects of the project.*
- ***Natalya Griko Ph.D., Senior Scientist.*** Dr. Griko is the Senior Scientist at Ayass Bioscience from the past 8 years where she is responsible to oversee and manage high-complexity genetic testing and lead numerous research projects. She has more than 24 years of experience in protein chemistry, molecular biology, microbiology, functional and structural biology in both academia and biotech industry settings. She earned her Ph.D. in Molecular Biology at the Institute of Protein Research in the scientific center of the Russian Academy of Sciences near Moscow. *Dr. Griko will be responsible for designing and developing the scientific strategy of this project.*
- ***Trivendra Tripathi Ph.D., Scientist.*** Dr. Tripathi has expertise in designing and validating clinical flow cytometry assays for immunophenotyping in leukemia and lymphoma, profiling and subsetting cells such as lymphocytes (T cells and B cells), stem cells, myeloid cells, macrophage and monocyte subpopulations, intracellular staining, and rare cell detection. He is part of the R&D team at Ayass Bioscience and is involved in developing *in vitro* diagnosis and targeting therapies for many diseases. He is also responsible for designing an immune profile flow cytometry panel for COVID-19 patients and correlating the findings to mass spectrometry. He earned his Ph.D. degree in Biochemistry at Aligarh Muslim University, India. *Dr. Tripathi will be responsible for supervising, conducting and analyzing the immunology aspect of the project.*
- ***Jin Zhang, M.D., Epidemiologist.*** Dr. Zhang has more than 10 years of public health/research experience (chronic and infectious diseases). She has great expertise in experimental design, planning, data analysis, modeling and projections, bioanalytical parameter determinations, and validation of various assays and clinical sample bioanalysis. She received her M.D. degree from the School of Medicine, China Three Gorges University, China. She earned her Master's degree in Pharmacology and Toxicology from the University of Mississippi Medical Center and MPH degree in Epidemiology and Biostatistics from the School of Public Health, Jackson State University, USA. *Dr. Zhang will be responsible for statistical analysis, risk assessment and all ethical considerations related to this project.*

- ***Victor Pashkov Ph.D., Research Scientist.*** Dr. Pashkov is a Research Scientist at Ayass Bioscience with the responsibility to conduct high-complexity genetic testing and participate in research projects. He has multiple years of experience as a biomedical research scientist with expertise in molecular biology, molecular genetics, and genotyping. He is involved in the design, development, and validation of high-complexity genetic testing. He demonstrates advanced skills in biological and biotechnological systems through the optimization of several protocols for DNA and RNA extraction, PCR, genotyping by mass-spectrometry, and data analysis. He earned his Ph.D. in Biochemistry at Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, of the Russian Academy of Sciences. *Dr. Pashkov will be responsible for experimental design, execution and analysis of the experiments for this project.*

**Key Advisors**

- ***Massoud Motamed, Ph.D.*** Dr. Motamed hold the position of Vice President of Quality at Nanoscope Therapeutics. His most recent role was as a CMC reviewer for the Gene Therapy Branch at the Center for Biologics Evaluation and Research (CBER), a division of the US Food and Drug Administration (FDA) responsible for regulating biological products for human use under applicable federal Jaws. He is honored to have received several awards, including the FDA's Outstanding Service Award from the Office of Regulatory Affairs.
- ***Jeremiah Gassensmith, Ph.D.*** Dr. Gassensmith is an Associate Professor – Chemistry & Biochemistry at The University of Texas, Dallas with appointments in Imaging at the UT Southwestern Medical center. He is an Elected Fellow at the Royal Society of Chemistry (FRSC). His research focuses on the intersection of organic and solid-state chemistry with biomaterials, particularly engineered virus-like particles.
- ***Xuebin Qin MD, Ph.D.*** Dr. Qin is a Professor of Medicine at Tulane University, and his research primarily centers on defining the role of innate immunity, including the complement system and monocyte activation, in the pathogenesis of various human diseases. These include HIV infection, HIV-associated cardiovascular diseases, SARS-COV-2 infection and long COVID-19.

**Other resources**

- ***Texas Biomedical Research Institute (Texas Biomed)****.* It is an independent, nonprofit biomedical research institution established in 1941 with a focus on protecting global health. Headquartered in San Antonio and originally founded as the Southwest Foundation for Research and Education, Texas Biomed specializes in infectious disease and immunology research with an emphasis on developing diagnostics, vaccines, and therapeutics. Key focus areas include virology, microbiology, genetics, physiology, and primatology leveraging specialization in nonhuman primate models. Notable contributions include helping establish the national primate research center network, developing screening programs that make blood transfusions safer, improving assisted reproductive technologies in humans and endangered species, and advancing knowledge to fight viral threats like COVID-19 through partnerships and internal assets like a BSL4 lab for maximum containment research. *Texas Biomed will be performing animal studies for this project.*
- ***InspectIR Systems****.* InspectIR Systems, founded in 2015, is a research, development & device company dedicated to community wellness and health. They are the creators of the first breathalyzer to receive any level of FDA authorization. The team has pioneered the combined use of machine learning and mass spectroscopy to deliver cutting-edge analytical and laboratory solutions at the point-of-need for multiple industries delivering breath and environmental analysis, VOC detection, and chemical identification. They have worked closely with the Ayass Bioscience's team during the pandemic to sequence COVID samples and identify variants of concern as part of determining the sensitivity of our developed breathalyzer. *InspectIR Systems will be combining their capabilities and infrastructure with us to significantly bolster collective success of AYA2012004_L aptamer.*

## C - MARKET, CUSTOMER AND COMPETITION

### *Market*

The COVID-19 infection market was valued at USD 18.69 billion in 2021 and is expected to reach USD 48.99 billion by 2029, registering CAGR of 12.80% during the forecast period of 2022 to 2029. The global antiviral drugs market is expected to reach the value of USD 107,700.57 million by 2030, with a CAGR of 5.5% during the forecast period[2]. Ayass Bioscience is planning to market AYA2012004_L aptamer globally, starting with the U.S. that represents the largest market.

The COVID-19 therapeutics market includes NIH recommended small-molecule antivirals [Ritonavir-Boosted Nirmatrelvir (Paxlovid), Remdesivir and Molnupiravir], convalescent plasma and Interferons (IFN Beta and PEG-IFN Lambda) and monoclonal antibodies. COVID-19 solutions have comprised the fastest growth subsector since 2020. The rapid growth of the market is fueled by a strong pipeline of therapeutics under development as well as the pressing need for an effective therapeutic agent due to emerging new variants.

The COVID-19 therapeutic landscape still represents immense short-term revenue potential despite widespread vaccination, with 65K new U.S. cases daily, ongoing healthcare system burden, millions of elderly and immune-compromised individuals facing severe early infection, plus millions more aggressively seeking interventions thwarting recurrence and emerging SARS-CoV-2 genetic derivatives demonstrating resistance against authorized neutralizing antibody formulations.

Total addressable market (TAM) & Service available market (SAM). The current average positive COVID-19 cases in the USA are approximately 65K. At this number, then at a direct-to-consumer price of $500 per treatment course per patient, the incident market for AYA2012004_L aptamer will approximately be $5.93B. If one assumes that 1% of the infected population may be treated with Ayass Bioscience's AYA2012004_L aptamer, then the potential prevalent market opportunity is approximately $59M.

***Competitors***

The competitive landscape for Ayass Bioscience's aptamer for COVID-19 therapy is shown in Fig. 3. There is no existing inhaled therapeutic treatment for COVID-19 with the capacity to neutralize the current and emerging variants of SARS-CoV-2, so AYA2012004_L aptamer has no direct competitor in terms of ease of self-administration and accessibility. A few monoclonal antibody therapies developed or investigated for treating COVID-19 can be considered as direct competitors. These bind directly to the S protein and block the S protein's ability to bind to the host receptor (ACE2) and inhibit the virus' ability to infect host cells. However, the monoclonal antibodies including casirivimab + imdevimab, cilgavimab + tixagevimab, bamlanivimab + etesevimab, and sotrovimab were inactive against Omicron variant[25–28].

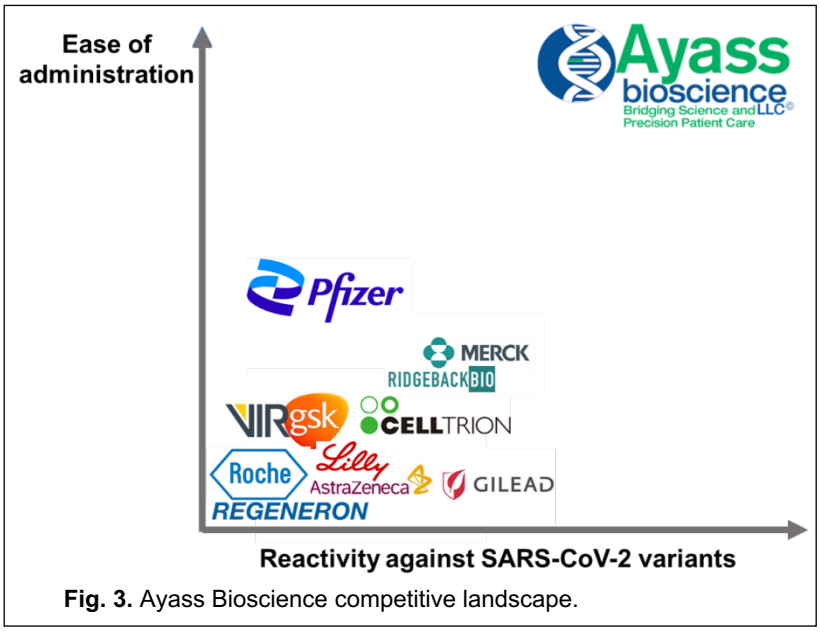


**Fig. 3.** Ayass Bioscience competitive landscape.

a. Direct competitors:

- Casirivimab (REGN10933) and imdevimab (REGN10987) [Ronapreve™; Roche and Regeneron]: A combination "cocktail" of two monoclonal antibodies given via intravenous infusion, bind to the SARS-CoV-2 spike protein, blocking virus attachment and entry into cells[29,30].
- Tixagevimab (AZD8895) and cilgavimab (AZD1061) [Evusheld™; AstraZeneca]: A spike protein directed monoclonal antibody combination that needs to be injected intramuscularly[31]. On January 26, FDA announced that combinations of Casirivimab + imdevimab and Tixagevimab + cilgavimab are not currently authorized for emergency use in the US because these therapeutics are unlikely to be active against more than 90% of the SARS-CoV-2 variants currently circulating in the U.S.[27].
- Bamlanivimab (LY3819253) and etesevimab (LY3832479) [Etesevimab; Eli Lilly]: A similar monoclonal antibody pair approach has been authorized under FDA EUA. However, some cases of COVID-19 symptoms were observed after bamlanivimab intravenous infusion, involving signs and symptoms such as fever, hypoxia, breathing difficulties, arrhythmia, and fatigue[32,33].
- Sotrovimab [Xevudy®; GlaxoSmithKline and Vir Biotechnology]: This monoclonal antibody given by intravenous infusion demonstrated neutralizing ability and protection against SARS-CoV-2[34]. Although Sotrovimab was used world-wide including in the U.S. under an FDA EUA, the FDA canceled the EUA in April 2022 due to lack of efficacy against the Omicron variant[26].
- Regdanvimab (Regkirona™; Celltrion): A monoclonal antibody therapy specifically targeting the SARS-CoV-2 variant Delta spike protein and given by intravenous infusion[32,33]. The most common side effects include infusion-related reactions, including allergic reactions and anaphylaxis[35]. It is approved for emergency use in some countries outside U.S.[35].

b. Indirect competitors (NIH recommended therapies):

b.1 Antiviral drugs

- Paxlovid™ (PF-07321332) [Pfizer]: Paxlovid™ is an oral antiviral tablet discovered by Pfizer, combining nirmatrelvir (SARS-CoV-2 3C-protease inhibitor that prevents the growth of the virus) and ritonavir (a boosting agent, which helps nirmatrelvir work better)[36]. The National Institutes of Health (NIH) and WHO recommends Paxlovid drug only for older (age above 65) people with a high risk of

hospitalization. The side-effects are dysgeusia, diarrhea, anaphylaxis, serious skin reactions, and other hypersensitivity reactions (HSRs)[37]. Moreover, Pfizer has priced their five-day course of Paxlovid at around $1,390[38].

- Remdesivir [Veklury™; Gilead Sciences]: Remdesivir is a broad-spectrum antiviral medication. It is an RNA polymerase inhibitor that binds to a virus-related RNA-dependent RNA polymerase and prevents RNA virus replication by ending RNA transcription. Therefore, remdesivir was used against the SARS-CoV-2 infection[39]. It is administered via injection into a vein. The FDA approved remdesivir for non-hospitalized children, adults, and older people on April 25, 2022. The associated side-effects include nausea, ALT and AST elevations, HSRs, and increase in prothrombin time[37] In developed countries, Gilead Sciences have priced Veklury™ at $2,340 for a 5-day treatment course[40].
- Molnupiravir (EIDD-2801) [Lagevrio™; Ridgeback Biotherapeutics and Merck]: Lagevrio (molnupiravir) is an oral antiviral drug that inhibits the replication of certain RNA viruses and therefore used for the treatment of COVID 19[41]. The NIH guidelines only suggest using molnupiravir only for mild-to-moderate infection if Paxlovid or Remdesivir is unavailable because it is less effective than other therapies for COVID-19. It is only authorized under an FDA EUA for the treatment of mild to moderate COVID-19 in high-risk individuals aged ≥18 years and not in people aged <18 years due to major potential effects on bone and cartilage growth[37]. Other minor side-effects include diarrhea, nausea and dizziness[37]. Moreover, as per the EUA, the 5-day course of MOV has a low risk for genotoxicity too[37].

b.2 Convalescent Plasma

Intravenous transfusion of plasma from donors who have recovered from COVID-19 is authorized under an FDA EUA for the treatment in patients who are immunocompromised or who are receiving immunosuppressive treatment. However, this therapy can cause adverse side effects including Transfusion-related acute lung injury (TRALI), Transfusion-associated circulatory overload (TACO), allergic, anaphylactic, febrile nonhemolytic and hemolytic reactions, hypothermia, metabolic complications, transfusion-transmitted infections, thrombotic events, theoretical risk of antibody-mediated enhancement of infection and suppressed long-term immunity[37]

***Competitive advantages of AYA2012004_L aptamer*.** Aptamers sidestep the shortcomings of the current therapies through ease of chemical synthesis affording drastic reductions in production complexity, superior thermal stability persisting reliably regardless of environmental conditions, negligible risks of immunogenic responses allowing repeated delivery, and higher tissue penetrance conferring superior potency at target sites. AYA2012004_L aptamer provides ease of use and avoidance of complex infusions, enabling self-administration immediately upon symptom onset, thereby improving outcomes. It also extends access for entire demographics who today remain untreated when encountering barriers reaching healthcare settings promptly. Compared to the current therapies, AYA2012004_L aptamer offers versatility with broad reactivity across variants, ease of self-administration via inhalation, high stability and efficacy, low costs and high scalability given its ease of chemical synthesis, and lack of toxicity and immunogenicity.

***Unique selling point:*** AYA2012004_L aptamer is the first potentially convenient self-administered antiviral biologic therapy with broad reactivity for early COVID intervention.

## *Customers and Users*

Customers: Ayass Biosciences' initial customers will be patients infected with SARS-CoV-2 variants, followed by pharmaceutical companies that are interested in sublicensing AYA2012004_L aptamer, which will be prescribed by doctors and allergists. Ayass Bioscience's strategy is to partner AYA2012004_L aptamer with a large pharmaceutical firm once systemic clinical safety and efficacy are demonstrated in patients. Global pharma companies have the manufacturing and marketing capacities in place to allow the full development and worldwide marketing and distribution of AYA2012004_L aptamer upon approval. The competitors listed above with a gene/cell therapy footprint, including Pfizer, AstraZeneca, Merck and Roche would be likely potential acquirers. In the U.S. there are 6,129 hospitals[42]. AYA2012004_L aptamer may also be available as an over-the-counter drug in the 88,000 pharmacies all over U.S.[43].

*Needs*

- ✓ Reduced health and negative economic impact of COVID 19 infection and treatment.
- ✓ Novel, appealing solution to cure patients that is also safe, compliant with the latest regulations, and suitable for reimbursement.

*AYA2012004_L aptamer values*

- ✓ Reduces hospitalizations and follow-up visits.
- ✓ Innovative technology, extensive safety and pre-clinical performance, suitable for reimbursement schemes.

Users: Users of the technology will be Physicians, particularly pulmonary medicine specialists.

*Needs*

- ✓ Easy-to-use and safe administration
- ✓ No adverse immune response.
- ✓ Competitive price.

*AYA2012004_L aptamer values*

- ✓ AYA2012004_L aptamer can be easily self-administered via inhalation
- ✓ AYA2012004_L aptamer is highly purified and developed according to cGMP.
- ✓ Current per patient per treatment course is estimated at approximately $250 and $500 for bulk ordering and direct to consumer order respectively.

Final beneficiaries: Patients infected with SARS-CoV-2 variants. The total number of patients in the U.S. were found to be 193 million.

Willingness to pay: Pharma companies would be willing to pay as this product has an advantage over the other available therapies. While, the customers would be willing to pay because of the increased QoL and reduced financial burden.

***Marketing & sales strategy***

*Value chain and key stakeholders*. Fig. 4 shows the Ayass Bioscience's value chain at full roll-out. Ayass Bioscience project an integrated commercial model comprising direct-to-consumer online sales, channel distribution partnerships, and biopharma licensing arrangements. Ayass Bioscience will continue performing R&D activities to bring Ayass Bioscience to Phase II clinical trial stage for COVID 19 and related infections. The pharmaceutical company will manufacture and distribute AYA2012004_L aptamer to the hospitals and government institutions to treat patients with COVID 19.

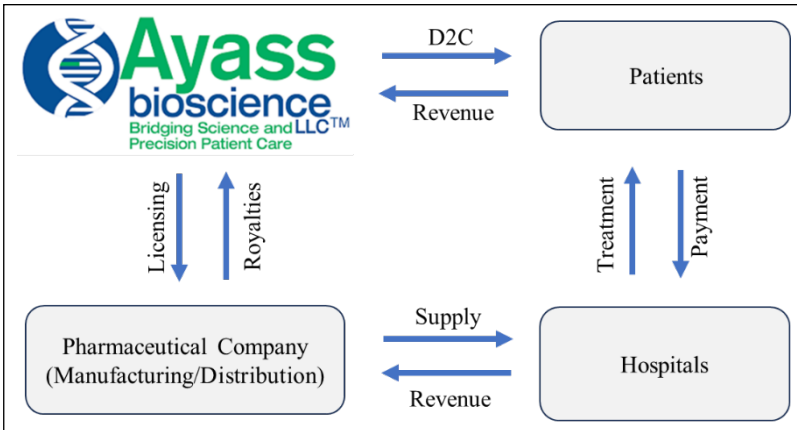


**Fig. 4**. Ayass Bioscience's value chain at full rollout

*Customer/Users.* COVID patients will be the initial customers, which will then expand to US hospitals systems managing COVID care and governmental agencies aggressively stockpiling new countermeasures. The hospital and government agencies will buy and provide AYA2012004_L aptamer to their doctors, who will be the active users of the product, delivering the treatment to COVID patients.

*Business model.* Ayass Bioscience proposes an integrated commercial model comprising direct-to-consumer online sales, channel distribution partnerships, and biopharma licensing arrangements.

Online Sales:

a. Targeting 20,000 units sold direct online by Year 2 at $500 per treatment course.
b. Scaling to 200,000 online orders annually by Year 6 as awareness and adoption increases.
c. Profit margins exceed 65% through online channel.

Channel Partners:

d. Contracting pharmacy chains, drug distributors, healthcare networks for fulfillment.
e. Taking 5-15% share of treatment cost as channel margin.

Licensing Deals:

f. Pharmaceutical corporations contracting development, manufacturing and commercialization licenses.
g. Modeling $10M+ upfront payments, milestone payments plus 10-15%+ royalty rates on treatment sales.

*Reimbursement*. The licensing Pharmaceutical Company will discuss reimbursement options with payers.

| **Strength** | **Opportunities** |
|---|---|
| ✓ Ease of self-administration through inhalation.<br>✓ Capability of broad reactivity against the original as well as new and evolving infectious strains.<br>✓ Aptamer approach is lower cost and scalable.<br>✓ AYA2012004_L aptamer shows stability and lack of immunogenicity. | ✓ Only Remdesivir and Paxlovid are currently FDA approved, with questionable clinical efficacy against emerging SARS-CoV-2 genetic derivatives.<br>✓ The steady growth of COVID-19 therapeutic market in general. |

| Weakness | Threats |
|---|---|
| ✓ Low brand awareness<br>✓ Regulatory hurdles for clinical grade manufacturing<br>✓ Complex and unequipped distribution network | ✓ Growing competition in the field.<br>✓ Skepticism of healthcare providers. |

## D - INTELLECTUAL PROPERTY (IP) PROTECTION

| Patents | | |
|---|---|---|
| Description | Application status | Owner |
| **PCT/US22/35718**<br>Viral protein specific aptamers and methods of use in diagnostics, therapeutic purposes | United States - Pending | Ayass Bioscience |
| **Copyrights and Trademarks** | | |
| Description | Status | |
| Company Name, Logo, and Website | Trademark: active | |

**IP management**

Ayass Bioscience has patented a synthetic DNA aptamer potently neutralizing SARS-CoV-2 with the aim of eventually developing the first potentially convenient self-administered antiviral biologic therapy for early COVID intervention.

Freedom to Operate (FTO): Ayass Bioscience conducted a thorough patentability search during its IP diligence. Ayass Bioscience were pioneers in the discovery of AYA2012004_L aptamer, so no pre-existing IP is anticipated. Ayass Bioscience will continue to ensure FTO by routinely conducting detailed literature searches, detailed patent searching using public repositories (e.g., ESCAPE and WIPO), and by analyzing data with Patsnap IP analytics tool. Depending on the date of commercial launch, a commercial license may be required, but would entail a low (<2%) royalty.

## E - FINANCE PLAN

AYA2012004_L aptamer has been developed with over $10M, financed through substantial non-dilutive funding from private organizations, foundations, and investors that recognize the rare upside potential for this category of investment. Moving forward, the company intends to use a combination of venture capital, strategic partnerships, and the requested grant funding. The proposed Project is expected to provide the necessary funding ($2.35M) to complete all of the pre-clinical and IND-enabling studies required to support clinical trials on of AYA2012004_L aptamer. With IM clinical data and a systemic IND in hand, Ayass Bioscience would raise up to $25M to advance clinical development and to build the management team. The funds will also be used to complete the development of the AYA2012004_L aptamer, conduct clinical trials, gain regulatory approvals, secure further intellectual property protection, and develop strategic business relationships to manufacture, market and launch the products.

## F - PRODUCTION AND MARKETING PLAN

***Production/operational plan***

Ayass Bioscience is preparing various novel aptamers for launch in multiple international markets and for a variety of clinical indications. Initially, the company is planning to develop AYA2012004_L aptamer for COVID-19 indication up to clinical Phase I safety testing, after which a Pharma company will be engaged to guarantee Phase II/III clinical trials and its launch in multiple international markets. The Roadmap for AYA2012004_L aptamer market launch is given in Fig.

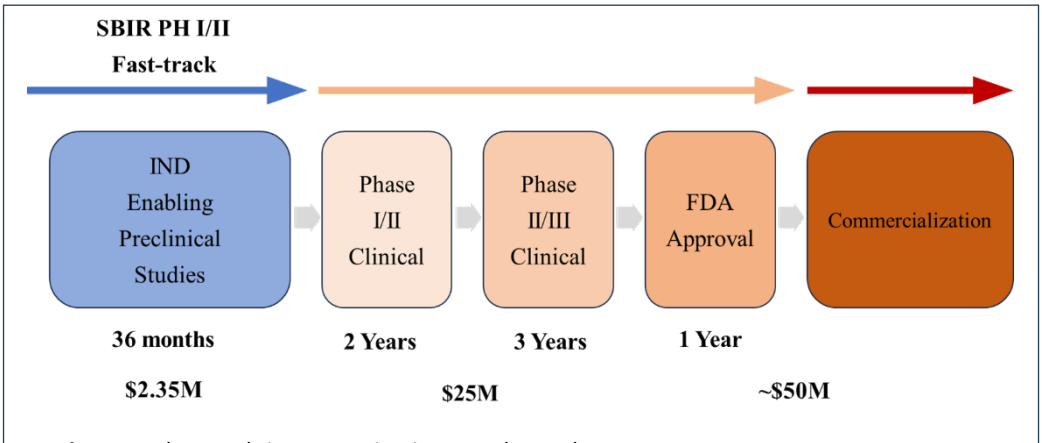


**Fig. 5.** Roadmap to bring Ayass Bioscience to the market

5. Towards this goal, the company will be expanding its scientific and management team by including CEO, CMO, CTO, CSO, CROs and project manager, and is undertaking the following significant development actions:

- ***Complete pre-clinical validation.*** Ayass Bioscience plans to gather preclinical evidence of AYA2012004_L aptamer's effectiveness and safety, during this project. The experimental plan is largely based upon IND-enabling activities to complete AYA2012004_L aptamer's pre-clinical validation. Specifically, Ayass Bioscience will perform extensive safety/toxicology, pharmacokinetic studies, and efficacy studies on two preclinical animal models. Studies will be conducted in collaboration with the Texas Biomedical Research Institute. The **Phase I** will focus on dosage optimization studies to determine the safest and most effective dose of AYA2012004_L aptamer using golden Syrian hamster model. In the subsequent **Phase II**, we will use the NHPs in IND-enabling studies, which will include: i) Determining maximum tolerated dose (MTD), ii) safety and efficacy. Completion of the proposed project will pave way for IND submission for AYA2012004_L aptamer which is expected in 2026-27.
- ***Corporate partnership.*** This project results will be used to raise the interest of Venture Capital and pharmaceutical companies for AYA2012004_L aptamer towards ***Phase I/II clinical trials.*** The clinical data obtained will enhance pharmaceutical companies' interest enabling Ayass Bioscience to successfully out-license AYA2012004_L aptamer for Phase II/III validation, FDA approval, and commercialization.
- ***Clinical validation.*** For systemic delivery clinical validation, Ayass Bioscience would replicate its inhalation therapy clinical plan, beginning with a Phase I/II trial at UMN. If the Phase I/II clinical study results are promising, the AYA2012004_L aptamer will be evaluated for Phase II/III clinical study (25-50 Patients). The successful outcomes of this last step will allow the marketing authorization of AYA2012004_L aptamer.
- ***Product Engineering.*** The licensee pharmaceutical company will be in control of manufacturing aspects including exploring economical options. The quality control and quality assurance aspects, packaging, and shipping will be performed by them.
- ***Parallel activities.*** With the royalties and upfront payment, Ayass Bioscience will continue the R&D on the aptamer technology. We will expand the application to other clinical indications and will further expand our portfolio. Ayass Bioscience will raise additional funds to conduct initial efficacy studies in new indications, such as cancer immunotherapy.

**Commercial and Marketing plan**

Ayass Bioscience is planning to develop AYA2012004_L aptamer through clinical phase I/II efficacy testing, a stage at which a pharma company will be engaged to complete clinical validation, obtain FDA approval and guarantee AYA2012004_L aptamer launch in the domestic market. Overall, AYA2012004_L aptamer could be ready for a BLA filing within 8-9 years. The product will be commercialized mainly through authorized distributors.

From a geographical point of view, the solution will likely be first marketed in the U.S. After the U.S., from the second year of commercialization, Ayass Bioscience plans to reach key European markets such as UK, France, Germany, and Spain. Upon successful market entry in the two major targeted regions (U.S. and EU), Ayass Bioscience will focus on Asia, starting with Japan, and then the rest of the world.

Ayass Bioscience will appoint a COO to plan marketing and communication activities to increase the visibility of the company and awareness for the technology platform to hospitals, KOLs in the field, pharmaceutical companies and venture capital firms. The company plans to implement the following methods:

- Website: Updated non-confidential information about the product, technological advancements at **https://ayassbioscience.com/**
- Social media posts and press releases: Updated information on project developments & results on LinkedIn and Twitter.
- Presentation of research data at international conferences: Suitable events will be drawn from a wide range, such as the meetings of World Congress on Infectious Diseases, IDWEEK, American society of Microbiology (ASM)Microbe, International conference on emerging infectious disease (ICEID), and World congress of infectious diseases (WCID).
- Publication on international, peer-reviewed scientific journals: Publication of study results in international journals like The Lancet Infectious Diseases, Emerging Infectious Diseases, BMI Open Respiratory Research, Clinical infectious Disease, Journal of infectious diseases and Journal of Virology.
- Business development meetings: e.g., Cell & Gene Therapy USA, J.P. Morgan Annual Healthcare Conference, Eyeforpharma, Biotech Showcase, Pharma iQ, Sachsforum-Switzerland, BioEurope, CPhI Worldwide and Bio International Convention.

- Reach out to centers of excellence and recognized KOLs in cell therapy and pediatric neurology: Ayass Bioscience already leverages the strong network of contacts in the US of Dr. Xuebin Qin (a leading researcher in innate immunotherapy), Dr. Massoud Motamed (expertise in FDA regulation) and Dr. Jeremiah Gassensmith (specialized in virology and drug delivery).
- Private fundraising activities: To support future fundraising for $25 M, Ayass Bioscience will identify and select new suitable equity investors and prepare a comprehensive Investor Package
- Pharmaceutical company outreach: During Phase I/II clinical trials, Ayass Bioscience will engage with pharma companies interested in licensing AYA2012004_L aptamer.
- Hospital and payers' involvement: Once a partnership is secured, Ayass Bioscience's final go-to-market strategy will be established with the partner biopharmaceutical company, which will cover the manufacturing and the commercialization costs. The initial target will most probably be the top 30 ranking hospitals for Pulmonary Medicine in the US. The drivers of the adoption will be: 1) Key Opinion Leaders endorsing AYA2012004_L aptamer therapy and 2) the fact that there is currently no specific cure for COVID-19.

## G – FINANCIAL IMPACT

### Revenue projections

Financial modelling suggests consumer sales scaling to $500M annually within 5 years as healthcare systems purchase quantities sufficient for public health preparedness stockpiles in anticipation of recurrent outbreaks.

Total projected 5-year revenue exceeds $625M including milestone licensing payments from large pharmaceutical corporations seeking to capitalize on complementary manufacturing and distribution competencies. The following table shows assumptions for net profit from year 1 (2029) to 5 (2034).

| Year | Direct Sales | Licensing | Total Revenue | COGS | R&D | Sales & Marketing | Administration | Total Expenses | Net Profit |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $3M | $0M | $3M | $1M | $3M | $500K | $500K | $5M | -$2M |
| 2 | $30M | $10M | $400M | $5M | $4M | $1M | $1M | $15M | $25M |
| 3 | $120M | $5M | $130M | $15M | $5M | $2M | $2M | $30M | $100M |
| 4 | $250M | $15M | $265M | $30M | $6M | $3M | $3M | $50M | $215M |
| 5 | $600M | $25M | $625M | $75M | $7M | $5M | $5M | $100M | $525M |

### Job Creation

The following shows stage of development for AYA2012004_L aptamer and expected jobs created by year:

*2026-27 IND Enabling:* 5 new jobs created: Chief Executive Officer, Chief Medical Officer, Project Manager, Head of Regulatory, Head of Preclinical Development

*2027-28 Phase I/II Clinical:* 9 new jobs created: Chief Scientific Officer, Clinical Coordinator, Head of Manufacturing, Head of Analytics, Project Manager 2, Finance Manager, Head of Operations, Admin 1, Admin 2.

To take a product through Phase II/III pivotal trials and receive BLA approval, it is expected that Ayass Bioscience would require at least $25 M and total and a team of over 24 people.

## FACILITIES AND OTHER RESOURCES

### ***Ayass Bioscience's Facilities***

Ayass Bioscience is a growing biotech company headquartered in Frisco, Texas. With over 30,000 square feet of space, spread across 3 buildings, Ayass Bioscience has ample room for its employees. The main building (Building IX) houses Ayass Bioscience's executive offices and several departments including sales, marketing, human resources as well as laboratory space with 12 bench areas where Ayass Bioscience's scientists and researchers work to develop new technologies and groundbreaking science. The lab has instruments to run standard as well as specialized molecular and cellular biology wet labs *(see Equipment list).* Building 7 provides open office space as well as a shipping and sample receiving area, as well as more laboratory space with 10 bench spaces. The third building contains office space for the data science department. The multiple buildings allow teams to collaborate when needed, while also providing the specialized spaces required for Ayass Bioscience's innovative R&D work. The centralized location fosters a tight-knit company culture and enables inter-departmental communication.


### ***Management, Leadership and Scientific Team***

- **Mohamad Ammar Ayass M.D., Founder and CEO.** Dr. Ayass is a practicing physician specialized in pulmonary and critical care medicine and researcher with over 30 years of pulmonary, immunology thrombosis and molecular research experience. He received his medical doctor degree at Damascus University College of Medicine, then completed his post-doc training at the University of Michigan and University of Tennessee. He completed his board certification in internal medicine and pulmonary disease and opened his own pulmonary clinic in west Texas and the DFW area. He is the founder of Ayass Lung Clinic, PLLC, Ayass Laboratory, LLC, and Ayass Bioscience, LLC, Aptamer Diagnostic, LLC, Ayass Research Institute, LLC and Apsilon Financial Services, LLC. *Dr. Ayass is responsible for Ayass Bioscience's R&D as well as business development and financial operations.*
- **Lina Abi Mosleh Ph.D., Principal Scientist and Vice President.** Dr. Abi Mosleh is an accomplished research scientist and leader with over 10 years of experience spearheading innovative scientific programs and discoveries that improve patient outcomes. She combines her expertise in molecular biology with cross-functional leadership skills to build high performing research teams focused on transformative science and personalized medicine. She is very well equipped to lead research initiatives in an executive role that directly advance patient care and health. She received her Ph.D. in Molecular Genetics and Biochemistry at the University of Texas Southwestern Medical Center at Dallas in the laboratory of Nobel laureates Drs. Michael S. Brown and Joseph L Goldstein. *Dr. Abi Mosleh is responsible for Ayass Bioscience's R&D in addition to overseeing, managing, and leading daily operations of both the clinical and research aspects of the project.*
- **Natalya Griko Ph.D., Senior Scientist.** Dr. Griko is the Senior Scientist at Ayass Bioscience from the past 8 years where she is responsible to oversee and manage high-complexity genetic testing and lead numerous research projects. She has more than 24 years of experience in protein chemistry, molecular biology, microbiology, functional and structural biology in both academia and biotech industry settings. She earned her Ph.D. in Molecular Biology at the Institute of Protein Research in the scientific center of the Russian Academy of Sciences near Moscow.
- **Trivendra Tripathi Ph.D., Scientist.** Dr. Tripathi has expertise in designing and validating clinical flow cytometry assays for immunophenotyping in leukemia and lymphoma, profiling and subsetting cells such

as lymphocytes (T cells and B cells), stem cells, myeloid cells, macrophage and monocyte subpopulations, intracellular staining, and rare cell detection. He is part of the R&D team at Ayass Bioscience and is involved in developing *in vitro* diagnosis and targeting therapies for many diseases. He is also responsible for designing an immune profile flow cytometry panel for COVID-19 patients and correlating the findings to mass spectrometry. He earned his Ph.D. degree in Biochemistry at Aligarh Muslim University, India.

- **Jin Zhang, M.D., Epidemiologist.** Dr. Zhang has more than 10 years of public health/research experience (chronic and infectious diseases). She has great expertise in experimental design, planning, data analysis, modeling and projections, bioanalytical parameter determinations, and validation of various assays and clinical sample bioanalysis. She received her M.D. degree from the School of Medicine, China Three Gorges University, China. She earned her Master's degree in Pharmacology and Toxicology from the University of Mississippi Medical Center and MPH degree in Epidemiology and Biostatistics from the School of Public Health, Jackson State University, USA.
- **Victor Pashkov Ph.D., Research Scientist.** Dr. Pashkov is a Research Scientist at Ayass Bioscience with the responsibility to conduct high-complexity genetic testing and participate in research projects. He has multiple years of experience as a biomedical research scientist with expertise in molecular biology, molecular genetics, and genotyping. He is involved in the design, development, and validation of high-complexity genetic testing. He demonstrates advanced skills in biological and biotechnological systems through the optimization of several protocols for DNA and RNA extraction, PCR, genotyping by mass-spectrometry, and data analysis. He earned his Ph.D. in Biochemistry at Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, of the Russian Academy of Sciences.