Universidad de
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Departamento de Economía

Caspr Biotech, plataforma de detección molecular basada en CRISPR.
Plan de negocios, tracción y perspectivas de mercado

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Executive Summary

Caspr Biotech is a startup developing a platform for precise molecular detection, powered by CRISPR [1] as the underlying technology. This platform is set to transform diagnostics in healthcare (and molecular detection in other industries such as agriculture, farming) given it's precision, portability and accessibility.

Existing technologies for molecular testing are limited to complex settings in sophisticated clinical labs, requiring expensive equipment and trained personnel. This means that it is performed in a centralized manner in specific institutions which have the resources and expertise to perform such tests, making the average waiting time for molecular detection a matter of days or even weeks. PCR (Polymerase chain reaction) has remained for the past decades as the *gold standard technology*.

Caspr Biotech is about to transform this with their fast, accurate and portable diagnostics. Caspr has developed a portable point-of-care molecular detection platform, which is set to enable a sample to result response in less than 30 minutes, at a fraction of the cost of current alternatives. Caspr uses this to identify within samples (blood, saliva, urine, etc) signature DNA sequences that belong to infectious diseases and genetic mutations.

Caspr Biotech arises from the linking of a group of three scientists (Carla Gimenez, Federico Pereyra Bonnet and Lucía Curti) which originally belonged to CONICET and a business entrepreneur (Franco Goytia). The scientific group had been working with CRISPR and wanted to move on to give a technology market application; on the other hand, Goytia had recently had his first successful experience leading a tech startup and wanted to pursue new ventures in something that could have a positive global impact. Goytia immersed himself into the scientific community of Argentina through CONICET and found that the country had a comparative advantage with regards to the other countries in the region, shown in terms of the number of researchers (per capita researcher is the highest in Latin America[2]) as well as the quality of the work (leading the ranking of scientific Nobel Prizes in the region[3]).

The company has achieved scientific and commercial traction since it's funding in 2018. It's key milestones include: successfully validating for Health and Agriculture relevant infectious diseases, filing a Provisional Patent in US, and having raised $ 450.000 from IndieBio[4] and GridX. This has established Caspr Biotech as one of the pioneer companies in the world in the usage of CRISPR for molecular detection, being featured by news sites such as Contxto, IB, La Nacion, amongst others.

The current thesis shows the problem from the underlying available molecular detection technologies, tendencies in the market, the opportunity Caspr Biotech is set to disrupt through its CRISPR based detection platform and the current traction the company has generated.

[1] Bacterial adaptive immune systems use CRISPRs (clustered regularly interspaced short palindromic repeats) and CRISPR-associated (Cas) proteins for RNA-guided nucleic acid cleavage. This system has been reingeneered as a biotechnology tool of great applications since it's discovery in 2012.
[2]World Bank, 2016 - Argentina leads the ranking of Researchers per Capita of Latin America with 1.202 researchers per million inhabitants. https://data.worldbank.org/indicator/SP.POP.SCIE.RD.P6
[3] Nobel Prize - https://www.nobelprize.org/ - Argentina has three science Nobel Prizes (Houssay, Leloir and Milstein)
[4] Leading Early Stage Biotech Accelerator in US

Introduction

The global problem with current diagnostic solutions

Studies conducted by the CDC (Centers for Disease Control, 2016) estimate that between 30% to 50% of the antibiotics currently supplied in the US are unnecessary[5], this being a problem which scales at a global level. The global burden is not only in terms of the economic inefficiency of spending in the healthcare system, but rather much more significant in terms of the generation of multi-resistant bacteria and antibiotic resistance within the population due to the unnecessary use of them . Antibiotic resistance (in English known by the acronym "AMR" as antimicrobial resistance) has been declared by many specialists as one of the greatest threats to health that humanity will face in the coming decades. According to a report made by the AMR Review (2016), 700,000 people die every year due to problems associated with this phenomenon. By 2050 it is estimated that it will become the leading cause of death in the world, given that drug-resistant infections will directly cause 10 million deaths per year and a cumulative total of US $ 100 billion in economic loss[6].

One of the main variables responsible for this misuse of antibiotics is the fact that current diagnostic tools can't inform professionals such as doctors with the correct results, in the appropriate context and at a viable cost.

There are currently two main technologies used to diagnose, the culture and the polymerase chain reaction (PCR). These are the techniques or tools that are most commonly used for all kinds of detections, including viruses, infections and resistance. They have basically remained unchanged for decades.

The *culture* as its name suggests is based on the culture of bacteria from a sample (such as blood), it has remained basically unchanged for centuries since its discovery in 1881. Culture takes at least 36 hours to confirm the type of infection. It not only implies long waiting times (in general, it takes 2-3 days for hospitals to take on average to conduct the study and interpret the results), but it is also an intensive technique in terms of the human resources needed to perform and evaluate this process for each sampling.

On the other hand, PCR is faster (the results may be available in less than 4 hours in certain cases), but it is expensive and is limited to clinical labs, meaning that it can only be

[5] Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Healthcare Quality Promotion (DHQP)
[6] Tackling Drug-resistant Infections Globally: Final Report And Recommendations, The Review On Antimicrobial Resistance, Chaired By Jim O'Neill, May 2016

performed in a centralized manner. Specific equipment and trained personnel are needed to operate and interpret the results, which is why it is practiced exclusively in clinical laboratories. For example the Argentine leading healthcare provider Swiss Medical carries out all its PCR studies in “batch” from a centralized lab for the entire Province of Buenos Aires. Not only does this imply high logistics costs, but it also tends to further delay sampling results for treated patients.

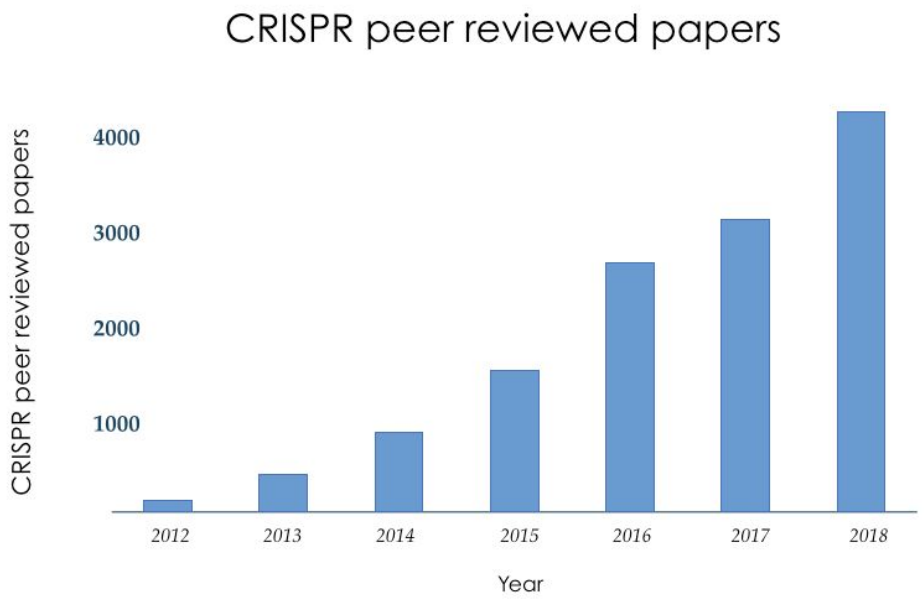
It is from the limitations of these tools that doctors are currently constantly dealing with each patient in a situation of uncertainty and pressure. A patient has to be treated for whom an accurate diagnosis is not available in the first few days. It is from this that doctors (beyond urgency) initially provide or prescribe antibiotics. There is a flaw in the system and an opportunity to position a tool that allows access to this type of information quickly, accurately, decentralized and accessible. This problem scales beyond to other industries and their respective professionals such as farmers and veterinarians.

CRISPR as the technology powering a molecular revolution

CRISPR is the most powerful molecular tool for searching unique and specific DNA sequences. Originally, CRISPR is the name of a recently discovered system present in nature within the vast majority of bacteria and archaea. This system acts in such a way as to defend against attacks by bacteriophages (viruses that infect bacteria), and is a system that has been evolving over millions of years. Bacterial adaptive immune systems use CRISPRs (clustered regularly interspaced short palindromic repeats) and CRISPR-associated (Cas) proteins for RNA-guided nucleic acid cleavage. CRISPR-Cas12a (Cpf1) proteins are RNA-guided enzymes that bind and cut DNA as components of bacterial adaptive immune systems.

There are two components of particular relevance in the process: a nuclease called Cas and an RNA molecule called a probe or guide. The guide identifies the DNA of the virus because it has the information to find it in part of its sequence, which is complementary to its target. By joining the guide to the Cas, the CRISPR complex can recognize viral DNA and cut it in a sequence-specific manner. In this way the formation of the virus is not viable and the bacteria is not affected.

In 2012, the breakthrough and discovery of this technology took place. CRISPR was isolated from bacteria and adapted for use as a biotechnological tool to manipulate DNA in animal cells - including human cells - or independently in vitro in the laboratory. Due to the simplicity of its use and its low cost, CRISPR implied the beginning of a bio-revolution, being presented as the technology of the moment in the most important specialized journals such as Nature or Science. Its use was viralized by many laboratories around the world, which enhanced scientific advances and the number of publications related to CRISPR.



Source: Adii M., Nature Communications, 2018

It is not only on the academic level that CRISPR has impacted in recent years but ,also, in the private framework of companies or startups that have emerged from this technology. Within the health industry, most have a focus on the therapeutic possibilities that arise from CRISPR. From the promise of the possibility of genetically editing living beings, and curing diseases such as cancer, blindness, among many others. All of these have been financed in the magnitudes of tens or hundreds of millions of dollars. All with valuations of more than u$s 1 Billion. Some companies based on this technology have quickly done IPO's and are listed on NYSE some examples being CRISPR Therapeutics ($ CRSP), Intellia Therapeutics ($ NTLA) and Editas Medicine ($ EDIT), all with multimillion or even billion dollar market capitalizations.

Under the first patents related to CRISPR, two groups were leading a long confrontation: the University of California Berkeley (UCBerkeley) with Jennifer Doudna as principal investigator and the Broad Institute (MIT and Harvard) under Feng Zhang's scientific supervision In 2017, there was a first ruling in favor of Broad Institute patents. Then a few months ago the USPTO[7] ratified the same; to the detriment of Berkeley. This decision benefits the generation of new startups based on CRISPR, since Broad has an open licensing model called the Inclusive Innovation Model.

Technical Fundamentals

Caspr differential arises from the novel CRISPR technology, which consists of a pair of molecules that function as the search engine for DNA fragments. Caspr uses CRISPR to

[7] United States Patent and Trademark Office

look for DNA from viruses and bacteria in a sample and thus detects the presence of target(s) of infections or resistance. This same technology is what gives the aforementioned "platform" feature in which it is easy to adapt the existing structure to detect infections that are preferred for the country, context or even industry in which new opportunities are found.

Each detection kit will be designed to direct the CRISPR Guide to the specific target to be detected. It will have three key components: the Cas enzyme, the guiding molecule and a molecular reporter that generates a fluorescent signal when the sample contains the pathogen. To apply CRISPR in diagnosis, Caspr will use the CRISPR system that contains the Cas12a enzyme. Specifically when the CRISPR complex finds its target (match), the enzyme changes its conformation and enters an activated state that unspecifically cuts any single stranded DNA molecule (activation). The reporter molecule is a single stranded DNA linked at its ends to a fluorophore and an inhibitor that masks the fluorophore signal. When CRISPR-Cas12a is activated, the reporter molecule will be cut off, releasing the fluorophore and generating a fluorescent signal (Fig 4). As an output or result, it will be seen that the sample of a patient that contains the specific DNA / RNA sequence which was configured for detection. This procedure has been proven in the research agenda of the group led by Doudna. [8]

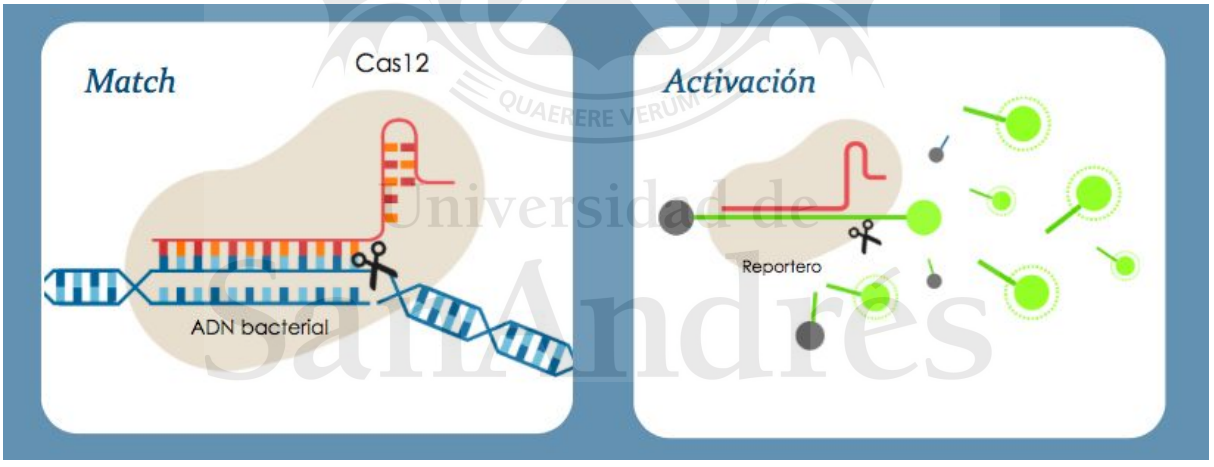


Fig. 4. Scheme of the operation of CRISPR applied to the detection of pathogenic DNA in a patient sample with its two key stages: match and activation.

Coupled to an isothermal amplification by Recombinase Polymerase Amplification (RPA), CRISPR can be repurposed as a very precise DNA/RNA detection platform at one-pot detection method with attomolar sensitivity (RPA-CRISPR detection). Rapid and sensitive detection of viruses and bacteria directly from bodily fluids can be performed if a fast heating step is added before enzyme detection.Even more, the ssDNA[9] molecule reporter cutting by CRISPR-Cas12a allows simple pathogen DNA/RNA detection using a colorimetric readout

[8] Chen JS, Ma E, Harrington LB, Da Costa M, Tian X, Palefsky JM, Doudna JA. CRISPR-Cas12a target binding unleashes indiscriminate single-stranded DNase activity Science (2018). 360(6387):436-439.

[9] single stranded DNA

as lateral-flow strips. Overall, the whole process can be done in 30-60 minutes. In summary, this platform is as sensitive and specific as amplification-based nucleic acid diagnostics (as PCR based-diagnostics) with speed and equipment requirements similar to those of rapid antigen tests at a very low cost.

Scientific Team

Caspr Biotech was born from one of the leading and pioneer groups in the usage of CRISPR within Latin America. This group belonged to CONICET, and had been working with the technology towards its application in cellular reprogramming and epigenetics.

Carla Giménez, BSc, PhD
CSO
CRISPR Biomedicine

Carla is the Chief Scientific Officer (CSO) and combines the scientific knowledge of CRISPR with a great capacity for leadership and vision on how to grow the project in the future. She is a biotechnologist at the National University of Quilmes and is ready to obtain a PhD degree in CyT. The focus of his doctoral thesis was the use of the CRISPR system in biomedicine. She began her study with CRISPR in 2013, at the very beginning of technology in the world. This extensive experience in the subject positions it as one of the pioneers of the use of CRISPR in the region. She has publications on the subject and gave several talks, workshops and advice to several research groups. Its main motivation is that our investigations translate into products or services that have an impact and solve social problems.

Dr. Federico Pereyra-Bonnet F. BSc, PhD
CONICET Deputy Researcher
CRO
Synthetic Biology

Federico is the Chief Research Officer (CRO), and one of the most outstanding CRISPR professionals in Argentina. He has a degree in Biological Sciences from the Universidad del Comahue and a PhD from the University of Buenos Aires. He is currently working as Deputy Researcher of CONICET at the Institute of Translational Medicine and Biomedical

Engineering CONICET-University Institute at Hospital Italiano de Buenos Aires. During his academic career he specialized in cloning, genetic and epigenetic editing in mammals; as well as in the field of biomedicine in stem cells and synthetic biology. Passionate about the formation of human groups that work synergistically taking advantage of their full potential and in the planning and execution of cutting-edge technology projects. With more than 20 publications, 100 congresses, 1 patent, experience in collective financing and several high-level technological advice, today he seeks to land in the industry with projects of high social and economic impact through the formation of biotechnology-based companies.

Lucia Curti, BSc
CONICET doctoral fellow
Junior Scientific Researcher
Synthetic RNAs

Lucia is a Junior Scientific Researcher in Caspr, with a degree in Genetics from the National University of the Northwest of Buenos Aires (UNNOBA). During her thesis she specialized in synthetic biology, particularly in synthetic RNAs. She is currently a Doctoral Fellow of CONICET and is developing his project in CRISPR and ARNs.

The Product

Phantom 1.0 Molecular Platform

Caspr Biotech is developing a portable device that acts as a platform for precise molecular detection. The device will be called Phantom 1.0.

This platform is set to transform diagnostics in healthcare (and other industries such as agriculture, farming) given it's precision, portability and accessibility. The following represents a render of the device Caspr is set to develop, with modular cartridges configured for different types of detections. Results within the handheld and portable device being directly accessible from a smartphone app that can be interfaced to other kinds of online databases.

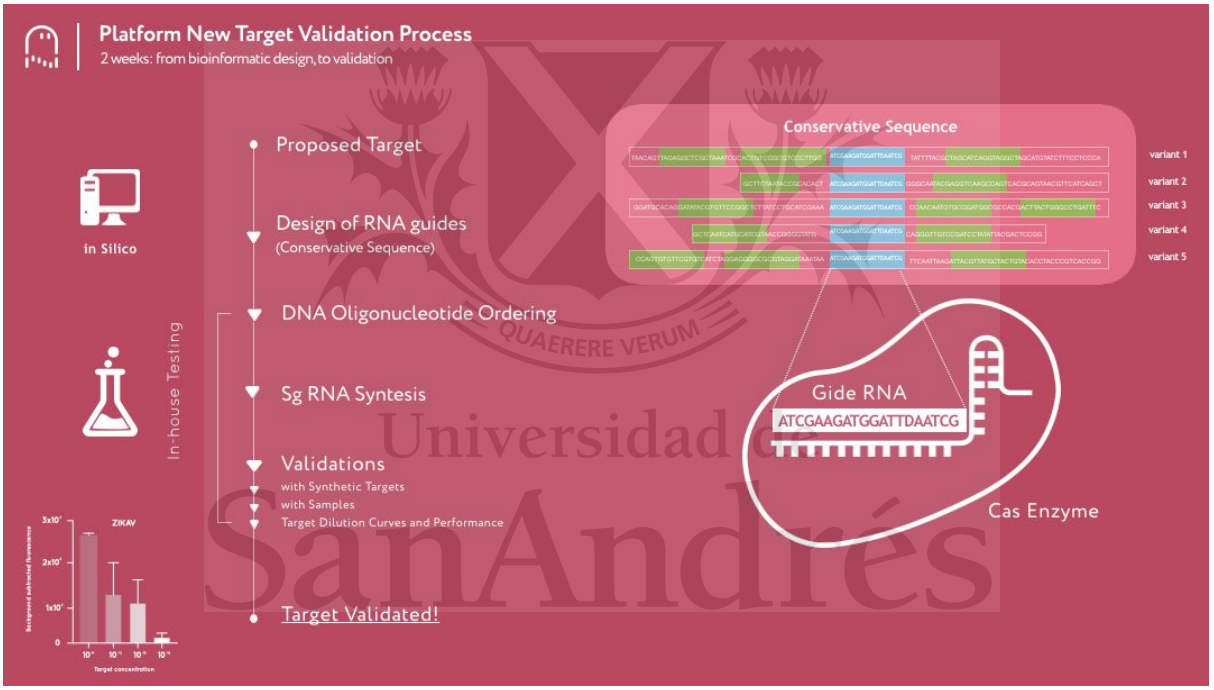
The proposed molecular detection solution has the following characteristics as part of its value proposition:

- Accessible (U$D 10 / cartridge)
- Fast (results in less than 30 minutes)
- Portable (no need for specific equipment)
- Precise (High specificity and attomolar sensitivity)

All these points to transform it into an unprecedented development for the current changing and globalized world in which infections grow and adapt at high speed.

Scientific Validations & Traction

Caspr Biotech has performed validations of its CRISPR based molecular detection platform for multiple targets in industries such as Healthcare (Dengue, Zika, Hantavirus, KPC, NDM, OX) Agriculture (Soy resistance, transgenic sequences) and animals. These validations have been performed on occasions with external research groups, hospitals and companies. The company emphasizes the concept of a "platform" for molecular detection with diverse applications, given the ease of reconfiguration that CRISPR has as a system of moleuclar detection. Caspr is capable of designing the detection system for a new proposed target in less than 14 days. This is a process that includes the in-silico design, as well as a lab testing. The specifics of the process can be found in the graph below:

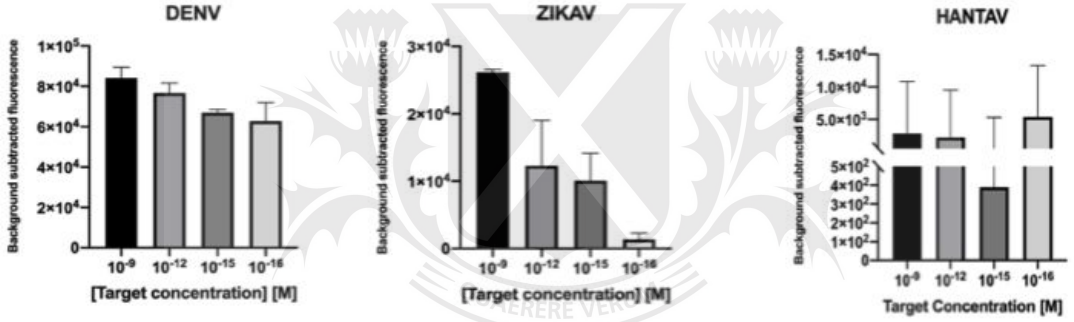


The key steps of the design and validation process are the following:

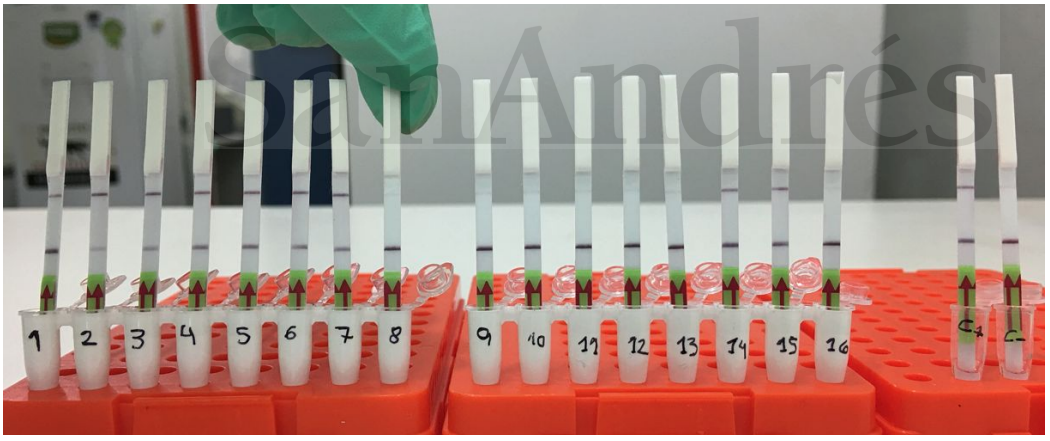
1. Target gene sequence identification - The National Center for Biotechnology Information (NCBI) database was used to select and delimit the target gene area to be identified with CRISPR.
2. Guides designed in silico molecules - To do this, we used the online Breaking-Cas program, which works with an algorithm that helps identify gene zones that meet the requirements to serve as guides for CRISPR-Cas12a
3. Guides produced in vitro - From DNA oligonucleotides we obtained the specific RNA guide molecules in the laboratory using PCR protocols fill in and In vitro Transcription (IVT). Details of the protocol can be found in the bibliography

4. Synthetic target produced in vitro - For the optimization of the guide molecules, a synthetic infectious target (only the part of the DNA that represents the pathogen) is created by means of oligonucleotide synthesis and molecular cloning within a plasmid or DNA vector. This allows avoiding the use of biosecurity facilities in the first stage of selection and optimization of guide molecules.
5. Fluorescence test - Briefly, the guide molecule was associated with the Cas12 enzyme to form the CRISPR complex and the FAM reporter molecule (emitted at 520 nm) was added in a specific buffer. The system was finally tested with positive controls (the Target to be detected is added) or negative controls (no target present). A background control was the buffer along with the reporter molecule. It is then placed in a fluorescence reader and the signal is observed at its maximum peak (20-40 min).

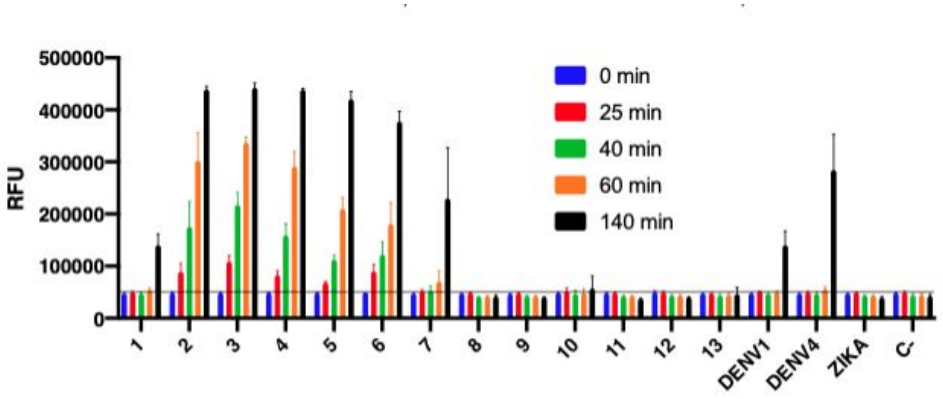
A relevant validation was performed by Caspr for detection of Dengue using as input RNA from human patient samples with the Albert Einstein Hospital in Sao Paulo, Brazil.



The readout was performed in lateral flow strips:



And validated with a fluorescence plate reader:



The results prove that the scientific team was able to detect Dengue virus on positive qPCR confirmed samples (#1-6) with a combined CRISPR complex (equal quantities sgRNAT1-3 and sgRNAT4) to recognize any dengue virus subtype. No signal is observed in healthy donor samples (#12-13) or in zika genome RNA. Future experiments should be done with larger RNA quantities as many detection methods use at least 10 times more as input. This would increase the detection speed. Also, future qPCR validation must be done for the unknown status samples.

Intellectual Property

Caspr Biotech has built a biodiscovery platform to discover novel CRISPR enzymes and systems that can power transformative applications across a range of applications within human health, starting with molecular diagnostics.

Although CRISPR is a system found in nature, a CRISPR - Cas complex becomes a non-naturally occurring system and hence is viable for a patent application under the laws of the United States Patent & Trademark Office.

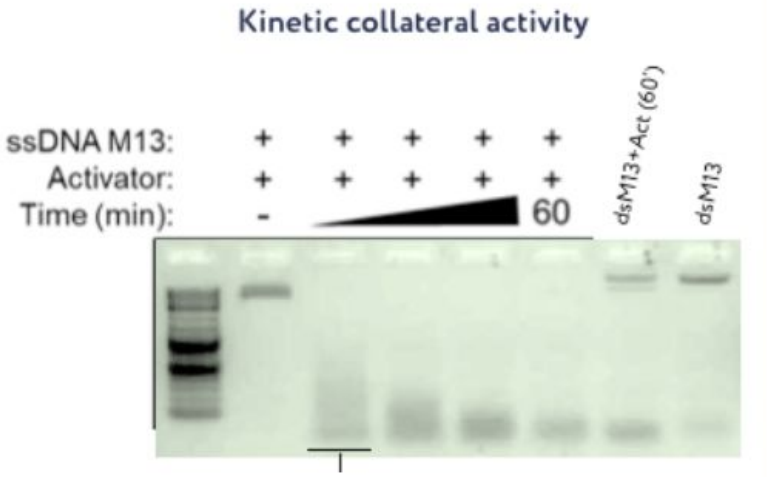
Novel CRISPR - Cas enzymes could provide Caspr Biotech with a barrier of entry through proprietary technologies which improve their molecular detection platform. The company has started generating its own IP Portfolio by filing a provisional patent US 62/898,340 (Inventors: Gimenez, Repizo, Pereyra Bonnet, Curti, Goytia, Farías) Titled: “CLASS 2 CRISPR–CAS RNA-GUIDED ENDONUCLEASE VARIANTS’

These Novel CRISPR Cas variants (Cas 12 and Cas 9) were discovered by a bioinformatic processing of metagenomic data from extreme environments (with unpublished characteristics). These enzymes have the following characteristics:

- **Key amino acid sequences** - which makes it belong to Cas 12 class
- **Low Percentage Identity** - 25%-50% compared to any other Cas enzyme

These enzymes can lead to improved diagnostics in key features such as sensitivity, specificity and stability. Their performance has already been validated and they are being

fully characterized by the scientific team of Caspr. The following figure shows that the proprietary Caspr Cas12a1 enzyme degrades ssDNA in less than 10 minutes.



This IP Strategy of Caspr is set to extend through diverse initiatives in the following fields:

- New antiphage detection systems through our bioinformatic discovery of our unpublished metagenomic DBB
- Protein design & engineering
- New readout methods (DNA origami)
- Lab on Paper Technology

POC microfluidic Device Development

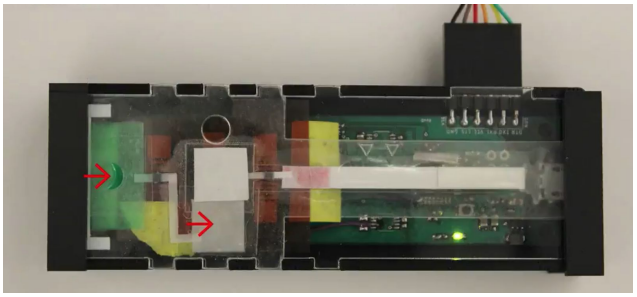
Caspr is integrating its already optimized CRISPR Lateral Flow based reading into a fully automated microfluidic POC device. The device will automate the sample preparation process, heating as well as readout; powered by capillary fluidics and resilient heating controls. This will create a portable platform for rapid NIPT detection at POC.

The development is set to be done though it's inhouse team (biomedical engineers, chemist, etc) as well as through service agreements with specialized microfluidics CONICET research groups in Argentina, and a Programmable Lab on a Chip group at Purdue University (US, Lafayette).

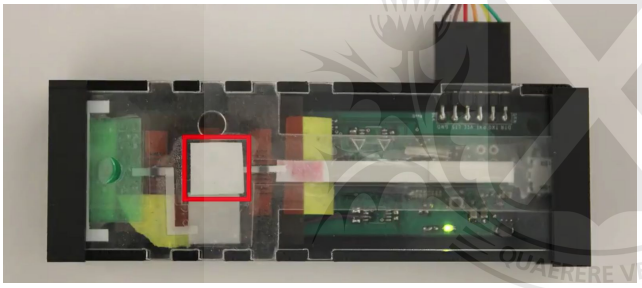
The development is of a fully-integrated sample-to-answer platform that:

1. Isolates cell-free fetal DNA from sample,
2. Amplifies ccffDNA by RPA and detect by CRISPR detection using pre-dried RPA-CRISPR reagents and
3. Automatically transports the CRISPR reporter molecule to an integrated LFIA for simple visual interpretation of results within 30 minutes of sample application.

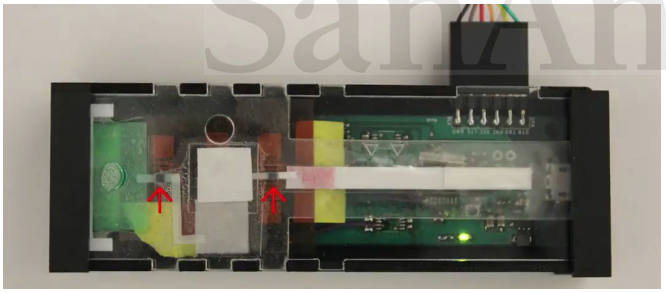
All this would be performed in 4 steps: deposit the sample and DNA wash (1), heating start (2), incubation (3) and result analysis by LFIA (4). An internal control would be included in the same test run to confirm a valid test. To more detail on device function see next figures 4-7.



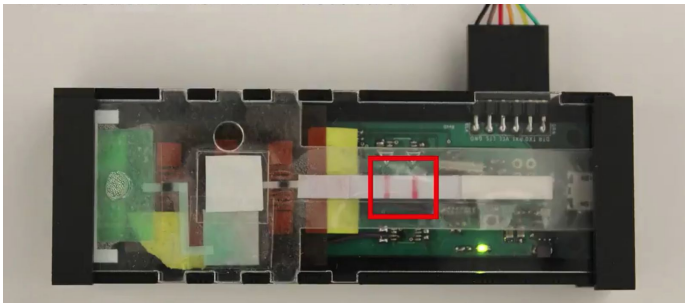
Sample and wash buffer loaded to inlets, DNA wash and reagent deposit



Amplification and CRISPR detection zone heated to 37 degrees for 30 min.



Valves heated to 40*C for 2 minutes to leave reaction transportation.



Lateral flow results analyzed after 45 minutes of sample deposition.

The POC device will provide a sample-to-answer for NIPT detection, in less than 30 minutes. It will be battery powered and rechargeable, enabling it's usage in various contexts. It will be based on 2 components:

- MicroCart - Disposable cartridge (which integrates the sample processing and lateral flow strip)
- Device (integrating the heating, optics and mechanics)

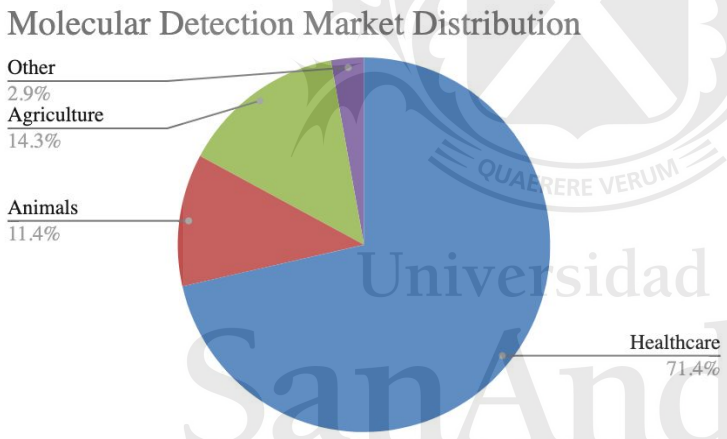
A software development will complement the optics readout enabling the results to be interpreted directly in a smartphone application. This could be connected through wiring or bluetooth (Figure 8)

Figure 8- Schematic of development pipeline from Lateral Flow (current) to Cartridge + Device and Integrated App

Economic Appraisal. Market Size

The Global Molecular Detection market is composed of three main industries; Healthcare, Animals and Agriculture. We estimate the total market sales to be of approximately U$D 35 Bn; with Healthcare accounting for +70% with an estimated $25 Bn in yearly spending[10], Agriculture ($ 5Bn)[11] and Animal (U$D 4 Bn)[12] molecular detection, follow as relevant industries within the market. This can be seen in the following chart and graph:

Market	Market Size (U$D)	% Market Share
Healthcare	$25,000,000,000	71.4%
Animals	$4,000,000,000	11.4%
Agriculture	$5,000,000,000	14.3%
Other	$1,000,000,000	2.9%
Total Market Size	$35,000,000,000	



The bulk of the Molecular Detection market is concentrated in developed countries, with the United States, Canada, Europe and Asia accounting for over 80% of global sales[13]. Latin

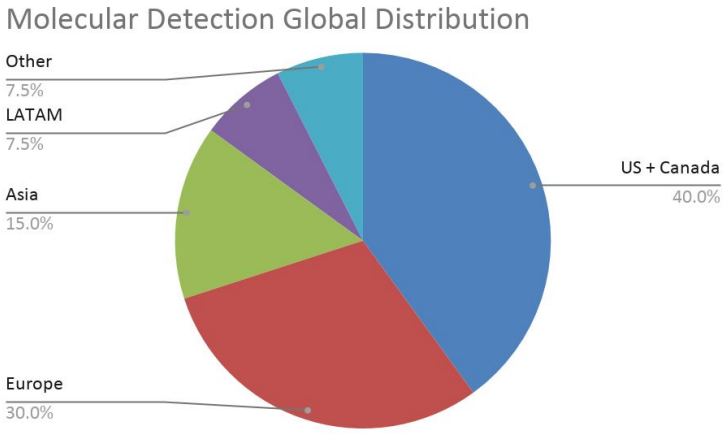
[10] "Ensuring innovation in diagnostics for bacterial infection: Implications for policy [Internet]. Show details Observatory Studies Series, No. 44. Morel C, McClure L, Edwards S, et al., editors. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2016 https://www.ncbi.nlm.nih.gov/books/NBK447315/",

[11] Global Newswire - Selbyville, Delaware , "Animal Diagnostics Market will grow at 8% CAGR to hit $5.5 Bn by 2025: GMI" https://www.globenewswire.com/news-release/2019/08/26/1906401/0/en/Animal-Diagnostics-Market-will-grow-at-8-CAGR-to-hit-5-5-Bn-by-2025-GMI.html

[12] Agricultural Testing Market by Sample, Application, Technology, and Region - Global Forecast to 2022 https://www.marketsandmarkets.com/Market-Reports/agricultural-testing-market-203945812.html

[13] Morel C, McClure L, Edwards S, et al., editors. Ensuring innovation in diagnostics for bacterial infection: Implications for policy [Internet]. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2016. (Observatory Studies Series, No. 44.) 3, Overview of the diagnostics market. Available from: https://www.ncbi.nlm.nih.gov/books/NBK447315/

America represents an approximate 7.5% of the global market, which would equal to more than $ 2.6 Bn.



The most relevant country within Latin America is Brazil, accounting for about 40% of the region's spending, followed by Mexico (15%), Argentina (12%) and Colombia (10%).

Country	% Market Share	Total Amount of Molecular Tests / Year
Brazil	40%	280,000,000
Mexico	15%	105,000,000
Argentina	12%	84,000,000
Colombia	10%	70,000,000
Chile	8%	56,000,000
Other Countries	15%	105,000,000
Total		700,000,000

Source: "Latin America molecular diagnostics market Segmented by Technology, Application, Product, End User, and Geography " (2016) https://www.marketsticker.com/latin-america-molecular-diagnostics-market

Although there is no official information of the number of molecular tests performed per year within the region, we elaborated a model from first hand information we were provided by the largest molecular detection company of Latin America (and the 5th biggest in the world), DASA. This prospective client of Caspr, headquartered in Sao Paulo, shared information of the 250M diagnostic tests it performs on a yearly basis, ⅓ of which are molecular tests. This means that the company performs about 82.5 M molecular tests per year. Additionally, according to their market estimates, the company captures 30% of the Brazil market, meaning that the total Brazil molecular detection market is of 280 M tests per year. Given the fact that Brazil is 40% of the region's total molecular detection market, we can estimate that 700M molecular tests are being performed per year in Latin America.

Diagnostics Number of Tests Performed by Year

Segment	Cases	Variable	Amount	Comments
DASA Diagnostics Total	250,000,000			250M diagnostics tests / year
DASA Molecular Detection	82,500,000		33%	About 1/3 of those tests in DASA are of Molecular Detection
Brazil Market	280,000,000	%	30%	DASA ~ 30% of total molecular diagnostics tests performed in BR.
Total LATAM	700,000,000	%	40%	Brazil accounts for 40% of the LATAM molecular diagnostics market

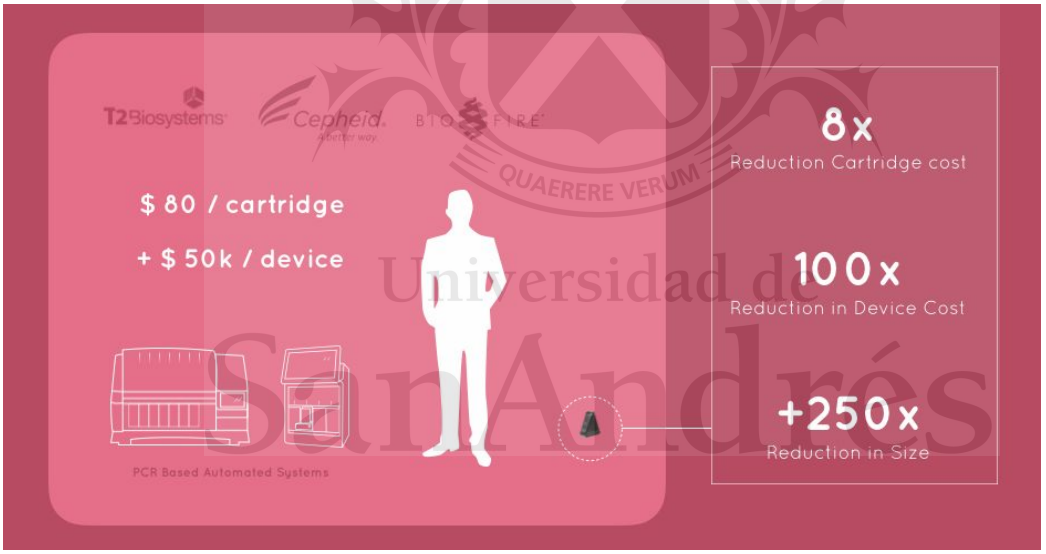
The molecular diagnostics market in Latin America was valued at $ 3.0 billion in 2015 and is expected to exceed $ 5.1 billion by 2024[14]. According to the Market Sticker Report (2018) Brazil's share of revenues exceeded 40.0% in 2015 and was at the forefront among other countries due to the presence of a unified health infrastructure such as the SUS. This is complemented with the fact that molecular diagnostics tends to be significantly higher in Latin American countries when compared to the rest of the world. According to a study elaborated by Drexler et al[15] (2009) RT-PCR reagents in Latin America are usually 100%–200% more expensive than in developed countries, linking this phenomena mostly to the fact that all of these are imported and carry high taxation and distributor margins.

Competitor Landscape

The current solutions for molecular diagnosis are based on equipment with specific machinery that requires inputs for each sampling. The technique they use is multiplex PCR with fluorophores labeled probes. All of them are based on the detection of pathogenic DNA, with a high level of sensitivity and specificity. GeneXpert (Cepheid) and Filmarray (Biofire) are automated systems which integrate PCR technology in an automated device. Even though these have improved the time to response for molecular detection, they remain overall inaccessible due to their costs and size. These devices start at $50.000 and require consumables which cost approximately $ 80 per cartridge. The smallest models come in a size of 40 cm x 40 cm x 30 cm and weigh more than 10 kgs.

[14] Market Stiker - Latin America molecular diagnostics market Segmented by Technology, Application, Product, End User, and Geography - Growth, Trends and Forecast (2012- 2022)
[15] Drexler JF, Kupfer B, Petersen N, Grotto RM, Rodrigues SM, Grywna K, et al. A novel diagnostic target in the hepatitis C virus genome. PLoS Med. 2009;6:e31. 10.1371/journal.pmed.1000031

Caspr Biotech's Phantom 1.0 will be sold for $200 and each cartridge $10. This is an 8x reduction in costs for the cartridge, and 100x when comparing the device cost. The device and cartridges will be manufactured by Caspr and commercialized in mixed models (direct sales, distributors and co-developments with partners).



Unit Economics

The estimated production cost (at scale) for the components are the following:

- **MicroCart** with CRISPR reagents $ 2.57
- **Phantom 1.0 Device** $ 70.00

The full details of the involved reagents and components can be found in the Annex.

Taking into account these component costs and the previously stated sale price, the following would be the detailed unit economics for both the MicroCart and Phantom 1.0 Device.

MicroCart	
Unit Sale Price + TAX	$10.00
Royalties (%)	5%
Royalty Fee	$0.50

A 5% royalty fee is estimated taking into account IP rights for CRISPR and other technologies to institutions (Broad Institute) and other possible partners.

Variable Costs (VC)	$2.57
VC + Royalties	$3.07
Net Margin (%)	69.26%

A net margin of almost 70% would result under the projected model for the MicroCart.

Phantom POC Device	
Device Price	$200.00
Unit Production Cost	$70.08
Net Margin (%)	64.96%

A Net Margin of almost 65% for the Phantom POC device.

Development, Operations & Launch Strategy

Caspr Biotech has based its development pipeline on the support from Venture Capital Investors. The company has so far raised U$D 450.000 from VCs Grid Exponential and IndieBio, in equity backed rounds.

Caspr is now in the process of securing its Seed funding round ($ 3M) from strategic institutional investors in order to accelerate the development of it's Phantom 1.0 platform and the MicroCarts. This will provide a runway of 18-24 months to achieve a functional MVP and a design freeze, enabling the company to then raise a Series A by 2022 for the production and commercialization of the product.

The strategy to market is primarily based in "non-regulated" industries (such as Agriculture and Animal Molecular Detection). Then being able to scale towards Healthcare Diagnostics were FDA (or equivalent) approval is needed in each of the intended commercialization territories (for example ANMAT in Argentina, ANVISA in Brazil).

For the initial Ag focused commercialization, Caspr Biotech has already generated interest and is negotiating possible commercial / co-development contracts with leading companies within the sector such as: BASF, Bioceres and Adecoagro, amongst others. In 2020 the company is set to advance in the initial commercial relationship with these clients, in some possible scientific validation initiatives for each of the company's targets of interest.

For example Bioceres is interested in the Phantom 1.0 device in order to detect it's proprietary transgenic crops in ports and customs. Current technologies require the company to ship the products to a centralized lab, hence losing time and many times losing the opportunity to monetize on their proprietary and enhanced crops.

The first year of commercialization will be focused on the internal Argentine market, later in 2023 opening up its export channel (and in-house team) in Brazil. By 2025 the company will start to expand it's platform to targets beyond Agriculture, with solutions tailored for both Animal (farm and veterinary) molecular detection as well as developing the first human related diagnostics solutions.

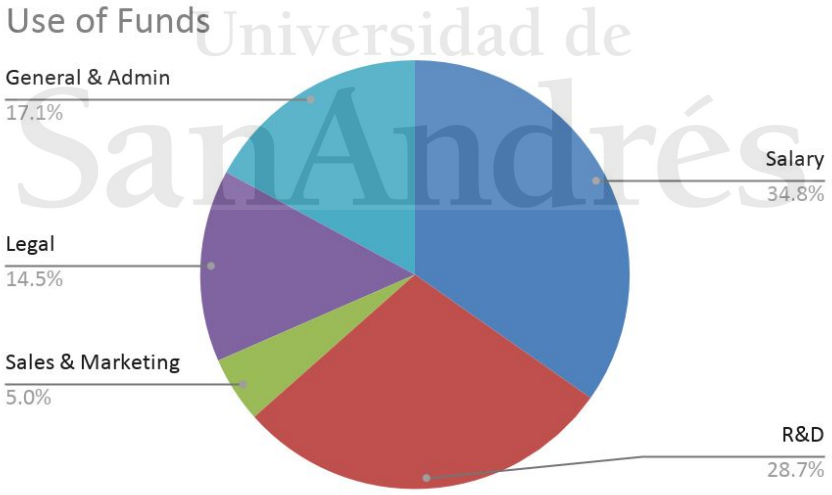
By 2029 it is estimated that the company will have a commercial presence exporting to the main countries of Latin America, with it's molecular detection platform developed to a variety of targets within multiple industries.

Use of Proceeds

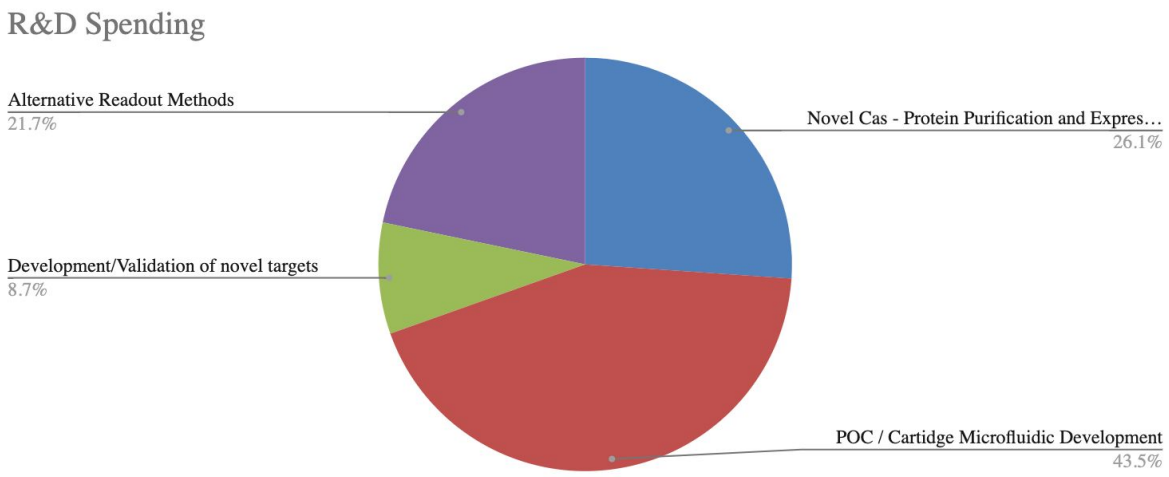
The breakdown of the use of funds for the next 18-24 months (2020 - 2022) can be elaborated based on the following 5 categories:

- General / Admin
- Legal
- Salary / RRHH
- Sales & Marketing
- R&D

Using these, we are able to establish a distribution of the Use of Funds for the mentioned period



Source: own elaboration based on general use of expenses

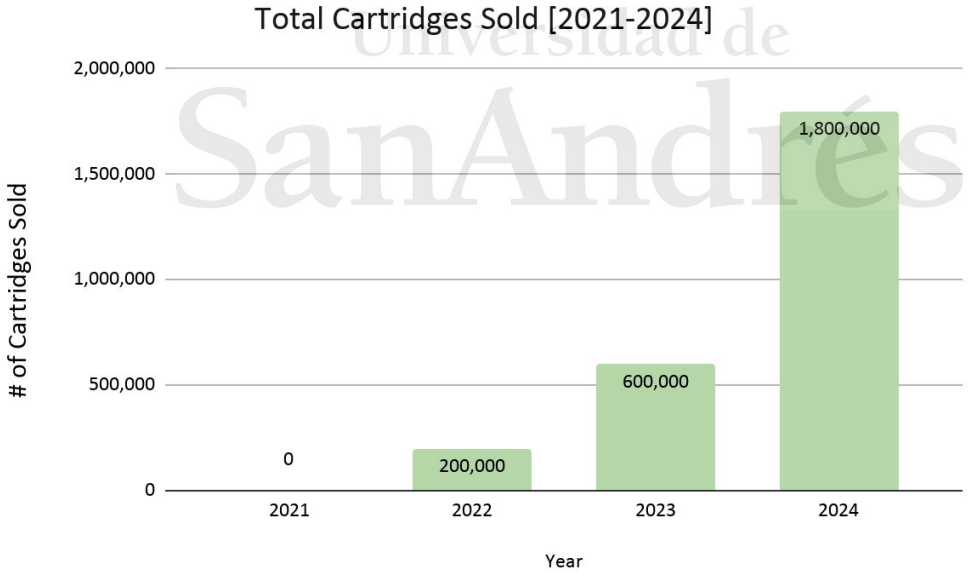


Source: own elaboration based on general use of R&D expenses

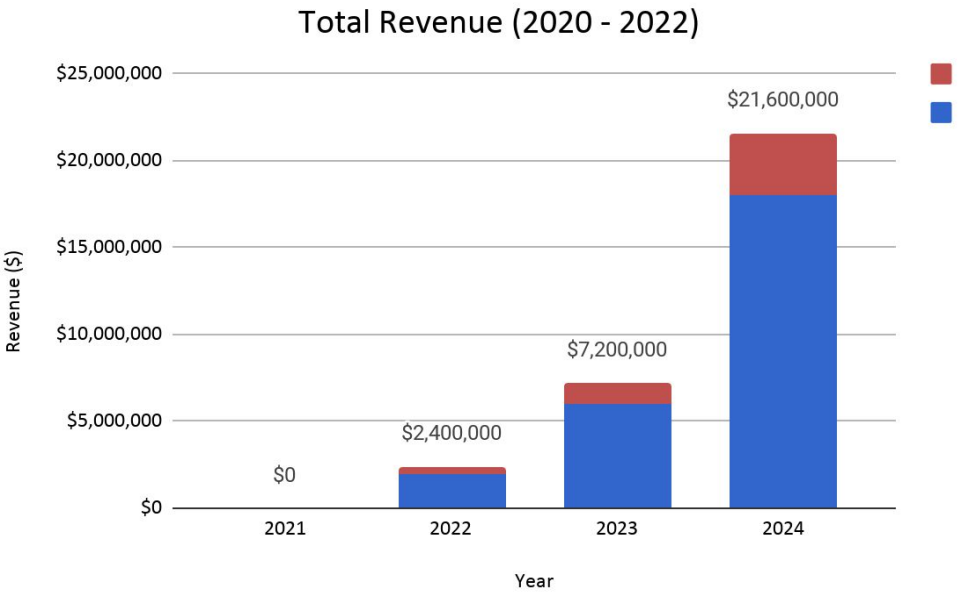
Financials

Even though the contribution margin for each unit sold will be positive from the first unit sold (2022), the company is estimated to be operating at a loss for the first 5-7 years (backed by venture capital).

The following tables show the estimated number of units sold for a 4 year period (2021 - 2024), as well as the associated revenue for those sales.



Source: own elaboration based on general sale estimates

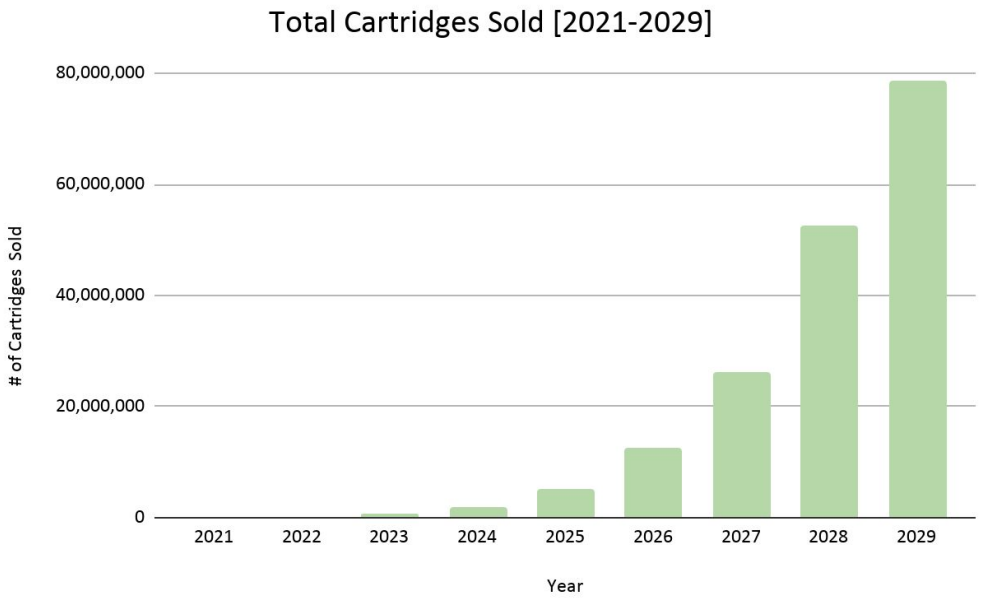


Source: own elaboration based on general sales estimate

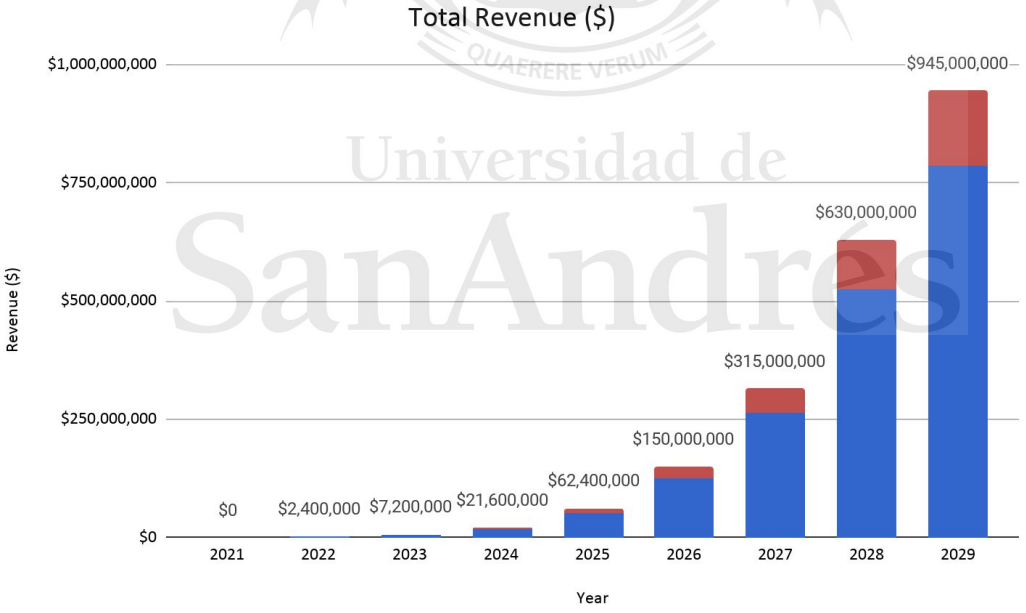
The following table shows the estimates of the number of units sold (cartridges & devices), revenue, COGS, Expenses, EBITDA, amongst other variables.

	2020	2021	2022	2023
Total Number of Cartridges Sold	-	-	200,000	600,000
Growth Rate%				*200%*
Total Number of Devices Sold	-	-	2,000	6,000
Revenue				
Revenue Cartridges	$ -	$ -	$ 2,000,000	$ 6,000,000
Revenue Devices	-	-	400,000	1,200,000
Total Revenue	**$ -**	**$ -**	**$ 2,400,000**	**$ 7,200,000**
COGS				
Cartidges COGS	$ -	$ -	$ 514,702	$ 1,544,105
POC Device COGS	$ -	$ -	$ 140,160	$ 420,480
Royalty Payments	$ -	$ -	$ 100,000	$ 300,000
Total COGS	$ -	$ -	$ 754,862	$ 2,264,585
Gross Profit	**$ -**	**$ -**	**$ 1,645,138**	**$ 4,935,415**
Gross Margin			68.5%	68.5%
Operating Expenses				
Salary	$ 359,500	$ 484,000	$ 1,628,000	$ 2,348,000
Legal	$ 171,000	$ 300,000	$ 300,000	$ 300,000
R&D	$ 231,000	$ 378,000	$ 1,380,000	$ 1,380,000
Sales & Marketing	$ 48,000	$ 60,000	$ 450,000	$ 1,080,000
General & Admin	$ 114,000	$ 324,000	$ 648,000	$ 720,000
Total G&A	**$ 923,500**	**$ 1,546,000**	**$ 4,406,000**	**$ 5,828,000**
G&A as % of Revenue			183.6%	*80.9%*
EBITDA	**$ (923,500)**	**$ (1,546,000)**	**$ (2,760,862)**	**$ (892,585)**
EBITDA as % of Revenue			-115.0%	*-12.4%*
Taxes	$ -	$ -	$ -	$ -

If projections are extended over a longer period of time (9 years) between 2021 - 2029, the company is set to achieve a continuous growth, selling almost 80M cartridges in 2029 (and 800.000 devices that same year).



Source: own elaboration based on general sales estimate



Device Direct Sales
MicroCart Direct Sales

Totaling a revenue of almost $ 1Bn in 2029.

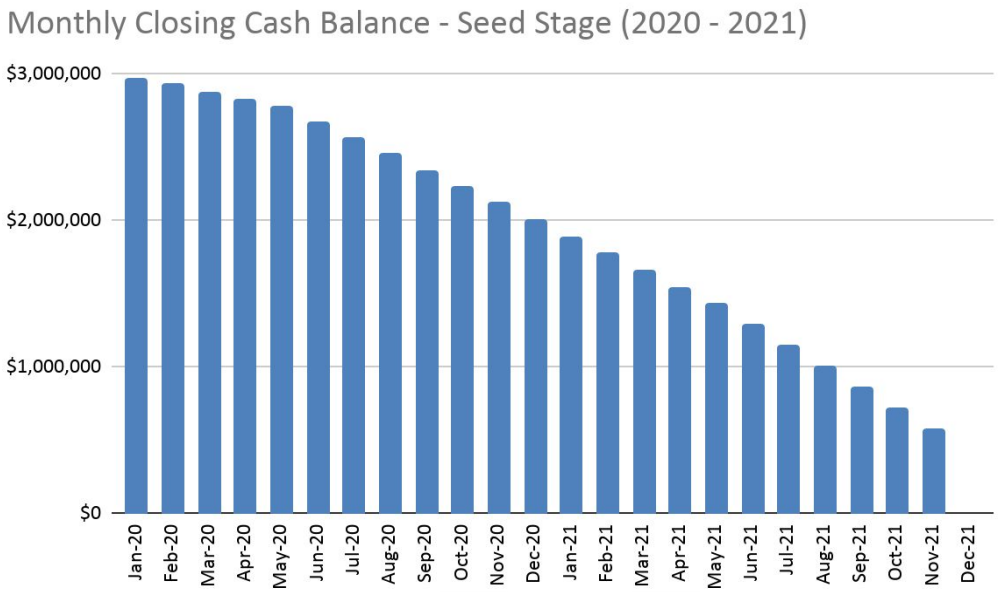
Cash Flow

The following chart shows the projected cash flow for 2020-2023; starting with an initial balance of $50.000 and a $3M investment. With $10M in Series A[16] funding added in 2022.

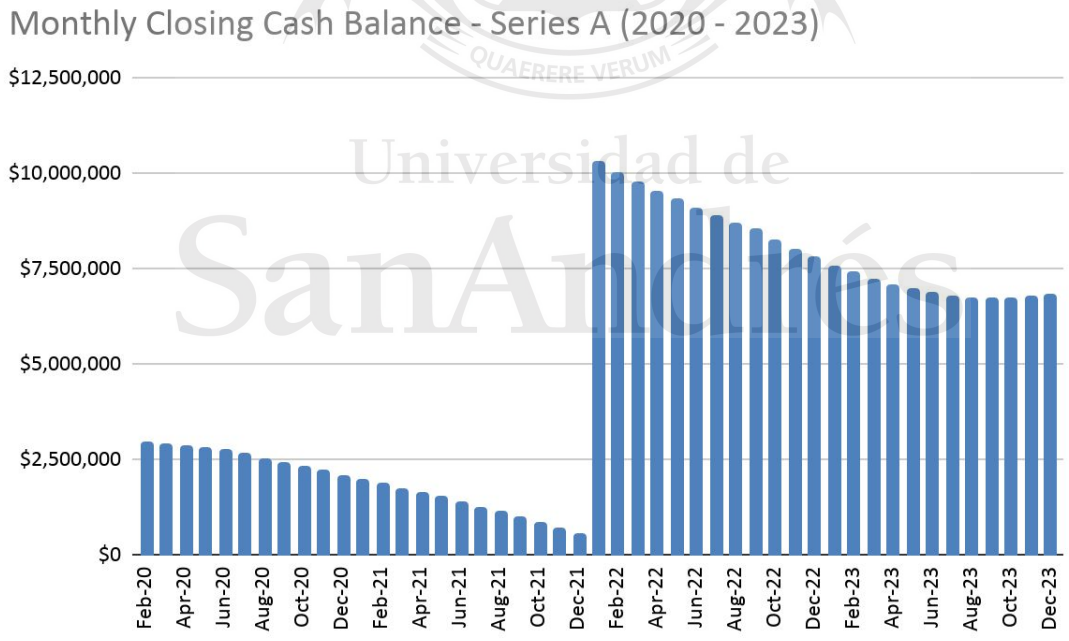
	2020	2021	2022	2023
CASH INFLOWS				
Investment	$ 3,000,000	0	$10,000,000	0
Credit Sales	$0	$0	$2,400,000	$7,201,200
Total Inflows	$ 3,000,000	0	$12,400,000	7201200
CASH OUTFLOWS				
COGS	$0	$0	$754,861	$2,264,960
Fixed Costs	$ 923,500	$ 1,546,000	$ 4,406,000	$ 5,828,000
Tax	$0	$0	$0	$51,637
Total Outflows	$923,500	$1,546,000	$5,160,861	$8,144,597
NET CASH FLOW	$ 2,076,500	-$1,546,000	$7,239,139	-$943,397
Opening Balance	$50,000	$2,126,500	$580,500	$7,819,639
Closing Balance	$2,126,500	$580,500	$7,819,639	$6,876,242

The following charts show the evolution of the Cash Flow for the 2020-2022 period. The management team should procure to secure the Series A funding before Dec 2021 as the cash in bank at that period would be at almost $580.000 and the runway for the company would be of few months (6) in case no additional funding is achieved.

[16] Series A is the next funding instance for a priced equity round (following a Seed round) in a startup/company. These rounds generally net between $5M - $15M depending on the industry. After Series A, common nomenclature for subsequent funding rounds is considered as Series B, C, D, etc.



The following graph shows the Monthly Cash Balance after a $10M capital injection in January 2022. As the company achieves break-even in 2023, the runway for the company extends and cash flow starts to become positive by Oct 2023.



Even though this model shows that the company would be achieving profitability in 2024, the company may opt in delaying profitability in pursuit of fast growth (rapid expansion in LATAM and the rest of the world). This could be achieved through a further series of Financing (Series B) which could be between $50-100M given current market comparables for biotech companies with $5-10M in revenue (projected 2023 figure).

Hiring

Caspr Biotech decided to locate its product and development offices in Argentina, given the ease of access to qualified biology and engineering human capital the company can access (primarily through researchers formed by CONICET). The company has elaborated a growth plan for 2020-2022 which includes the required human resources for the development and commercialization of it's products. The detail of hiring for each quarter can be found in the following table:

Overhead			
CEO	Hired	2019	FTE
CSO	Hired	2019	FTE
CRO	Hired	2019	FTE
Lead Scientist	Hired	2019	FTE
Bioinformatic	Hired	2019	FTE
Lead Sales Rep	Q2.2020	2020	FTE
Molecular Biologist	Q2.2020	2020	FTE(s)
Bioinformatic	Q2.2020	2020	FTE
COO	Q2.2020	2020	FTE
IP Specialist	Q2.2020	2020	FTE
Clinical Pathologist	Q2.2020	2020	FTE
Clinical Engineer	Q3.2020	2020	FTE
Director of Sales	Q3.2020	2020	FTE
Director of Operations	Q3.2020	2020	FTE
Director of Marketing	Q3.2020	2020	FTE
CFO	Q4.2020	2020	FTE(s)
Sales Rep (5)	Q1.2022	2022	FTE(s)
Area Sales Manager (X3)	Q1.2022	2022	FTE(s)
Biomedical Engineers (x3)	Q1.2022	2022	FTE
Customer Support (x3)	Q1.2022	2022	FTE(s)
Customer Success (x5)	Q1.2022	2022	FTE(s)
Operations (x10)	Q1.2022	2022	FTE(s)
HR (x2)	Q1.2022	2022	FTE(s)
Marketing (x5)	Q1.2022	2022	FTE(s)
Finance (x3)	Q1.2022	2022	FTE(s)
Software Engineers (x3)	Q1.2022	2022	FTE(s)
Regional Expansion Team (x40)	Q4.2022	2022	FTE(s)
Consultants	Outsourced	rced	Outsourced
Regulatory	Outsourced	rced	Outsourced

Additionally, aggregated figures can be obtained for this growth, as shown in the table below:

Category	2019	2020	2021	2022
New Hires in period	5	13	0	78
Headcount at end of period	5	18	18	96

Conclusion

Caspr Biotech is a startup which was founded at the conjunction of a group of scientists and a business entrepreneur. The company is addressing a growing market with innovative technology such as CRISPR. The need for their product is shown in the commercial interest Caspr has generated from other companies, researchers and hospitals.

As a general perspective, the success of the company will depend on execution, commercial efficacy, and funding efficiency. It is important to note that the company has centered its development schedule and objectives through a Venture Capital model. This model enables the company to delay profitability and commercialization perspectives in stake of prioritizing product development and innovation. This is a positive strategy as long as current Venture Capital tolerance for high risk (no revenue) companies remains vigent. Shifts in investment preferences (in terms of risk) from the Venture Capital market could limit the possibilities of subsequent funding in future instances for the company, and hence attempt against the success possibilities of Caspr Biotech.

Caspr Biotech is a positive case study of a *startup* as a vehicle for scientists to apply their basic research toward concrete product oriented applications, trying to solve the world's greatest problems.

Annex

Commercialization Strategy by Segment & Captured Market Percentage

Year		Cartridges Units Sold	POC Device Units Sold	Revenue - Cartridges (U$D)	Revenue - Phantom 1.0 (U$D)	Total Revenue (U$D)	% & Captured Segment
1	2020	0	0	$0	$0	$0	
2	2021	0	0	$0	$0	$0	
3	2022	200,000	2,000	$2,000,000	$400,000	$2,400,000	0.05 [AR] Agriculture
4	2023	600,000	6,000	$6,000,000	$1,200,000	$7,200,000	0.025 [BR,AR] Agriculture
5	2024	1,800,000	18,000	$18,000,000	$3,600,000	$21,600,000	0.075 [BR,AR] Agriculture
6	2025	5,200,000	52,000	$52,000,000	$10,400,000	$62,400,000	0.2 [BR,AR] Agriculture + NIPT
7	2026	12,500,000	125,000	$125,000,000	$25,000,000	$150,000,000	0.25 [BR,AR,MX] Agriculture + NIPT + Animal
8	2027	26,250,000	262,500	$262,500,000	$52,500,000	$315,000,000	0.075 [LATAM] POC Molecular Detection Market
9	2028	52,500,000	525,000	$525,000,000	$105,000,000	$630,000,000	0.15 [LATAM] POC Molecular Detection Market
10	2029	78,750,000	787,500	$787,500,000	$157,500,000	$945,000,000	0.225 [LATAM] POC Molecular Detection Market

MicroCart - Unit Reagent Cost

Component	Cost	Manufacturer	Type
Cas 12 Protein	<$0.01	Produced Inhouse	CRISPR Mix
RNAse alert	$0.02	IDT bulk 2 nmol tubes	CRISPR Mix
crRNA	<$0.01	1 NEB T7 transcription kit	CRISPR Mix
T7/rNTPs	$0.02	1 kit (Thermo)	CRISPR Mix
RNAse inhibitors	$0.15	1 vial (NEB Murine inhibitors)	CRISPR Mix
RPA	$0.43	1 kit (Twist Dx)	CRISPR Mix
Subtotal	$0.61		

MicroCart - Hardware / Paper Components

Component	Cost	Manufacturer	Type
LFIA	$ 1.80	USTAR	LF
Glass fiber	$ 0.02	Millipore	Cart-Component
MF1 blood separator	<$0.01	GE Life Sciences	Cart-Component
0.22 µm polyethersulfone (PES)	$ 0.03	Millipore	Cart-Component
Wax valve strips	<$ 0.01	Whatman & Xerox	Cart-Component
Cellulose L	<$ 0.01	Whatman	Cart-Component
polyethylene terephthalate (PET)	<$ 0.01	Apollo	Cart-Component
Laminate	$ 0.05	Swingline SelfSeal	Cart-Component
polystyrene gasket	$ 0.01	Lohmann Precision Die Cutting	Cart-Component
Double-sided adhesive	<$ 0.01	Silhouette	Cart-Component
Subtotal	$1.96		

Phantom 1.0 Device Components

Component	Cost / Unit (U$D)	Manufacturer	Type
nanosilver ink	$ 0.03	Novacentrix	Resistive heating
Kapton substrate	$ 0.45		Resistive heating
Glass fiber	$ 2.14	Microchip Technology	TCU
Pogo Pins	$ 3.96	Mill-Max Manufacturing Corp.	TCU
MLX90614	$ 44.34	Melexis Technologies NV	TCU
AP3429	$ 0.42	Diodes Incorporated	TCU
Micro USB Female	$ 0.46	Amphenol FCI	TCU
Green LED	$ 0.27	Lite-On Inc	TCU
DAC6311	$ 5.22	Texas Instruments	TCU
N-MOSFET	$ 1.77	Infineon Technologies	TCU
2.2µH Inductor	$ 0.24	Bourns Inc.	TCU
6-pin Female Headers, Right Angle	$ 0.66	Sullins Connector Solutions	TCU
8MHz Crystal	$ 0.83	EPSON	TCU
Tiny Rectangular Button	$ 0.56	C&K Components	TCU
22µF capacitor	$ 1.38	Samsung Electro-Mechanics America, Inc.	TCU
10µF capacitor	$ 1.26	Samsung Electro-Mechanics	TCU
100n capacitor	$ 0.70	Samsung Electro-Mechanics America, Inc.	TCU
22p capacitor	$ 0.30	Samsung Electro-Mechanics America, Inc.	TCU
10k resistor	$ 0.60	Stackpole Electronics Inc.	TCU
0.1Ohm resistor	$ 1.35	Panasonic Electronic Components	TCU
1k resistor	$ 0.40	Bourns Inc.	TCU
300k resistor	$ 0.10	Yageo	TCU
95.3k resistor	$ 0.10	Yageo	TCU
Printed circuit board (PCB)	$ 0.50		TCU
plastic housing	$ 1.89	Stratasys	Plastic housing
acrylic lid	$ 0.15	Shape Products	Plastic housing
Reusable Component Total	$70.08		

Caspr Team with Lino Barañao (Minister of Science, Technology and Innovative Production of Arg.) - September 2019

Goytia in IndieBio (Batch 8) DemoDay Presentation [June 2019]