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Bioceres: AG Biotechnology from Argentina

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ABSTRACT

In this case we present a business decision-making situation in which the CEO of an Argentine Ag Biotech company, Bioceres, has to decide the best way to commercialize a new drought-tolerant transgenic technology. The company was founded by twenty three farmers, who shared a common dream that Argentina could become a benchmark in the development of Ag biotechnology. The case has strategic and financial implications, as well as decision-making situation involving a joint venture with an American biotechnology company. It also introduces to discussion the business models of Ag biotechnology companies in developing countries.

Keywords. Business Case; Ag Biotechnology; Joint-Ventures; Business Models

1 Introduction

Back in February 2012 Federico Trucco, CEO of Bioceres, an Argentine ag-biotechnology firm with offices in the city of Rosario^{*}, was about to held a meeting with the board of directors of his company. The central issue of the meeting was the decision regarding the signature of a joint venture agreement with an American firm called Arcadia, for the development and commercialization of a new transgenic technology for soybean crops.

Bioceres managers had contacted their colleagues in Arcadia when the research institute of the company opened its new premises in December 2010, in the city of Rosario. This event was attended by many well-known personalities from the scientific, political and business arena in Argentina; and even though the Arcadia managers could not attend, they were able to come to visit the Argentine Republic some time afterwards, in April 2011. After meeting with the Bioceres managers and visiting the firm's facilities, they were very impressed by the infrastructure and the prestige/reputation of the company.

Arcadia saw in Bioceres a potential ally, due to its biogenetic know-how in soybeans and the patents they held in drought and salt tolerance technologies for soybeans. Bioceres, on the other hand, saw in Arcadia a company with a professional management team and expertise in ag biotechnology, as it had a sound background as the company that obtained the first three approvals from the American government for genetically modified organisms[†]. It also held several patents related to efficient usage of nitrogen and water. Furthermore, this company had the financial support of John Sperling, a professor who turned to

^{*} A city of one million people in the middle of the most fertile agricultural area of Argentina, known as the "Humid Pampa"; equivalent to the 'Corn Belt' in the US.

^{*} When the managers of Arcadia were working for Calgene, which produced the first GMO tomatoes.

be a billionaire when he created an on-line university[‡]. (For details about Arcadia, see **Annex 5.**)

After Arcadia managers' visit to Argentina, both companies started to develop a shared interest in working together. The topic that interested them most was the possibility of developing and commercializing biotechnological events to increase crop performance at a worldwide scale. With this goal in mind, they decided to explore the possibility of establishing a 'joint venture', a strategic alliance to set a company with resources both from Bioceres and Arcadia. This venture would be called "Verdeca", and would operate as a business unit for Bioceres Holding and Arcadia Biosciences.

The board had to evaluate this agreement, knowing that signing a 'joint-venture' agreement with Arcadia would allow them to become an 'international player' in the world of the ag biotechnology, which was not the most usual growth path for a company with the characteristics of Bioceres. This road implied some new risks, such as competing with a giant like Monsanto, which had in its pipeline similar events, plus the fact that they should share the potential profits that this technology could render. Why did they not license their patents to one of the 'big six' firms (Monsanto, Du Pont, Bayer, Syngenta, Dow, and BASF), and even if they would hand over some potential profits, they would be facing significant lower commercial and financial risks? After all, the world of ag biotechnology is dominated by a few large companies, such as Monsanto, Du Pont, Bayer, Syngenta, Dow, and BASF, with wealthy financial and technological resources.

Moving forward with the joint venture with Arcadia was an option that conveyed many challenges: Did Bioceres have the adequate skills at the scientific, management and commercial levels? Could they obtain the governmental regulatory approvals for their transgenic events in subjects such as 'environmental safety', and 'human and animal security' not only in Argentina but also in other countries? Did they have the financial resources to go through the different stages of this project? What did the stockholders think about this agreement, and how does it align with the strategy of the company? Could two companies from two countries with very different cultural background work together smoothly?

1.1 Bioceres Origins

Bioceres was founded in 2001 by twenty three stakeholders from the agricultural sector, and linked by their membership in a non-for-profit organization called AAPRESID, a pioneer institution in Argentina in the field of no-till farming and productivity. These first shareholders shared a common dream: that Argentina could become a benchmark in the development of ag biotechnology, and at the same time, that these inventions may lead to an increase in competitiveness. (For Bioceres history milestones, see **Annex 1**.)

It was established as an investment society focused on the creation, management and funding of ventures linked to the development of technologies, products and knowledge in ag biotechnologies and related fields. By the year 2012 it had 260 shareholders, most of them farmers, none of whom had more than 4% of the total stock package. (For Financial Information, see **Annex 2**.)

The business model of Bioceres, at the beginning, was similar to what is known as a 'pool': It consisted of the outsourcing of all the contributions of a biotech-based project, in which each participant contributed with some resource (inputs, land, funding, knowledge) and Bioceres focused on the management and coordination of all the components. Early enough they concluded that such model had an unavoidable flaw: it would prevent Bioceres from capitalizing from their 'failures'; this is, to learn from those initiatives that did not thrive in order to leverage that knowledge into other projects. This possibility was a key element in a biotechnology project, "as in biotechnology, just as in any other science, you learn from your mistakes; so you need to capitalize the failed projects to know what to do and what not to do in the future. In the 'pool' model, this knowledge was capitalized by the provider of the 'research services' but not by Bioceres, who was limited to the coordinating role"[§].

INDEAR

The change in their business model, due to the perception that the 'pool' model was no the most adequate, lead Bioceres to create its own research and development center; which they called Institute of Agro Biotechnology of Rosario (INDEAR). It became the heart of Bioceres, not only because it was their R&D arm to support the different projects, but also because it was the 'scientific service' area, which provided these 'high-end' services to other institutions and biotech companies. Bioceres developed the

⁺ He founded the for-profit University of Phoenix. See Wired "John Sperling Wants You to Live Forever", <u>http://www.wired.com/wired/archive/12.02/immortal_pr.html</u>

[°] Interview with the CEO.

capacities to manage these biotechnological processes cost-efficiently; other labs from public universities could not afford to do so.

As a payback for these services, the firm had the first option over the intellectual property of the project in which it participated. (See Glossary of technical concepts in Appendix.)

Through INDEAR, Bioceres could make strategic partnerships with other research groups, normally through 'public-private' agreements, which was a key feature to manage the risk these projects involved. By means of these partnerships Bioceres entered into research projects through INDEAR, obtaining a first option in those successful projects. This allowed them to have many projects with different profiles in terms of risks and timing, where they committed 33 cents for their 'scientific services' (the cost) provided and obtained 1 dollar (the market value) from their participation of the project. In this way they were able to mitigate the risks involved in the 'valley of death' of the biotechnological projects. In this way INDEAR was constituted as the "central node of biotechnological knowledge" of the firm, and allows Bioceres to access to many biotech projects developed by public labs, adding swiftly new projects for the short and long term; and thus gaining a scope of initiatives with different regulatory profiles, different timing and approval mechanisms. INDEAR is organized under four technological platforms:



The genomic and bio-information platform performs the sequencing of the deoxyribonucleic acid(DNA) and the information processing at a high scale. This allows accelerating the research projects, processing and sequencing the genomic information that is needed for the development of biotech events, and producing massive amounts of sequences of DNA that is provided for the different projects. The technology involved in this platform is 'state of the art' and unique in the country, therefore, participation in the R&D consortia with other public and experienced research groups becomes strategic.

The Synthetic Biotechnology and Metabolic Engineering platform develops genetically optimized organisms, which enables the production of high value compounds from very cheap raw materials with a low environmental impact. One example of this is the use/employment of glycerin as a raw material to obtain second-generation biofuels, and the production of bio-plastics such as the polyhydroxyalkanoates (PHA).

In the Molecular Biology and Routines platform the molecular analysis of transgenic events is performed, as well as the identification of genes of interest and the regulatory sequences. All this is done with the goal of generating new technologies oriented to improve the efficiency in the use of resources such as water, nitrogen, and phosphorus. This platform is also important to aid at the developmental stages of genetically modified crops. Finally, the Proteins Technology platform is responsible for the protein characterization of new products developed by INDEAR, and the purification strategies of the proteins produced in plants in the area of 'Molecular Farming'.

All these technologies are related to plant transgenesis, which is the process of introducing an external gene (called 'transgene') from the genome of one plant and incorporating into the genome of another, so that this plant will exhibit a new property and transmit this property to its <u>offspring</u>. <u>Transgenic</u> plants are able to express foreign genes because the <u>genetic code</u> is similar for all living organisms.

1.2 Description of the Holding Companies

Because of the change in its model, Bioceres became a cell-organized group, in which the cells (firms of the group) are part of the same body, Bioceres Holding. Being part of this body implied freedom to act, and at the same time, the need to act in a coordinated way: to know 'who we are', 'what we do', 'when we say yes and when no', etc.

"From an organizational point of view we can say that Bioceres is as an entire company on itself, as there is a core decision-making center with a CEO and 11 managers, common processes to all the business units, as well as a common philosophy and one group of shareholders"^{**}. However, the cell organization based on different companies allowed Bioceres to partition its assets, aiming at maximizing them. This is, the firm can serve different 'clients' from different industries from different 'counters': Those who are linked to seeds will be served from Bioceres Seeds; those related to energy, from another area and the bioreactors, from another, etc. (For the Organizational flowchart see **Annex 3**.)

The overall structure of the portfolio of the group is the following:



Bioceres Seeds

'Bioceres Seeds' is a seed company that develops and commercializes wheat, soybeans, corn, sorghum, and sunflower products for the Bioceres group. In the firm model, Bioceres Seeds is a key business to capture value from the biotechnological events that they produce. In this way, intellectual property is generated from the projects which are set in the different 'joint-ventures' that the firm holds with strategic partners. However, the next step is to make those projects profitable through 'Bioceres Seeds', which acts as an outlet for the event enabling Bioceres to obtain better deals with potential licensees of the technology. Additionally, Bioceres Seeds enters the market with an integrated and tangible product (the genetic material of the crop plus the transgenic event) which results in farmers willing to pay to get access to them.

SEMYA

SEMYA is a strategic alliance between Bioceres and a 'micro biology agricultural' company called Rizobacter. They intend to work together in an integrated development of biotechnological events, germoplasm, bio-fertilizers, and bio-pesticides, with the goal of achieving true synergy in seed treatment. These technologies help increasing the productivity of the crops, reduce the environmental impact, and improve an efficient use of resources.

SEYMA seeks to identify the 'microbiological characterization' of soils used to plant crops in order to sell a 'customized' product (seeds, bio-fertilizers, bio-pesticides)'. This means that the product is developed to match the microbiological characteristics of the soil, so that the farmer chooses his seeds according to the most appropriate attributes (drought tolerance, efficiency in the use of nitrogen, soil characteristics, etc.). In this way SEMYA and Bioceres Seeds complement each other: While Bioceres Seeds validates the model of a customized product, SEMYA helps protect the intellectual property.

INMET

INMET is a company focused on metabolic engineering: it uses bacteria as bio-reactors to produce compounds of commercial interest, such as those from low-cost raw materials. One example is the case of the bio-plastics, in which the chemical-based product is substituted by a biotechnology based alternative.

^{**} Interview with Bioceres CEO

Another example is the above mentioned: the use of glycerin for the production of second-generation biodiesel.

These types of technologies are the 'growth platforms' for the company: At the beginning of 2012 Bioceres focused on biotechnological products linked to the world of food, and these projects would mature as of2016. Those projects linked to biomolecules would be developed between 2012 and 2016, and those related to second-generation bioenergy platforms have a longer deadline, by 2020. (For Bioceres Patent families, see **Annex 4**.)

2 Funding the Research Projects

The portfolio of projects of Bioceres is divided in two types, according to progress:

- a) Projects already technologically developed that enter into the commercial stage.
- b) Projects in the developmental research or pre-competitive stage.

Among the first type of projects we can highlight the production of chymosin, obtained from safflower seeds, which is now-a-days at a 'national commercialization' stage and at a 'pilot plant scale'. Bioceres is searching to achieve an agreement with an international partner, to start the construction of a production facility with the goal of exporting chymosin globally. The transgenic event project for drought tolerance and salinity (called 'HB4'), which has several international patents, and is advancing in the subsequent steps of 'de-regulation' and 'commercialization' is also worth mentioning. These projects at the commercial stage should be financially evaluated just like any other investment project.

For the projects at a pre-competitive stage, Bioceres needs to use different financial tools in order to obtain funds from national and international institutions:

- The NRCⁱ They are 'non-returnable contributions' to technological companies, as subsidies granted by the Ministry of Science, Technology, and Productive Innovation in Argentina for those projects considered as 'innovative' and which involve new products, services and processes. Bioceres received its first NRC in 2005, in 2006 they got two more, and from 2008 onwards, between seven and ten each year for different projects. These grants involve 100-200 thousand –dollar subsidies.
- 2. Consortia: They are public-private associations of research institutions for large R&D projects with long execution times in the pre-competitive stages, at a national or international level. Up to now Bioceres has been involved in seven consortia: Three of which are at a national level and related to subjects including transgenic pastures, drought tolerance and salinity, and metabolic engineering for the conversion of glycerin into biodiesel, jet fuel, and potential applications to bio-pesticides, and bio-polymers. There are also two international consortia with the European Economic Community connected to projects related with Mediterranean pasture sequencing and the development of functional food (or nutraceutical, the introduction of vitamins, antioxidants, etc. into food products). Finally, we can mention the Mercosur Consortium to study the sequencing of the soybean genome, and another consortium with the Ibero-American Program for Science and Technology for Development, (CYTED, made up by institutions and companies from Ibero-American countries) for the sequencing of the 'common bean' (Phaseolus vulgaris L.).

3 Verdeca Project

The goals defined for the 'joint-venture' with Arcadia are the development, de-regulation, and commercialization of biotechnological events for the improvement of the soybean^{t†} in the five principal production markets: Argentina, Brazil, China, USA, and India, and two consumption markets: Japan and the European Union.

The key contribution of Bioceres in this agreement is its core transgenic technology: HB4®, which provides tolerance to draught and salinity. This transgenic technology has been developed not only for

⁺⁺Glycine max: It is a <u>plant</u> classified as an 'oilseed' legume, grown for its edible bean, especially as a cheap source of proteins to feed <u>livestock</u>.

soybeans, which is a more advanced stage of development, but also for crops such as corn, wheat, and alfalfa^{‡‡}.

Bioceres and Arcadia would participate in the 'joint-venture as a 50-50 percent agreement regarding the capital investment and the distribution of profits. They have committed to channel all their available technologies to soybeans, and also to contribute with 10 million dollars each, for the 'de-regulation' of their first products of this oilseed, the first of which is the HB4[®]. The contributions that each company would make to the joint-venture can be summarized in the following table (See Annex 6: Bioceres and Arcadia's Platforms.):

Bioceres	Arcadia
Among its 260 stockholders, most of them are farmers, producing soybeans in Argentina and Latin America in an area of approximately 2.5 million hectares	Experience management; most of them had worked in Calgene, the company that introduced the three first events for genetically modified foods.
It has its own seed company (Bioceres Seeds)	International relationships in the sphere of research and global commerce.
The HB4 transgenic technology (tolerance to drought and salinity), with proven effects on multiple field trials and in the initial stages of de-regulation	Knowledge about the 'de-regulation' process
It provides scientific services to the 'joint venture' through INDEAR	The NUE transgenic technology (nutrition use efficiency, especially for nitrogen)
	The WUE transgenic technology (water use efficiency)
	Animal nutrition technology

By means of this agreement, between Bioceres and Arcadia, Verdeca would intend to become an international provider of second-generation transgenic high quality events. Arcadia's portfolio includes, among others, the following technologies:

- Tolerance to drought and salinity;
- Nutrition use efficiency, especially for nitrogen (NUE);
- Water use efficiency (WUE)
- Technology for high quality animal nutrition

These technologies would be sold as a tangible product, bundled in the soybean seed. The first products to be sold would be those related with tolerance to drought and salinity for an estimated date of 2018, and the efficient use of nutrients and water for 2020. The product would be sold through their own channels: the seed network, direct sales to distributors and through licenses of the HB4 technology to the principal seed companies in the different international markets in which they may be operating.

The field trials made during three years validated the HB4 transgenic event, by which there were productivity improvements of an average of 15%, with 8% to 10% under low stress environments, and up to 30% under high stress conditions (See **Annex 9**: Commercial Plan for Soybean HB4).

The benefits of these productivity improvements could be captured in the price of the seed, multiplied by the percentage of producers who bought them. At a world level, the soybean has a market of 100 million

⁺⁺ http://www2.bioceres.com.ar/verdeca-next-generation-soybean-traits/

hectares, with a yield of around 250 million tones in production, mostly in USA, Brazil, and Argentina, which concentrates a 70% of all market. (See Annex 7: Soybean Markets.)

Having developed the technology, the next steps to get to the market are the 'de-regulation' or approval of the transgenic event by government organizations, the multiplication of the seed through agreements with other seed companies, and finally, the commercialization of the transgenic seed.

The 'de-regulation' process involves obtaining the approval by different government institutions, each one in the countries in which the seed or grain is produced and/or commercialized. The evaluation covers: product efficiency, environment impact, and food safety for animals and humans. More specifically, the evaluation involves aspects such as the genetic modification of the plant, the security of the proteins, and their levels of expression. There are also studies carried out regarding the 'substantial equivalence' of the crop compared to plants with no genetically-modified plants, the agronomic behavior of the crop, and the environmental impact of the crop grown at a larger scale.

The different stages of the 'de-regulation' take place at the same time as the development process of the product, in a period of time of up to four years. At the early stages of development the 'concept proof' in model plants is performed (this can be done without the need of any regulatory requirements). At the second and third stages, the validation of the proof of concept is applied to the crop of interest, using non-commercial varieties. At this point it is necessary to have regulatory authorities' permits cleared to proceed with the field trials, and the focus of the evaluation is centered on the environmental perspective. Having completed this stage, the output is assessed for food safety issues, which should render the 'food safety dossier' permit. As mentioned before, the whole field trial process is very demanding and must be done in each country in which the firm expects to produce and/or sell its product. (See Annex 8 for HB4 de-regulation process.)

This project will require roughly a 20-million dollar investment for the development and de-regulation stages, a 5-million dollar investment per year during four years (between 2012 and 2015). Once the de-regulation status for the transgenic event is attained by 2015, Verdeca shall sign agreements with seed companies, which will multiply the seed with the transgenic event HB4[®] for two more years (2016-2017). Eventually, at this point the financial cash flow would be leveled, as no further investing will be required; instead, significant incomes would come along.

Only after 2018 the product would be ready to be sold in the different markets in which Verdeca will operate. At this stage, it is important to consider the financial requirements in order to be able to commercialize its products on a global basis, in which Bioceres would concentrate on Latin American countries, and Arcadia in the USA and the other markets through local partners. At the same time, Bioceres intends to use the same transgenic technology HB4 in crops such as wheat, corn and alfalfa, in partnership with other companies, using the model developed with Arcadia, with new opportunities but also with extra financial requirements and different business models.

To be able to meet all these commitments regarding the development and commercialization of the HB4[®] technologies, Bioceres would need to resort to external shareholders and public funds. In the case these funding sources were not available, Bioceres counts on the commitment made from a strategic part ner to invest in this venture with the goal to close the financial gaps that may exist. Consequently, Bioceres's three principal funding sources for all HB4[®]-based projects (soybean, corn, wheat, and alfalfa) were the following:

- Capital Expansion: By scaling up stocks using a financial tool called PROFIET (Program for Promoting the Entrepreneurial Investment on Technology^{§§}) by which each new investor that purchases Bioceres stocks will be eligible to obtain refunds from the Ministry of Science, Technology, and Productive Innovation in Argentina. The refunds amount to 50% of the net value of their stock investment, payable with bonds to be used to cancel domestic taxes in Argentina. This mechanism is meant to raise 10 million dollars.
- Subsidies from the public sector: Around 1.25-million dollar subsidies for research and development projects.
- Strategic Partners: An investment by a strategic partner of around 8 million dollars.

^{§§} In Spanish, "Programa de Fomento a la Inversión Emprendedora en Tecnología", <u>http://www.mincyt.gob.ar/convocatoria/profiet-convocatoria-2013-7981</u>

4 Analyzing the Alternatives

When the CEO of the company entered into his office he was thinking about the implications of signing the joint venture agreement with Arcadia. On the one hand, he should evaluate all the aspects related with the project feasibility, its potential profits, the project time-to profit/timing required till the project would become profitable, against the risks it would involve. In one word: Can Verdeca be a profitable venture? They also had to analyze if Verdeca was the only option to capture value for the HB4 transgenic technology or were the other alternatives. If so, which were those? And eventually, what profits and risks would those alternatives entail? Finally, the question of the challenges that the partners in the joint venture should face in order to become successful should be addressed.

On the other hand, he should analyze the possibilities to use similar mechanisms to apply HB4[®] to the rest of the crops (wheat, corn, and alfalfa), funding these ventures, and finding appropriate partners and developing the profitability analysis of them. All these issues should be added to the complex array of factors to be considered in the evaluation of the 'joint-venture' with Arcadia, which the CEO of the company should make jointly with the Board of Directors during the meeting that would take place within few minutes

Note

This case is based on a true business situation, and was prepared to provide material for class discussion; it is not intended to illustrate effective or ineffective handling of a managerial situation. The author may have disguised certain data to protect trade secrets and preserve confidentiality. Interested instructors at educational institutions may request access to a teaching note and additional material by contacting the editor of the IJFSD.

Annex 1 Bioceres History Milestones

Year and Milestone

2001	2004	2005	2006	2007	2010	2012
Bioceres founded in the city of Rosario Argentina with 23 shareholders	Bioceres starts selling seeds Signature of the agreements to develop the HB4 technology Patent application in 7 countries for HB4	Signature of the agreements to develop the HB10 technology	The construction of INDEAR (Research Facility) starts Patent application in 8 countries for HB10	Constitution of 'Bioceres Holding' 129 shareholders	Inauguration of the INDEAR (research facility)	260 shareholders

Balance Sheet				
Year	2009	2010	2011	2012
Current Assets	1.6	3.0	3.3	5.3
Cash and Banks	0.3	0.5	0.0	0.1
Account Receivables	0.6	1.7	2.1	2.3
Other Account Receivables	0.2	0.6	0.9	1.8
Inventories	0.6	0.1	0.3	1.1
Other Current Assets	0.0	0.1	0.0	0.0
Non Current Assets	5.8	7.7	8.8	10.6
Investments	0.0	0.0	0.0	0.0
Account Receivables	0.0	0.0	0.0	0.0
Other Account Receivables	1.0	1.5	1.9	2.0
Other Assets	1.7	2.0	2.8	5.0
Inventories	2.7	3.8	3.8	3.5
Intangible Assets	0.4	0.4	0.2	0.1
Total Assets	7.3	10.7	12.1	16.0
Current Liabilities	1.7	2.6	3.5	6.0
Account Payables	1.3	1.7	3.0	4.4
Loans	0.0	0.3	0.3	1.1
Salaries Payable	0.1	0.1	0.1	0.2
Taxes Payable	0.0	0.0	0.0	0.1
Payment Invoice	0.0	0.0	0.1	0.2
Other Current Liabilities	0.4	0.4	0.0	0.0
Non-Current Liabilities	1.1	1.0	1.2	1.1
Loans	0.5	0.8	0.9	0.8
Salaries Payable	0.1	0.2	0.1	0.0
Taxes Payable	0.0	0.0	0.2	0.2
Other Non-Current Liabilities	0.4	0.0	0.0	0.0
Total Liabilities	2.8	3.7	4.7	7.1
Participation of third parties in Controlled Societies	0.2	0.3	0.3	0.3
Equity	4.4	6.7	7.1	8.6
Liabilities + Equity	7.3	10.7	12.1	16.0

Annex 2: 'Balance Sheet' and Loss and 'Profit Statement' (2009-2011) (in millions of dollars)

Loss and Profit Statement (in Millions of US dollars)				
Year	2009	2010	2011	2012
Revenues	1.1	2.2	5.3	7.7
Sales Costs	-1.0	-1.9	-3.5	-3.0
Subtotal	0.2	0.3	1.8	4.6
Results due to seed multiplication	0.2	0.2	0.0	0.0
Expenditures	-0.8	-1.7	-2.9	-4.2
Financial and holding Results				
Generated by Assets	0.2	0.3	0.5	0.0
Generated by Liabilities	0.5	0.4	-0.1	-0.5
Other Incomes and Expenditures	-0.3	-0.2	0.0	0.0
Profits before taxes	-0.1	-0.8	-0.8	0.0
Taxes	0.2	0.4	0.3	-0.1
Result participation of third parties in Controlled Societies	0.0	0.0	0.1	0.0
Profits	0.1	-0.3	-0.4	0.0

Annex 3: Organizational FlowChart



Name	General Description	Abstract	Inventors	Asigned to	Date
Cox-5c (Patent 7,598,368 USPTP)	Is a gene intron for increasing expression level in cassettes, plant cells and transgenic plants	An isolated DNA molecule for enhancing gene expression of a coding sequence, fragment, genetic variant, cassette, vector, cell, plant and seed containing said molecule, wherein the molecule comprises introns for induce an increase in the expression level of a transgene, useful in DNA constructions for transforming plant cells, wherein the cell or plant has a construction containing one of these introns under control of a promoter and upstream of a coding sequence stably integrated in its genome displaying higher expression levels as compared to non- transformed cells or plants, or cells or plants transformed with constructions that lack the inventive intron, wherein the sequences of 5'-non-coding sequences of the genes mentioned above also comprise promoters and exonic sequences in DNA constructions displaying synergism with the effect produced by the intron, and wherein the 5'-non-coding sequences of COX5- c genes lacking said intron promote tissue-specific expression in pollen when they are comprised in DNA constructions for plant transformation.	*Chan; Raquel Lia (Paraje el Pozo, AR) *Gonzalez; Daniel H. (Paraje el Pozo, AR) *Curi; Graciela C. (Paraje el Pozo, AR) *Cabello; Julieta (Paraje el Pozo, AR)	*Universidad Nacional Del Litoral (Rosario, Santa Fe, AR) *Consejo Nacional de Investigaciones Cientificas y Tecnicas (Rosario, Santa Fe, AR) *Bioceres S.A. (Rosario, Santa Fe, AR)	July 31, 2006
Hahb 4 (Patent Application 20070234439 USPTP)	DNA constructs that contain Helianthus annuus Hahb-10 gene coding sequence, method for generating plants with a shortened life cycle and a high tolerance to herbicidal compounds and transgenic plants with that sequence	The present invention refers to a gene from Helianthus annuus encoding a transcription factor that comprises a homeodomain associated with a leucine zipper. This gene is named Hahb-10. The transcription factor Hahb-10 can be used in DNA constructs to transform host cells and plants. Transgenic plants that overexpress this transcription factor are more tolerant to herbicides, and have a shorter life cycle.	*Chan; Raquel Lia (Santa Fe, AR) *Gonzalez; Daniel H. (Santa Fe, AR) *Dezar; Carlos A. (Santa Fe, AR) *Rueda; Eva C. (Santa Fe, AR)	*Bioceres S.A. *Consejo Nacional de Investigaciones Cientificas y Tecnicas *Universidad Nacional del Litoral	October 6, 2006
Hahb 10 (Patent Application 20070180584 USPTP)	Transcription factor gene induced by water deficit conditions and abscisic acid from Helianthus annuus, promoter and transgenic plants	A new transcription factor coding gene induced by water deficit or abscisic acid of Helianthus annuus, having a homeodomain associated to a leucine zipper, was characterized. The transcription factor is useful to be cloned in DNA constructions for transforming host cells and plants. The transgenic plants comprising the transcription factor gene are tolerant and resistant to harmful environmental conditions such as water stress and high salinity. A nucleic acid promoting sequence is also provided wherein the sequence is induced by water deficit or abscisic acid. Constructions, host cells and transgenic plants that comprise the transcription factor gene are provided.	*Chan; Raquel Lia (Santa Fe, AR) *Gonzalez; Daniel Hector (Santa Fe, AR) *Dezar; Carlos Alberto (Santa Fe, AR) *Gago; Gabriela Marisa (Santa Fe, AR)	*Bioceres S.A. (Santa Fe, AR)	January 20, 2010

Annex 4 Details of the Patents Granted to Bioceres

Annex 5: Arcadia Biosciences⁹

Arcadia Biosciences was founded in 2002 in Davis, California, to pursue agriculture-based business opportunities through the development of products and technologies that improve the environment and human health. Arcadia got started when Eric Rey, who had worked at Calgene¹⁰ for 17 years, met a billionaire named John Sperling. This wealthy man had made a fortune with the for-profit 'Phoenix University', and since then has used his money to promote animal cloning, human life extension, saltwater agriculture and shrimp farming in Africa, among others. Eric Rey and John Sperling got to talking about how genetically-engineered crops could benefit the environment, and Sperling became a majority shareholder of privately-held Arcadia.

The company's purpose, according to Eric Rey, who became its CEO, is to "use the tools of plant biotechnology, and point them at saving the environment." "When developing a new crop variety", he said, "if we can't put our fingers on an environmental benefit or a human health benefit, we won't do it."¹¹

The company's Nitrogen Use Efficiency (NUE) technology produces plants with yields that are equivalent to conventional varieties and has the potential to reduce the amount of nitrogen fertilizer. It has successfully transformed canola, Arabidopsis (model crop), to bacco (model crop) and rice with the NUE technology. Most crops are inherently inefficient in their use of nitrogen fertilizer applied to fields. Nitrogen fertilizer is a critical input to enhance crop yield. Approximately one-half of the fertilizer farmers apply is not used by the plant and either volatizes into nitrous oxide, a greenhouse gas 300 times more potent than carbon dioxide, or enters ground and surface water systems. Arcadia's proprietary NUE technology enables farmers to achieve high yields using significantly less nitrogen fertilizer.

Arcadia Biosciences' Salt Tolerance technology allows plants to produce normal yields and quality under saline conditions through saltwater irrigation. The technology is applicable to a wide range of crops, including corn, rice, soybeans, wheat, alfalfa, vegetables and turf. Its salt-tolerance plant technology improves farming efficiencies and reduces the need for fresh water by allowing increased use of salinized irrigation water. It holds a patent for its Drought Tolerance technology in the US, and in August 2013 a new patent has been issued by the State Intellectual Property Office of China.

Arcadia Biosciences' Human Health Technologies are GLA-Enriched Safflower Oil and Extended Shelf-Life Produce. Its product Sonova[™] GLA-Enriched Safflower Oil a potent source for use in supplements, because its seeds contain oil with as much as 40% gamma linolenic acid that is used in nutraceuticals and functional foods and imparting multiple therapeutic benefits. The company is developing new lines of wheat with reduced gluten - Celiac-Safe Wheat.

Arcadia has a very experienced management team:

- Starting with its CEO, Eric Rey, with a 20-year background focused on food, feed, and industrial products from agricultural biotechnology, who served as vice president of operations for the Calgene Oils Division of the Monsanto Company. During the 17 years he was at Calgene, Mr. Rey was responsible for the establishment and management of the company's operational, product development, and agricultural infrastructure.
- Its Chief Technological officer is Dr. Knauf, also with more than 20 years of experience in agricultural product and technology. Before joining Arcadia, he had worked in Anawah, Inc. (formerly Tilligen,

⁹ Sources: DataMonitor, Marc Gunther, EBESCO, Arcadia: Seed of Change, Harvard Business Case (9-709-019), Arcadia Web Page

¹⁰ Creator of the first GMO food introduced into the market, the "Flavr Savr tomatoes",

see Cargene Harvard Business Case (9-502-041)

¹¹ "Biotech food for a warming planet"

http://www.marcgunther.com/biotech-food-for-a-warming-planet/ July 27, 2011

Inc.), Calgene and Monsanto. In Calgene he was responsible for developing, partnering and managing projects that required the integrated efforts of biochemistry, molecular biology, cell biology and conventional plant breeding in affiliation with major consumer brand food companies.

- Wendy Neal is the Chief Legal Officer and Vice president with more than 10 years of experience in intellectual property and business law. She is skilled in developing and implementing worldwide intellectual property protection and enforcement strategies, negotiating technology-driven business transactions, strategic counseling in the development of patent and trademark portfolios, and related multinational prosecution.
- We should also mention Don Emlay, Vice President, Regulatory Affairs and Compliance, who totals30 years of experience in regulatory matters associated with consumer, industrial and transgenic plant products. For the past 17 years, he has worked exclusively in the plant biotechnology area. He led the team of scientists, lawyers and regulatory specialists that brought the first genetically engineered whole food through the USDA and FDA regulatory approval processes. Subsequent to completing the FDA consultation and USDA de-regulation processes for the FLAVR SAVR tomato, he led the completion of the processes for BXN Cotton (tolerant to the herbicide bromoxynil) and Laurate Canola (canola containing a high level of lauric acid).

Arcadia's headquarters are located in Davis, California, with additional facilities in Seattle, Washington, and Phoenix, Arizona, in the United States. It has around 85 employees, mostly researches based in Davis, and has an annual income of around 6 million dollars.



Annex 6 Bioceres and Arcadia's Platforms

Annex 7: Soybean Markets

In the 2011/2012 season Argentina produced around 40 million tons of soybeans, with an average yield of 2.2 tons per hectare. This value is lower than the average for the last three years, in which de average production was 47 million tones with an average of 2.6 tons per hectare. The harvested area is of 18 million hectares, with a growing tendency.

Season	Harvested area (Millions of Ha)	Yields (ton/ha)	Production (Millions of Tons)
2005	14.0	2.728	38.3
2006	15.1	2.679	40.5
2007	16.0	2.971	47.5
2008	16.4	2.821	46.2
2009	16.8	1.847	31.0
2010	18.1	2.905	52.7
2011	18.7	2.607	48.9

Harvested Area, Production and Yield for Soybeans in Argentina. (2005-2011)

Source: Ministry of Agriculture Argentina

The Argentine production represents around 18-20% of the world market; with a global total production in the last three seasons of 250 million tones approximately. The average planted area in the world for the last three seasons was of 100 million hectares

Harvested Area.	Production and	Yield for So	vbeans World	Market.	(2005 - 2011)
					(/

Season	Harvested area (Millions of Ha)	Yields (ton/ha)	Production (Millions of Tons)
2005	92.5	2.318	214.5
2006	95.3	2.329	222.0
2007	90.2	2.437	219.7
2008	96.4	2.398	231.2
2009	99.0	2.255	223.2
2010	102.6	2.583	265.0
2011	103.0	2.533	260.9

Source: FAO.

Another important player in the soybean market is Brazil, with an average production of almost 70 million tones as an average in the last three seasons. This represents a 27% of the world production and 55% of the South American production.

Season	Harvested area (Millions of Ha)	Yields (ton/ha)	Production (Millions of Tons)
2005	22.9	2.230	51.2
2006	22.0	2.380	52.5
2007	20.6	2.813	57.9
2008	21.2	2.816	59.8
2009	21.8	2.637	57.3
2010	23.3	2.948	68.8
2011	24.0	3.121	74.8

Harvested Area, Production and Yield for Soybeans in Brazil. (2005-2011)

Source: FAO.

Analyzing the regional markets in the world, the South American Market, with 136 million tons, and the North American with 87 million tons, represent 85% of the world production of soybeans. Thus, they are key markets for companies selling soybean seeds.

Season	Harvested area (Millions of Ha)	Yields (ton/ha)	Production (Millions of Tons)
2005	40.2	2.381	95.8
2006	40.7	2.437	99.2
2007	40.4	2.822	113.9
2008	41.4	2.765	114.6
2009	42.7	2.233	95.3
2010	46.0	2.886	132.8
2011	47.5	2.862	136.0

Harvested Area, Production and Yield for Soybeans South America. (2005-2011)

(*) Includes Argentina, Bolivia, Brazil, Colombia, Ecuador, Paraguay, Peru, Uruguay, Venezuela Source: FAO.

Harvested Area,	Production and	Yield for Soybeans	North America.	(2005-2011)
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Season	Harvested area (Millions of Ha)	Yields (ton/ha)	Production (Millions of Tons)
2005	30.0	2.889	86.7
2006	31.4	2.882	90.5
2007	27.1	2.785	75.6
2008	31.4	2.676	84.1
2009	32.3	2.940	94.9
2010	32.5	2.923	95.0
2011	31.3	2.789	87.4

(*)Includes USA and Canada Source: FAO.

Crops with HB4®		2012				2013			2014			2015				
		II	III	IV	Ι	II	III	IV	Ι	II	III	IV	Ι	II	III	IV
Wheat		Field trials Equiva		Equivale studie	nce Field trials #5		Dossi preparat	er ion	Regulatory			vevaluation				
Corn		Material Field preparation #		Field tri #3	als	Equivalence Field studies #		Field tri #4	als	Dossier preparation			Regulatory evaluation			1
Soybean		Field trial #4 Field tri #5		als	Analysis and preparati of the dossier			on	n Regulatory evaluation							
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	Stage 1: Proof of concept			Stage II: Early development			d	Stage III: Advanced development			Stage IV: Regulatory and prelaunch					

Annex 9: Commercial Plan for HB4[®] Soybean

Commercialization Prices for the HB4[®] Soybean according to the Characteristics of the Product

Product	Price (Dollars)	Reference	Unit	Description		
Basic	28.24	8.5% of the value of a ton of soybean	40-kg (*) Bag	Germoplasm with resistance to herbicides (RH)		
Basic plus treatment	31.64	A 3.40-dollar value for Fungicides and inoculants	40-kg Bag	Germoplasm with resistance to herbicides (RH) and inoculants and fungicides		
HB4® Product	55.49	Productivity increase of 15%, capturing 30% of this benefit	40-kg Bag	Germoplasm with resistance to herbicides (RH) With treatment and with gene HB4®		

(*) We estimate two bags of 40 kg per planted hectare of soybeans

Source: Commercial Plan of Bioceres

Annex 9: Commercial Plan for HB4[®] Soybean (continued)

Planted Area of Soybeans per Country. Potential Markets for Verdeca. Millions of Hectares 2011/2012 Season

Country	Planted Area
Argentina	18.67
Brazil	25.00
China	7.89
EEUU	30.35
India	10.27

Source: Foreign Agricultural Service, USDA

Appendix 10: Glossary of Biotechnological and General Concepts^{*}

- Abiotic stress: The effect of non-living factors which can harm living organisms. These non-living factors include drought, extreme temperatures, pollutants, etc.
- **Bacterium:** Common name for the class of unicellular organisms, without a distinct nucleus. Bacteria are prokaryotes, and most of them are identified by means of Gram staining (q.v.). Bacteria usually reproduce asexually, by simple cell division, although a few undergo a form of sexual reproduction, termed *conjugation*.
- **Bio-informatics:** The use and organization of information of biological interest. In particular, it is concerned with organizing bio-molecular databases, in getting useful information out of such databases, in utilizing powerful computers for analyzing such information, and in integrating information from disparatebiological sources.
- **Biotechnology:** The use of biological processes or organisms for the production of materials and services of benefit to humankind. Biotechnology includes the use of techniques for the improvement of the characteristics of economically important plants and animals and for the development of microorganisms to act on the environment.2. The scientific manipulation of living organisms, especially at the molecular genetic level, to produce new products, such as hormones, vaccines or monoclonal antibodies.
- Clone: A group of cells or organisms that are genetically identical as a result of asexual reproduction, breeding of completely inbred organisms, or forming genetically identical organisms by nuclear transplantation.
 2. Group of plants genetically identical in which all are derived from one selected individual by vegetative propagation, without the sexual process.
- **Chymosin** (or rennin): is an enzyme found in rennet. It is produced by newborn ruminant animals in the lining of the fourth stomach to curdle the milk they ingest, allowing a longer residence in the bowels and better absorption. It is widely used in the production of cheese.

^{*}Adapted from FAO: Food and Agriculture Organization of the United Nations

- **DNA:** The long chain of molecules in most cells that carries the genetic message and controls all cellular functions in most forms of life. It can also be explained as the information-carrying genetic material that comprises the genes.
- **Enzyme:** A protein produced in living cells, which, even in very low concentration, catalyzes specific chemical reactions but is not used up in the reaction.
- Gene: Conceptually, the unit of heredity transmitted from generation to generation during sexual or asexual reproduction. More generally, the term is used in relation to the transmission and inheritance of particular identifiable traits. Since the molecular revolution, it is now known that a gene is a segment of nucleic acid that encodes peptide or RNA.
- **Genetic Engineering:** Changes in the genetic constitution of cells (apart from selective breeding) resulting from the introduction or elimination of specific genes through modern molecular biology techniques. This technology is based on the use of a vector for transferring useful genetic information from a donor organism into a cell or organism that does not possess it.
- Genetic marker: A DNA sequence used to "mark" or track a particular location (locus) on a particular chromosome.
- **Genome:** The entire complement of genetic material (genes + noncoding sequences) present in each cell of an organism, or in a virus or organelle. 2. A complete set of chromosomes (hence of genes) inherited as a (haploid) unit from one parent.
- **Germplasm**: The genetic material that forms the physical basis of hereditary and which is transmitted from one generation to the next by means of the germ cells. The genetic material that forms the physical basis of hereditary, and which is transmitted from one generation to the next by means of the germ cells.
- **Herbicide resistance:** The ability of a plant to withstand herbicide. Herbicide resistance has been one of the early targets of plant genetic engineering. If a herbicide is sprayed onto a field planted with such resistant crops, then all the plants except the crop would be killed, thus providing an effective method of weed control without having to develop herbicides specific to each weed type.
- **Hybrid seed:** Seed produced by crossing genetically dissimilar parents. 2. In plant breeding, used colloquially for seed produced by specific crosses of carefully selected pure lines, such that the F1 crop displays hybrid vigor. As the F1 crop is heterozygous, it does not breed true and so new seed must be purchased each season.
- Joint Venture: A business arrangement in which two or more parties agree to pool their resources for the purpose of accomplishing a specific task. This task can be a new project or any other business activity. In a joint venture (JV), each of the participants is responsible for profits, losses and costs associated with it. However, the venture is its own entity, separate and apart from the participants' other business interests.
- **Marker-assisted selection:** The use of DNA markers to increase the response to selection in a population. The markers will be closely linked to one or more quantitative traitloci (q.v.).

Marker gene: A gene of known function and known location on the chromosome. cf genetic marker.

- Molecular biology: The area of knowledge concerned with the molecular aspects of organisms and their cells.
- **Molecular cloning:** The biological amplification of a specific DNA sequence through mitotic division of a host cell into which it has been transformed or transfected.
- **Molecular Farming:** It involves the use of plants, and potentially also animals, as the means to produce compounds of therapeutic value.

- **Molecular genetics:** The area of knowledge concerned with the genetic aspects of molecular biology, especially with DNA, RNA and protein molecules.
- **Molecule:** A unit of matter, the smallest portion of an element or a compound that retains chemical identity with the substance in mass.
- Mutagenesis Change(s) in the genetic constitution of a cell through alterations to its DNA.
- **Mutation:** A sudden, heritable change appearing in an individual as the result of a change in the structure of a gene (= gene mutation); changes in the structure of chromosomes (= chromosome mutation); or in the number of chromosomes (= genome mutation).
- **Protein:** A macromolecule composed of one to several polypeptides. Each polypeptide consists of a chain of amino acids linked together by covalent (peptide) bonds. They are naturally-occurring complex organic substances (egg albumen, meat) composed essentially of carbon, hydrogen, oxygen and nitrogen, plus sulphur or phosphorus, which are so associated as to form sub-microscopic chains, spirals or plates and to which are attached other atoms and groups of atoms in a variety of ways

Recombinant DNA The result of combining DNA fragment differen Bioceres History Milestones Annex 1 Bioceres History Milestones

Recombinant DNA technology: A set of techniques which enable one to manipulate DNA. An organism manipulated using recombinant DNA techniques is called a genetically modified organism (GMO). Among other things, recombinant DNA technology involves: <u>identifying genetical cloring genes</u>; - studying the expression of cloned genes; and producing large quantities of the gene product.

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- Patent Transgenic: An organism in which a foreign gene (a transgene) is incorporated into its genome. The transgene is present in both somatic and grm/ cells, is expressed in one or more tissues, and is inherited by offspring in a Medicinal ashform.
- Vector: An organism, usually an insect, that carries and transmits disease-causing organisms. 2. A plasmid or phage that is used to deliver selected foreign DNA for cloning and in gene transfer.
- **Water stress:** The condition when plants are unable to absorb enough water to replace that lost by transpiration. The results may be wilting, cessation of growth, or even death of the plant or plant parts.

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