Pharma-Biotech program 2011-2014

Results Report

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

This document is the result of evaluation of the Pharma-Biotech program sponsored by FARMAINDUSTRIA, which since 2011 has organized regular meetings between pharmaceutical companies, small new drug development companies and research centers, with the aim of exploring common interests and achieving potential collaboration agreements.

Interviewing and information collection directly from the participants was carried out over the months from December 2014 to February 2015.

During the four years the Pharma-Biotech program has been operating, 12 meetings have been held in which a total of 60 Spanish drug development entities have participated (including small biotech companies, research centers and hospitals), of which 51 (85%) were surveyed.

On the other hand, of the 33 pharmaceutical companies that have taken part in one or various of these 12 meetings, information was collected from 22 of them (66%) through two different surveys, one written and the other with a direct personal interview.

The entire project has been undertaken by the following team: Javier Villoslada (Formas Asesores), Amelia Martín Uranga (FARMAINDUSTRIA) and Javier Urzay (FARMAINDUSTRIA)

Both the interpretation of the results and the field work as well as the rest of the analysis and conclusions included in this report are solely those of the writers of the study and do not necessarily reflect the point of view of FARMAINDUSTRIA.

Madrid, June 22, 2015

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Contents

1 EXECUTIVE SUMMARY

The development of new drugs is currently immersed in a series of important changes that are related, among others, with the following aspects:

- The general reformulation in investments in R&D

- The expiration of patent rights for blockbusters.

- The change in focus towards drugs of biological origin.

- The ever more widespread trend to outsource part of research.

The interest of the pharmaceutical industry in finding new drugs of biological origin is growing, and it needs to do so while maintaining costs are not very high, making attractive the approach of finding products in development in research centers or small start-up companies, in order to reach effective collaboration agreements with them. In this way, a large economic gain can be generated for both the pharmaceutical company and the biotechnology company or research center, which, lacking the boost that can be provided by such an agreement, would have enormous difficulties to take the project to advanced phases of clinical research.

Spanish biotechnology companies, recently created start-ups, have also had difficulty in finding funding for their projects, risky and with a long maturity period, to which it should be added that many of the researchers who have created these companies, spin-offs of research institutes, have initially sought (and been satisfied with) mostly public funding, since the way of getting it was familiar to them, the entrepreneurial ambition was not high and they sometimes saw the company as a "low intensity" business mechanisms still closely-linked to their institution. The sum of both effects is that currently in Spain there are more than a hundred small biotech companies with in many cases interesting and promising projects but that do not have the necessary financial resources to continue with preclinical trials and even less so with the full-scale clinical trials that are required for these developments to finally reach the market.

In this context and within the framework of the Spanish Technological Platform for Innovative Medicines, FARMAINDUSTRIA launched the Pharma-Biotech program in 2011 with the aim of providing the necessary information and promoting potential cooperation agreements between pharmaceutical companies, small Spanish biotechnology companies and research centers, to take advantage in the best way possible of the results of the research conducted in research centers and hospitals, and the positive preclinical findings that were obtained by these small start-ups.

The reception by pharmaceutical companies of this initiative of FARMAINDUSTRIA has been excellent from the start of the program, and 33 of them have actively participated in one or various of the 12 meetings carried out since then.

But equally extraordinary has been the receptiveness and interest shown by small Spanish biotech companies and research centers and hospitals working actively on the development of new drugs, systems of vehiculization of drugs to the focus of the disease, or final implementation of new and effective diagnostic or prognostic kits. The result of this has been the submission to the program of 357 R&D projects, which have been carefully analyzed to ensure that they are able to fulfill the expectations of interested pharmaceutical companies to optimize the effort to be devoted by each member of the project.

A total of 60 entities, including companies, research centers and hospitals, have submitted 86 products over these four years from 2011 to 2014. Most of these products have so far reached different stages in the process of interaction with pharmaceutical companies, from the most basic, which consists of making known their developments and the stage of development they are in, as well as their most relevant innovative qualities, to the most complex, which is reaching the stage of signing a complete agreement for technical, industrial and commercial cooperation. Between the two extremes, the scheduling of new meetings, more detailed presentations, or follow-ups subsequent to each meeting.

The objective of the program is not simply to add up cooperation agreements, but to create favorable conditions so that these agreements can be implemented over time, on the basis of:

- identifying real needs which exist,

- seeking, processing, and providing the appropriate information,

- generating the atmosphere of trust essential for effective and realistic cooperation.

After four years, twelve meetings, 86 projects and 93 agents involved, this document proposes to offer a general review of what has been done up to the moment, permitting, based on the experience gained, to set new goals for the next actions that need to be addressed in the service of the pharmaceutical industry and hence of the Spanish biotechnology sector, in the area considered here.

This program should continue because it favors a fluent development of the innovation ecosystem in the pharmaceutical sector to the extent that it contributes to the generation of beneficial intersections between the main agents involved.

2 THE PROGRAM

2.1 Genesis and development

In July 2010 FARMAINDUSTRIA presented a **study** on *Funding difficulties of recently created innovative companies in the health area*, whose conclusions and recommendations included some proposals for action aimed at promoting the transmission of information of "business value" between national and multinational pharmaceutical companies and small innovative companies recently created in Spain that could offer promising developments of new medicines.

For this, it was proposed to implement a simple pilot program capable of **facilitating personal meetings** between executives and managers of the **pharmaceutical industries and start-up** companies directly involved in the scientific-technological field related to human health, with the idea of simplifying communication channels and bringing closer supply and demand.

Thus, in November of that same year, FARMAINDUSTRIA, taking advantage of the impetus provided by the Spanish Technological Platform for Innovative Medicines, launched the **Pharma-Biotech program** with aim of contributing to closer ties between the pharmaceutical industry and the Spanish biotechnology sector.

The initiative sought from the start, through interactive meetings with a predetermined number of participants, to allow previously selected Spanish biotechnology companies to present to interested pharmaceutical companies **products in development with sufficient potential** (innovative, effective, protected) that represent an **opportunity of cooperation** to be explored by both parties.

Over the length of **2011**, four meetings were held (two in Madrid and two in Barcelona) each focusing on specific therapeutic areas: central nervous system, oncology, inflammation, dermatology, and respiratory system.

In **2012** three more meetings were held, one in Zaragoza and another in Bilbao (BioSpain), including drug developments carried out by public research entities, thereby broadening slightly the focus that had originally been placed exclusively on start-up companies. This diversification was very well received by the participating pharmaceutical companies, who had unanimously expressed interest in the submission of projects by both companies and public research groups, provided they were selected according to similar quality criteria.

In **2013** three new meetings were held, two in Madrid and another in Barcelona. The first two were focused on oncological therapies and the central nervous system respectively, whereas the third focused on cardiovascular disorders and autoimmune diseases.

Finally, in **2014** two new meetings were organized, one at the headquarters of FARMAINDUSTRIA in Madrid and the other in Santiago de Compostela (which was the twelfth of the program), taking advantage of the framework of the BioSpain 7th International Meeting on Biotechnology.

While in 2012 the search for new drugs in development was expanded to public and private biomedical research centers (thus going beyond the initial approach that was focused on small start-up companies), in 2014 the range of opportunities was expanded again by inviting also hospitals with highly qualified research groups working very close to medical practice.

Each meeting is configured as an individualized forum where it is sought to create a sufficient **atmosphere of interaction** to allow identification of an added value derived from the exchange of information between biotechnological demand and supply of a highly innovative and differential content in the field of new therapies and innovative drugs.

In this context it is of the utmost importance to continuously verify the extent to which pharmaceutical companies and proposing organizations (companies and research centers) perceive that their participation in the initiative has an effective value and how this perception evolves over time. To provide this information, participants are requested to complete a brief questionnaire after each meeting. The results obtained are later analyzed and compared.

Thus, in October 2013 a series of interviews were conducted with 22 pharmaceutical companies to collect first hand information about the added value this initiative represents for the industry and how it should move forward. All the companies surveyed expressed their satisfaction and interest in continuing to hold these meetings.

Similarly, in November 2014 an in-depth survey was initiated, encompassing all research centers, hospitals and biotech companies who participated in any of the twelve meetings carried out, to collect the necessary information to make a brief analysis of the tangible and intangible results of the Pharma-Biotech program, which will complete its fifth year of operation this year in 2015.

At each meeting there are on average ten to fifteen pharmaceutical companies participate and six to eight new drug projects are presented that have been previously checked to ensure they fulfill seven minimum criteria, which are the following:

1. therapeutic area of interest;
2. innovative mechanism of action;
3. degree of differentiation from other developments or existing products;
4. state of progress in development of the drug;
5. type of product (drug, release system, biomarker, etc.);
6. status of industrial protection;
7. interest of presenting entity in collaborating with the pharmaceutical industry.

In the preliminary phase to the holding of each meeting the projects most closely matching the above criteria were selected and an executive summary was prepared and sent to all pharmaceutical companies, so that, based on the proposed presentations, they could decide on their specific interest in participating in one meeting or another. This summary was written in English to facilitate its internal circulation within multinational pharmaceutical companies that have their center for evaluation of new drugs outside of Spain.

The document summarizing the content of each meeting is distributed in English at least three weeks in advance to potentially interested pharmaceutical companies, later requesting by email or phone their decision to participate or not based on the scope and content of the six to eight projects proposed for presentation at the meeting.

Organization of the meeting is then completed when the information about the interested pharmaceutical companies and the researchers who will present their respective projects is finalized, so that each meeting is considered of a restricted nature in which the previously announced content will be discussed.

The **agenda of each meeting** is organized around two blocks of 3 to 4 presentations with a duration of 20 minutes plus 10 minutes of questions for each presentation, with an informal interaction time before and after each block lasting 30 to 45 minutes.

A **uniform structure** is maintained for the format of all presentations, which facilitates following the key aspects to be highlighted of each project that are of interest to the pharmaceutical industry. The format contains the following points in this order:

- ***The Institution***
  - *Organization*
  - *Team*
  - *Pipeline*
  - *Other projects*
- ***The Product***
  - *Target Indications*
  - *Innovative mechanisms of action*
  - *Differential features facing the market*
  - *Current status of development*
  - *IPR protection*
  - *Pitfalls & Risks to be considered*
- ***Partnering Opportunities***

In addition to inform contacts between all attendees, some individual meetings are organized at the time or for later days and a brief evaluation questionnaire is handed out to collect the participants' opinions. This questionnaire basically covers the following aspects:

- General satisfaction with conduct of the meeting
- Degree of novelty perceived for each project presented
- Specific interest that each project could have for the pharmaceutical company
- Projected change the interest of each project could have in coming months
- Perception about the technical and financial risks or the low rate innovation of each project
- Suggestions to improve organization of forthcoming meetings

The main indicator of success that is sought, though not in the immediate term, is the **actual number of projects** presented that generate a genuine **technical and business interest** in pharmaceutical companies and, ultimately, if as a result of this initiative negotiations have been initiated for the signing of effective **cooperation agreements**.

For the group of the twelve meetings organized to date, the overall degree of satisfaction of all participants (pharmaceutical companies and biotech companies presenting projects) was very high, exceeding on average 8 points out of a maximum score of 10.

Of the participating pharmaceutical companies, 15 have shown **interest in some of the products in development presented**, which at first glance allows us to establish the good reception this experimental action is achieving.

Additionally, it can be noted that at least four companies associated with FARMAINDUSTRIA are completing or have **completed cooperation agreements** related to some of the products in development presented at the meetings.

Whenever possible it is attempted that the meeting is held in a specific therapeutic area because it is easy in this way for all the projects presented to be of interest for all the pharmaceutical companies attending. This is always done when new drugs in **oncology** or in the **central nervous system** are addressed. But in the case of other therapeutic areas, such as infection, nephrology,

pneumology, or cardiology, it is difficult to bring together a sufficient number of projects of sufficient interest to complete a meeting, and in such cases, it was opted to have a mixed agenda.

The therapeutic area addressed in each meeting together with the date and location where it was held are summarized in the following table.

Meeting	Date	City	Framework	Therapeutic area
Meeting 1	Feb-11	Barcelona	Farmaindustria HQ	Central nervous system
Meeting 2	Apr-11	Barcelona	Farmaindustria HQ	Oncology
Meeting 3	May-11	Madrid	Farmaindustria HQ	Oncology
Meeting 4	Jul-11	Madrid	Farmaindustria HQ	Several areas (1)
Meeting 5	Mar-12	Barcelona	Farmaindustria HQ	Several areas (2)
Meeting 6	Jun-12	Zaragoza	Aragonés Health Service	Several areas (3)
Meeting 7	Sep-12	Bilbao	BioSpain 6th int'l meeting	Oncology
Meeting 8	May-13	Madrid	Farmaindustria HQ	Several areas (4)
Meeting 9	Jul-13	Barcelona	Farmaindustria HQ	Central nervous system
Meeting 10	Nov-13	Madrid	Farmaindustria HQ	Several areas (5)
Meeting 11	Jul-14	Madrid	Farmaindustria HQ	Several areas (6)
Meeting 12	Sep-14	Santiago de Compostela	BioSpain 7th int'l meeting	Several areas (7)

(1) Respiratory, Inflammatory, Infectious, Nephrology and Dermatology Diseases
(2) Inflammation, Infection and Respiratory System
(3) Oncology, hepatitis C, pulmonary fibrosis and bactericides
(4) Oncology, tuberculosis and sleep disorders
(5) Autoimmune and cardiovascular diseases
(6) Inflammatory disease, autoimmune disease and oncology
(7) Central Nervous System and Oncology

The number of participants per meeting as well as the number and origin of the projects presented are listed in the following table.

Meeting	Number of Projects presented	New (N) Revised (R)	Research centers and hospitals	Small biotech companies	Participating pharmaceutical companies
Meeting 1	6	6 N / 0 R	0	6	19
Meeting 2	8	8 N / 0 R	0	8	13
Meeting 3	7	7 N / 0 R	1	6	14
Meeting 4	9	9 N / 0 R	0	9	14
Meeting 5	7	7 N / 0 R	4	3	14
Meeting 6	5	4 N / 1 R	3	2	6
Meeting 7	6	6 N / 0 R	0	6	Open meeting
Meeting 8	6	3 N / 3 R	1	5	12
Meeting 9	7	5 N / 2 R	4	3	7
Meeting 10	7	7 N / 0 R	5	2	10
Meeting 11	8	7 N / 1 R	7	1	10
Meeting 12	10	7 N / 3 R	4	6	Open meeting

In summary, a total of **86 projects were presented**, of which 76 were new and 10 were proposed again some time after their first presentation after identifying significant advances since the first time. Projects were presented by **37 small biotech companies** and **23 research centers** and **hospitals**. Finally, a total of **33 different pharmaceutical companies**, both national and foreign, actively participated in the meetings, many of which were present at several meetings, with an **average of 12 participating pharmaceutical companies** per meeting.

2.2 Proposals analyzed and projects presented

One of the most significant values of the program, according to the opinion expressed by representatives of the pharmaceutical companies attending the meetings, is the **process of identification and selection of proposal** with sufficiently attractive medium-term business potential.

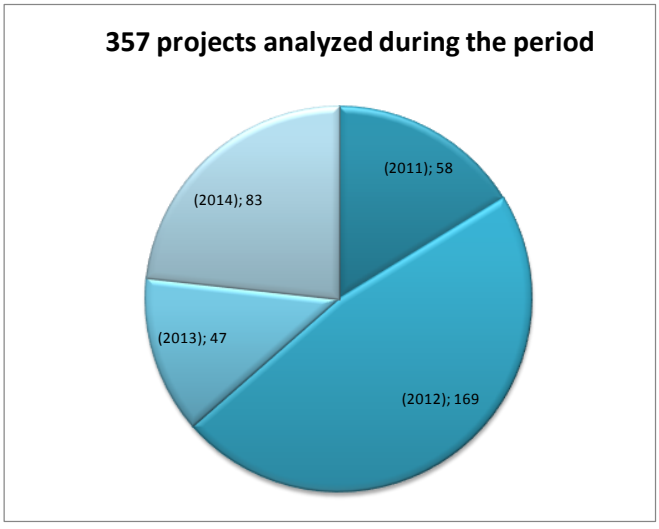
Each year the FARMAINDUSTRIA work team seeks, receives, and analyzes numerous projects in development from both small biotech companies and research centers and hospitals. This is implemented via a permanently open **electronic window** on the website of the innovative medicines platform *www.medicamentos-innovadores.org*, where any biotech company or research group can submit a development proposal in progress for its analysis.

In addition, the team has meetings and **regular contacts with OTRI** (Research Results Transfer Offices) of universities, research centers and hospitals, and other facilitator agencies, to be acquainted with the technological offering in the human health sector that each institution has available for presentation, taking into account the seven main selection criteria discussed in the previous section.

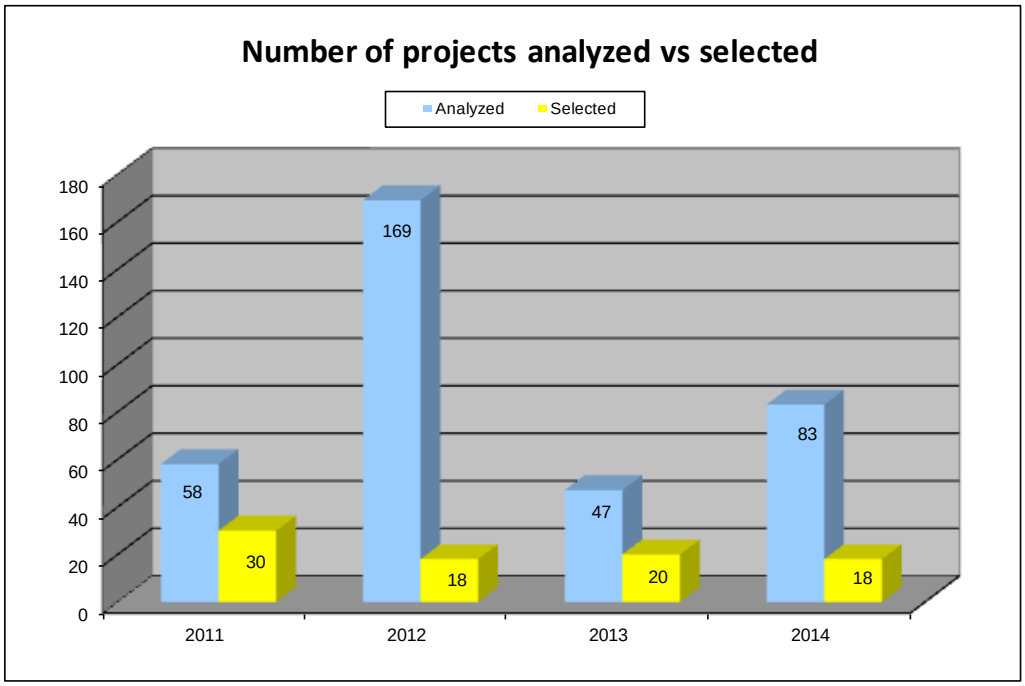
Every time a proposal of intent is received, a brief questionnaire is sent from FARMAINDUSTRIA to the interested party to make an initial evaluation by both about the project's potential to generate the interest of the pharmaceutical industry. When the questionnaire is returned, the status of the project is evaluated in terms of its actual degree of innovation, state of development, therapeutic area, patents and industrial protection. If the initial expectations are promising, a first face-to-face meeting is arranged with the researchers in order to specify in more detail the most critical aspects of the project and the key factors for its advance towards clinical phases. From this point on, and depending of the result of this meeting, the agenda is organized for each project presentation meeting.

As a result of this meticulous work of identification and selection, up to December 2014, **357 potential projects** were analyzed, of which finally **86 were selected** to participate in the different meetings organized (24%).

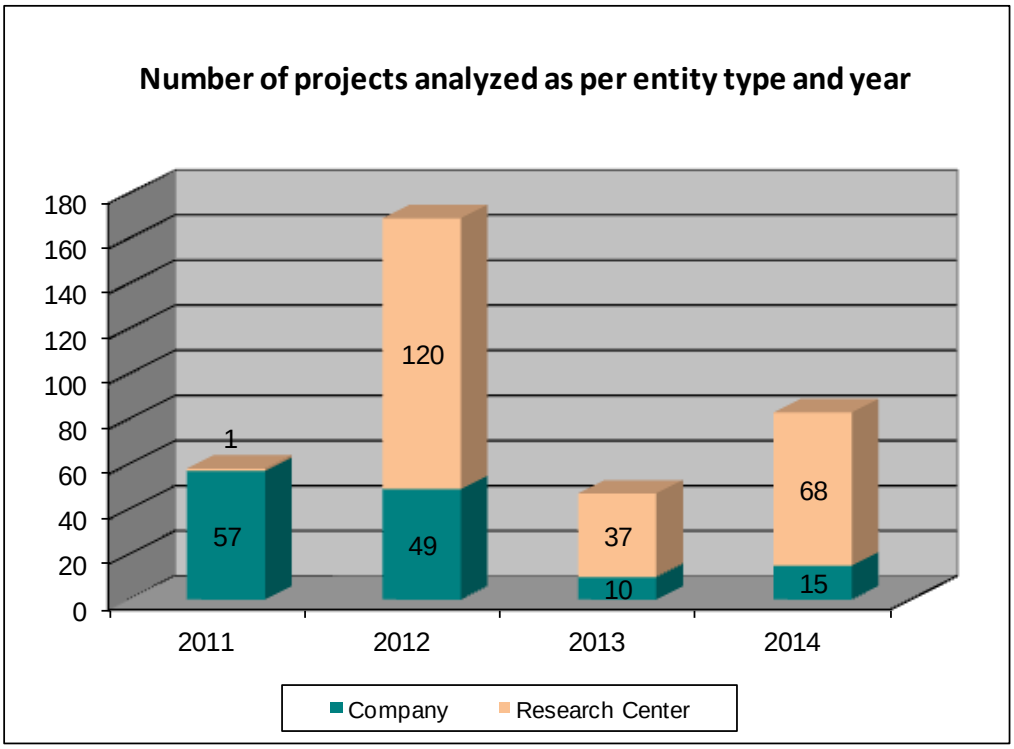
Some data on the number of projects analyzed and presented according to various categories is shown in the following charts.



A breakdown of the total number of projects received and selected for presentation within the program reveals that in 2012 was the year in which by far the largest number of proposals were received. This can be explained by the fact that 2012 was the year that reception was opened to proposals from research centers, which resulted at that time in a large injection of ideas and projects to be analyzed.



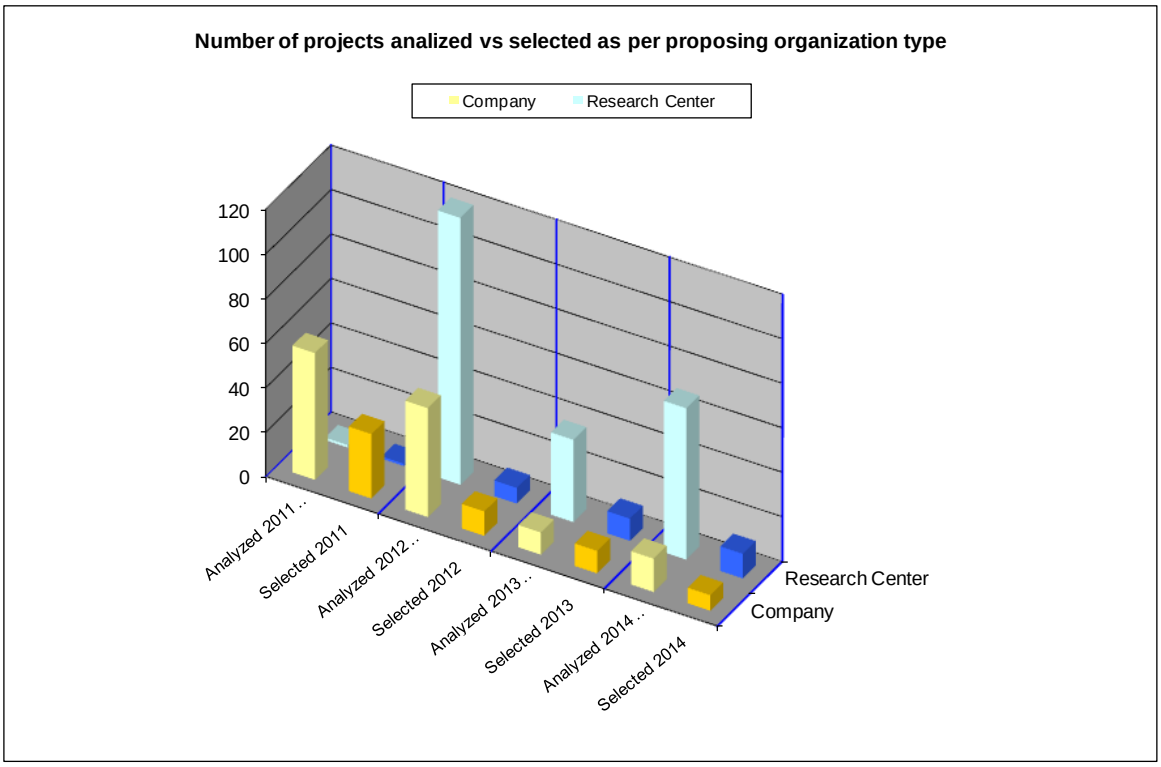
In particular, as shown in the following chart, while the number of proposals analyzed from small biotech companies remained practically constant in 2011 and 2012, those from research centers accounted for the majority of new proposals received in 2012.



In 2013 there was a sharp decline in the number of proposals received and analyzed, mainly because the large influx of proposals received in 2012 left a remainder to be used in the meetings scheduled for the following year. However, it is also true that after the first massive collections of proposals, the number of research projects not yet analyzed and reviewed decreased steadily, most likely as a result of the sharp drop in funding of biomedical research that has been occurring since the economic and financial crisis took hold of the budgets of institutions and companies.

On the other hand, it should be clarified that the number of projects selected for presentation at meetings decreased from 30 in 2011 to 18 in 2012, which was due to the fact that four meetings were organized in 2011 and only three in 2012, while maintaining the average of 6 to 8 projects to be presented at each meeting.

The ratio of proposals received to proposals approved is significantly different depending on their origin, as can be seen in the following chart.

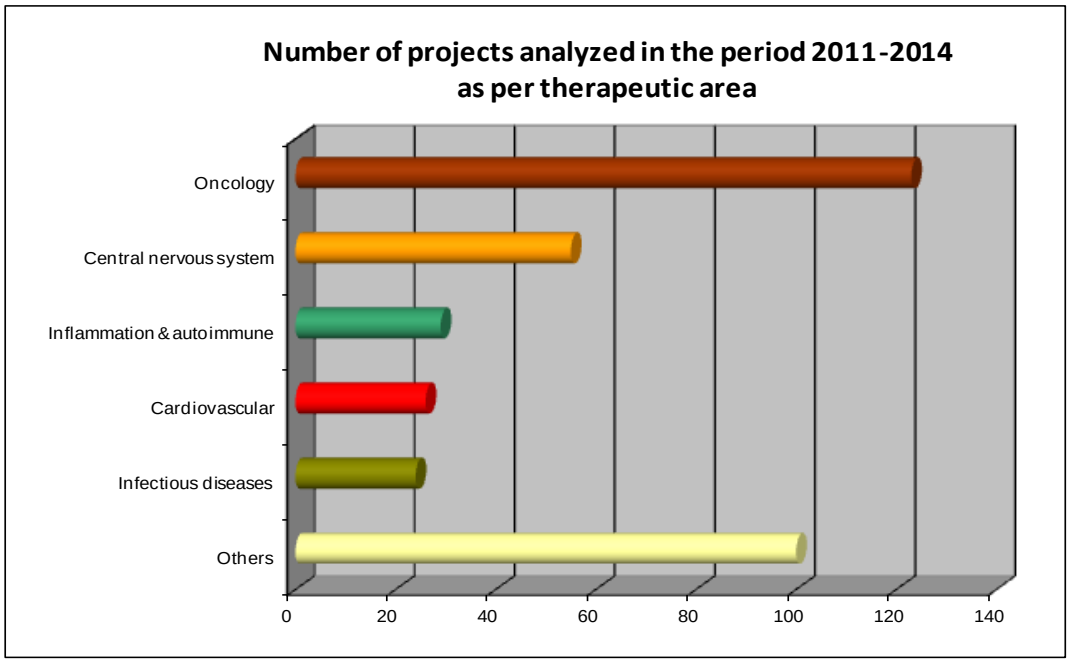


	2011		2012		2013		2014	
	Analyzed	Selected	Analyzed	Selected	Analyzed	Selected	Analyzed	Selected
Companies	57	29	49	11	10	10	15	7
Research centers	1	1	120	7	37	10	68	11
TOTAL	58	30	169	18	47	20	83	18

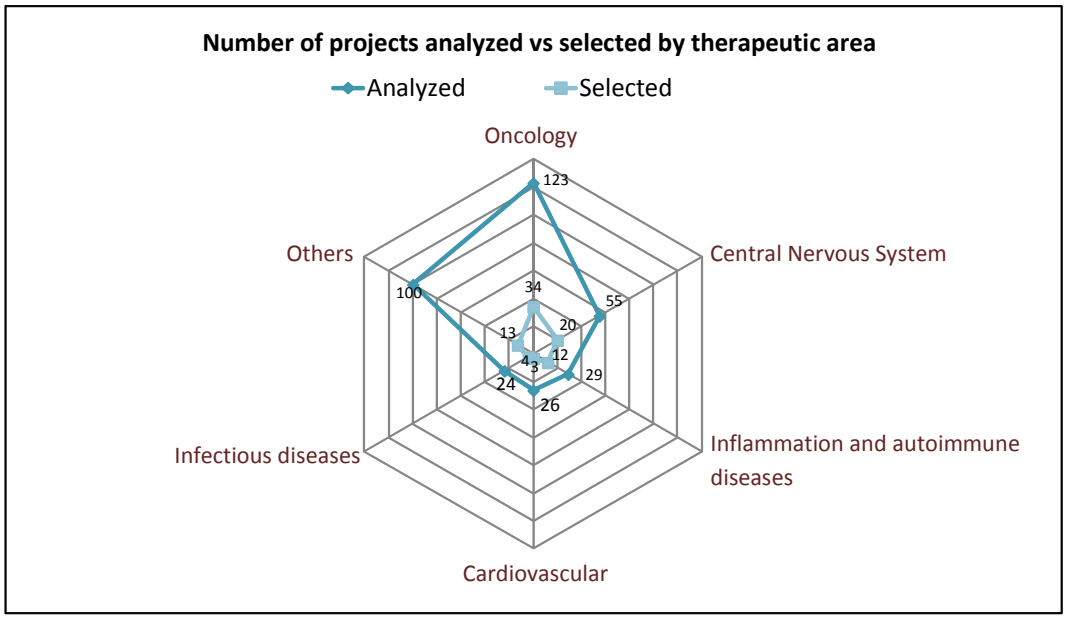
Over the four years of activity, **44% of the projects proposed by companies** were selected and **13% of projects proposed by research centers and hospitals**. There are two reasons to explain this difference: the first and most important reason is that companies generally show a considerably higher degree of development in their research projects than research centers and

hospitals whose projects are usually in more premature phases. The second reason is that while companies usually propose specific projects related to a single product, research centers may sometimes propose different research projects within the same family of compounds, and while they increase the number of projects analyzed, they end up presenting only one of them, generally the most advanced one.

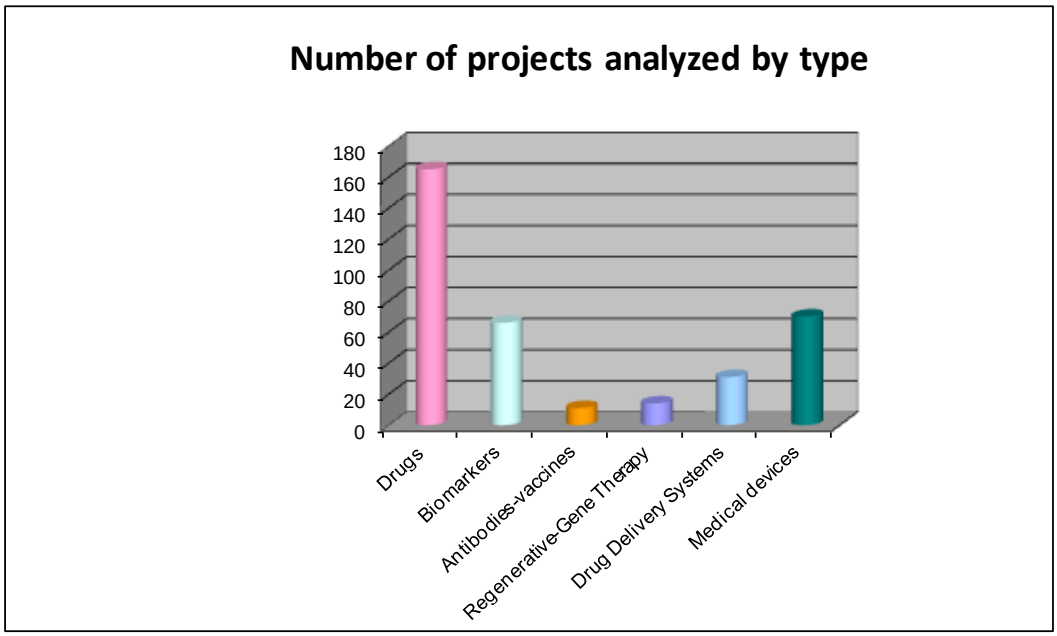
Another point is interest is to determine which **therapeutic areas** are covered by the projects analyzed and presented. It can thus be seen in the following chart that cancer encompasses by far the largest number of the proposals received, followed by drugs related to the central nervous system.



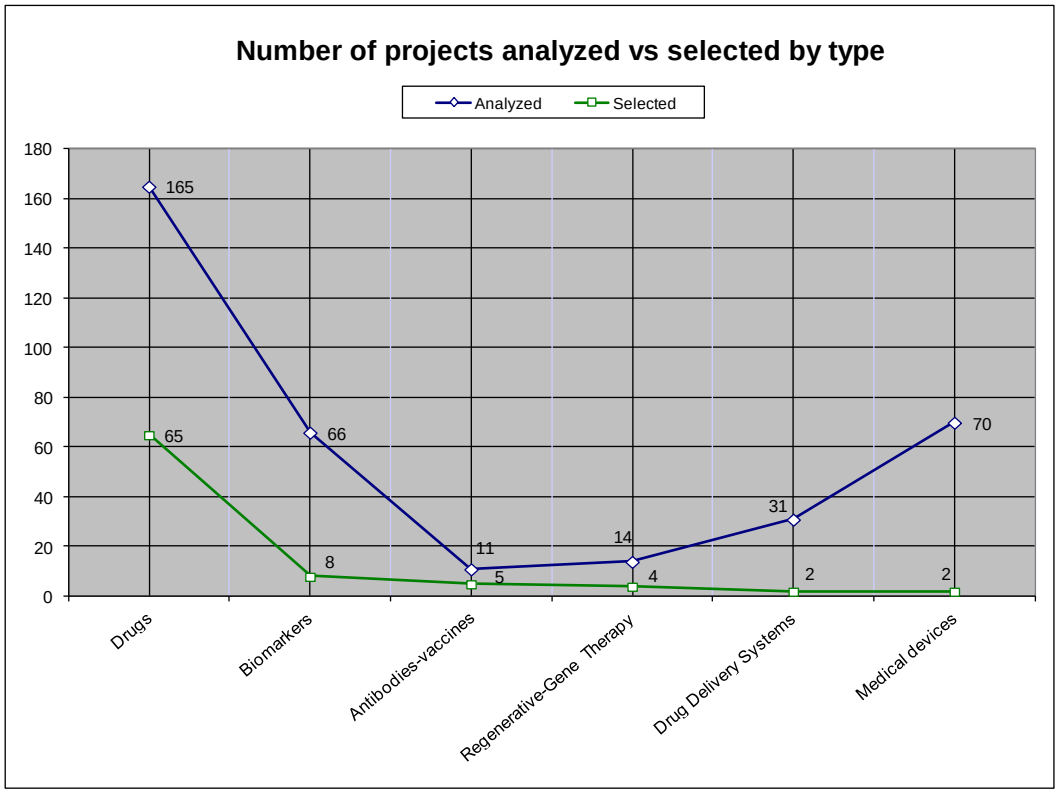
The projects selected for presentation at the meeting follow the same order, the largest number corresponding to oncology (34) followed by the central nervous system (20) and inflammation (12).



Finally, the following chart provides the distribution of the proposals received and analyzed according to the **type of product** involved, distinguishing between drugs, biomarkers, vaccines and antibodies, gene therapy and cell therapy, drug release systems and medical technologies.



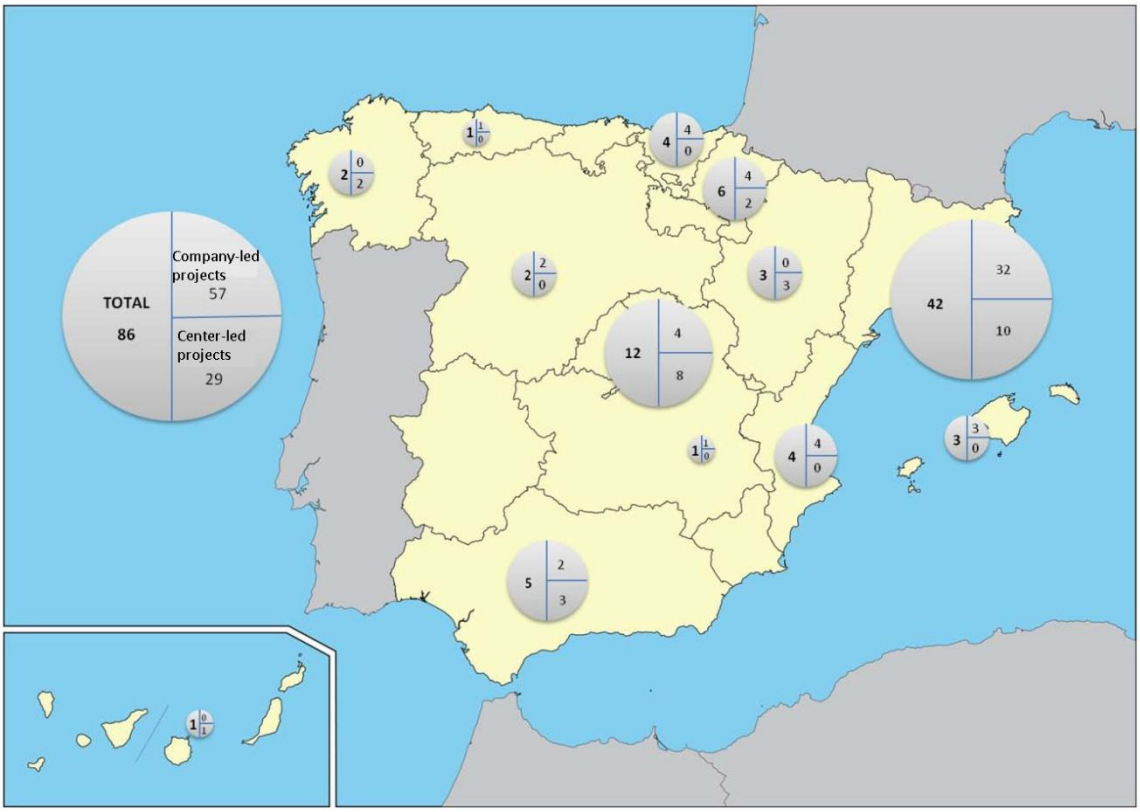
The main interest shown by the pharmaceutical industry from the start was to know **new drug developments**, so this was the most sought for category of projects and consequently the one for which more projects was received. It is also interesting to compare the number of projects proposed and the number of projects finally presented at the meetings, as shown in the following chart.



There is no doubt that a large amount of research is carried out on other types of products in addition to therapeutic drugs, but since the agendas of the meetings are prepared to fit the specific interests identified by the pharmaceutical companies, they ultimately establish which type of products should be presented since before closing the agenda of each meeting a preliminary document is distributed among potential participating pharmaceutical companies, requesting them to assess the interest of the initial selection for each company.

It is therefore quite significant to see that of 165 proposals related to drugs, 65 (40%) were presented, whereas of 70 proposals received that could be categorized as "medical technologies", only 2 (3%) were finally presented.

As regards the geographical origin of the projects selected, the following image offers detailed information about the origin of the 86 projects presented over the 12 meetings held up to now.



The most striking feature at first look is the preponderance of Catalonia, which has traditionally been the headquarters of a large part of the Spanish pharmaceutical-chemical industry. It is also notable that the program, as can be seen in the map, has tried to cover the whole national geography, with only 4 of the 17 autonomous communities without participation to date.

A more detailed look at the information offered in the above image shows in addition that in Catalonia there is a greater balance between projects from biotech companies and research centers, with predominance of the former over the latter. The second ranking geographical origin of the projects presented is Madrid, but here the great majority are from public research centers and hospital, with only 4 originating in start-up companies.

It may be relevant to point out that the place where the different meetings were held is distributed as follows: 5 in Madrid, 4 in Barcelona and 1 each in the cities of Zaragoza, Bilbao and Santiago de Compostela. Undoubtedly the place of the meeting helps to mobilize projects from

companies and research centers from the region, but in any case the selection of proposals is made based on the seven criteria, so the determining factor is fulfillment of those criteria.

A comparison of the origin of the projects selected with the relative number of proposals is given in the following table.

Total 2011-2014	Analyzed	Selected	Percentage
Andalusia	49	5	10.2%
Aragón	23	3	13.0%
Asturias	3	1	33.3%
Cantabria	1	0	0.0%
Castile–La Mancha	1	1	100.0%
Castile–León	7	2	28.6%
Catalonia	112	42	37.5%
Extremadura	---	---	---
Galicia	12	2	16.7%
Balearic Islands	3	3	100.0%
Canary Islands	2	1	50.0%
La Rioja	---	---	---
Madrid	91	12	13.2%
Murcia	---	---	---
Navarre	17	6	35.3%
Basque Country	20	4	20.0%
Valencia	16	4	25.0%
TOTAL	***357***	***86***	***24.1%***

2.3 Participating agents

In the 12 meetings carried out within the Pharma-Biotech program, a total of 93 agents have participated directly, in addition to FARMAINDUSTRIA.

33 pharmaceutical companies:

Abbott, Abbvie, Almirall, AstraZeneca, Bayer, Bial, Boehringer Ingelhem, Daiichi Sankyo, Esteve, Faes, Fardi, Ferrer, GSK, Ipsen, Janssen-Cilag, Lacer, Leti, Lilly, Lundbeck, Merck, MSD, Novartis, Nycomed (now Takeda), Pfizer, Pierre Fabre, Praxis Pharmaceutical, Reig Jofre, Rovi, Rubió, Sanofi Aventis, Servier, UCB Pharma, Viñas Laboratorios.

37 small biotech companies:

AB Biotics, Ability Pharmaceuticals, Advancell, Amadix, Ambiox Biotech, Ankar Farma, Archivel, Argon Pharma, Aromics, Asac Pharma, BCN Peptides, Bioncotech, Bionure, Biopolis, Digna Biotech, Enemce Pharma, Entrechem, Ikerchem, Immunonovative Dev., Janus Dev., Lifelength, Lipopharma, Lykera Biomed, Nanodrugs, Nanoimmunotech, Neuron Bio, Neurotec Pharma, Neuroscience Technologies, Oncomatrix Biopharma, Oryzon, Palau Pharma, Sanifit, SOM Biotech, Spherium Biomed, VCN Biosciences, Vivia Biotech, Zyrnat.

23 research organizations and hospitals:

Ciberes Gr. 29, CIMA, CLINIC Corporació Sanitària, CNIC, CNIO, Hospital Universitario La Princesa de Madrid, Hospital Universitario Ramón y Cajal de Madrid, Hospital de La Paz de Madrid,

Hospital Nª Sª de Valme de Sevilla, Hospital Virgen del Rocío de Sevilla, Instituto Aragonés de Ciencias de la Salud (IACS), Instituto BIFI de la Universidad de Zaragoza, Idibaps, Idibell, IDIS Santiago de Compostela, Institut de Neurociencies de la Universidad Autónoma de Barcelona, IQAC-CSIC de Cataluña, Instituto de Investigación de la Salud Germans Trias i Pujol, The Protein Targets Group de la Universidad de Zaragoza, Universidad de Barcelona, Universidad Complutense de Madrid, Universidad Pompeu Fabra, Universidad de Vigo.

3 TECHNOLOGIES, COMPANIES AND RESEARCH CENTERS

The ultimate rationale of the Pharma-Biotech program to help the **scientific and technological developments being carried out in Spain** in the field of human health to have the best possible expectations **of being utilized for the benefit** of society. It is known that for a drug to cover all the necessary stages to guarantee its efficacy and ensure its tolerability requires much time (often more than ten years) and many financial resources (which can be counted in hundreds of millions of euros).

There are numerous diseases requiring treatments that still do not exist and which are the field of study of a large number of researchers working at universities, institutes, centers, hospitals, foundations and companies. It is generally recognized that Spain has a **high-quality scientific level** and well-organized resources, which, despite the economic and financial crisis in recent years and the cutbacks made in the funding of R&D&I, is able to maintain a high level of international competitiveness.

Through the Pharma-Biotech program over its four years of operation many **good projects** have become known, with a variable degree of development but always having demonstrated at least a **preclinical proof of concept** and which were presented to the pharmaceutical industry with the purpose of generating the greatest possible number of interactions between both environments: one closer to the discovery of new molecules and new treatments and the other closer to the market, that is, manufacturing and distribution of drugs that have successfully completed the path from the laboratory to the patient.

Some problems are known and remain without an easy solution, among these are the impossibility for developments made in public research centers and universities to be self-financed beyond the initial preclinical trials, and the scant probability on the other hand that pharmaceutical companies or venture capital funds can accelerate their development in a generalized way for all, given the **high cost** and the low probability that a new molecule or an innovative therapeutic approach **will finally complete its path** from preclinical and clinical trials to approval by the national drug agencies.

However, the fact that the problem exists and is recognized is an incentive for carrying out meetings such as those generated through the Pharma-Biotech program, with the idea that the more opportunities will arise the more the interested parties are brought into contact with each other. It is obvious that financing of R&D&I in any sector and even more so in the pharmaceutical sector is a complex and costly enterprise that requires a sufficiently attractive incentive to outweigh the risk and high investment. But it is also true that they are not starting from scratch, as shown by the set of quality projects presented in the Pharma-Biotech program, which, at least in their initial phases of scientific development, have been largely financed with public funds and should be capable of better use.

Probably there is an increasing need for a large international agreement to make more efficient not only the process of discovery and development of new medicines for treating and curing generalized illnesses such as cancer or Alzheimer's disease, but also for diseases more prevalent in third world countries and hundreds of rare diseases for which it is even more difficult to find suitable funding, as there are in fact projects and discoveries that technologically could be effective for such goals.

3.1 Products in development presented at the meetings

Below are listed the **86 projects** that have been presented at the 12 Pharma-Biotech meetings that have taken place over the four years since the start of the program. For each project, the product in development presented, the therapeutic area concerned and the company, research center or hospital that presented the product and its geographic location are specified.

It should be recalled that although 86 project presentations were made, not all correspond to different products since in some cases the presentation consisted of explaining the advances made in a previously presented product, especially when two or more years had elapsed between presentations and it was considered that the new trials performed justified returning to the same product.

On the other hand, it can be seen that various companies and institutions have participated in more than one meeting presenting different products, in some cases referring to the same therapeutic area and in other with developments aimed at diseases very different from each other.

PRODUCTS in development PRESENTED A THE 12 PHARMA-BIOTECH MEETINGS

(In alphabetical order of entities)

Company or Entity	Therapeutic area	Product presented
AB BIOTICS Catalonia	Genetic analysis	New genetic biomarkers
ABILITY PHARMACEUTICALS Catalonia	Liver cancer	ABTL0812: an oral, safe mTORC1/C2 and DHFR inhibitor in phase I/Ib in lung and pancreatic cancer
	Solid tumors	Novel derivatives of polyunsaturated fatty acids for the treatment of Lung and pancreatic cancer
ADVANCELL Catalonia	Leukemia	ATH001- Acadra (Acadesine) is a small molecule, in development for the treatment of leukemia and lymphoma of B-cell origin
	Plantar syndrome	ATH008 - Topical treatment of palmar-plantar erythrodysestesia syndrome (Hand Foot syndrome or PPES)
	Dermatology	Dermosome Technology®, nanomedicines for the treatment of Actinic Keratosis
	Multiple sclerosis	Oral NT-KO-003 for the Treatment of Multiple Sclerosis
AMADIX Castile-León	Colorectal cancer	miColon* - Non-invasive screening test for Advanced Adenomas and Colorectal Cancer in blood
AMBIOX BIOTECH Madrid	AIDS prevention	Preventing the spread of HIV / AIDS through the use of nanotechnology
ANKAR FARMA Madrid	Retinal dystrophy	Innovative pharmacological treatment for retinal dystrophies
ARCHIVEL FARMA Catalonia	Asthma	Use of the immune-modulator Ruti® for prevention and treatment of stational rhinitis and asthma

		Tuberculosis	Ruti®: adjunctive immunotherapy to the standard antibiotic treatment for preventing tuberculosis in infected individuals
	ARGON PHARMA Catalonia	Oncology	ENAX003: Preclinical development of an oral wide spectrum antitumoral drug for pancreatic cancer
	AROMICS	Mesothelioma	Novel Berberine derivatives as antitumor agents for cancer
	ASAC PHARMA Valencia	Psoriasis, Dermatology	CUPS. New contribution to plaque psoriasis treatment
	BCN PEPTIDES Catalonia	Inflammatory pain	DD04107, the first peptide of a new class of long-acting analgesics
	BIFI UNIVERSIDAD DE ZARAGOZA Aragón	Hepatitis C	Allosteric inhibitors of the NS3 protease from the hepatitis C virus with a new action mechanism
	BIONCOTECH Valencia	Oncology	Anticancer therapy based on tumor self degradation
		Oncology	Ephrin B2 as a therapeutic strategy against angiogenesis
	BIONURE Catalonia	Multiple Sclerosis	Neuroprotective BN201 for multiple sclerosis and orphan CNS indications
		Neurodegeneration	BN201: a paradigm-shift (neuroprotection) in the treatment of neurodegenerative diseases
		Multiple sclerosis	Neuroprotective therapy with G79 candidate
	BIOPOLIS Valencia	Celiac disease	New probiotics with novel functional effects against celiac disease and infection by Helicobacter pylori
	CIBERES 29 ENFERMEDADES RESPIRATORIAS Canary Islands	Inflammation	1,2,3,5-tetrasubstituted pyrroles: new molecules with potent antiinflammatory activity in acute lung injury
	CIMA Navarre	Alzheimer's disease	Novel strategy for symptomatic and disease-modifying treatment of Alzheimer's Disease
		Oncology	New epigenetic agents: therapeutic approach in cancer
	CNIC Madrid	Inflammation	Selective inhibitory peptides of the calcineurin phosphatase activity
		Autoimmune diseases	Development of Novel Anti-Calcineurin Drugs for the Treatment of Inflammatory and Autoimmune Diseases
		Cardiovascular	Usage of the calcineurin variant CnAβ1 with gene therapy to treat heart failure
	CNIO Madrid	Oncology	Advanced PI3K inhibitors
	IQAC-CSIC Catalonia	Rheumatoid arthritis	Early diagnosis and prognosis of rheumatoid arthritis based on citrullinated peptides

DIGNA BIOTECH	DIGNA BIOTECH Navarre	Multiple Sclerosis	Methylthioadenosine: immunomodulation and neuroprotection for the multiple sclerosis treatment
		Cervix carcinoma	EDAHPVE7 as a therapeutic vaccine against cervix carcinoma
		Lung fibrosis and melanoma	Efficacy of P17, a TGFbeta1 inhibitor peptide, in lung fibrosis and melanoma
		Cervix carcinoma	EDAHPVE7 as a therapeutic vaccine against cervix carcinoma
Enemce Pharma S.L.	ENEMCE PHARMA Catalonia	Cardiovascular	NMC, a new antithrombotic candidate aimed to a multibilion dollar market
entrechem biotechnology	ENTRECHEM Asturias	Oncology	EC 70124, a kinase inhibitor of NF-kB pathway, targets initiating cancer cells (cancer stem cells)
FAES FARMA www.faes.es	FAES FARMA Basque Country	Solid tumors	Nielix: New antitumoural drug for leukaemia, melanoma, colon and ovarian cancer
ferrer	FERRER Catalonia	Sleep disorders	Lorediplon: “best-in-class” product for insomnia treatment
Virgen de Valme	HOSPITAL Nª Sª DE VALME UNIV. SEVILLA Andalusia	Inflammation	Antibodies for the Diagnosis, Prevention and Treatment of Diseases Involving Alteration of the Inflammatory Response
Hospital Universitario Ramón y Cajal	HOSPITAL RAMÓN Y CAJAL Madrid	Brain ischemia/stroke	Quinoline and steroidal nitrones with neuroprotective activity for the treatment of ictus
IP	HOSPITAL UNIV. LA PRINCESA UV. COMPLUTENSE Madrid	Autoimmune diseases	VIP serum levels as prognostic biomarker in patients with rheumatoid arthritis
Virgen del Rocío	HOSPITAL V. DEL ROCÍO UNIV. SEVILLA Andalusia	Colorectal cancer	Selected miRNAs as biomarkers for Advanced Colorectal Cancer (CRC) Response to Chemotherapy
		Multiple myeloma	Cannabinoid agents for the treatment of multiple myeloma and related conditions
CLÍNIC Corporació Sanitària IDIBAPS	CLINIC Coporació Sanitària IDIBAPS Catalonia	Heart failure	Soluble protein AXL as a Heart Failure biomarker
IDIBELL	IDIBELL Catalonia	Autoimmune diseases	Hasc-Sst2: Human adipose tissue-derived mesenchymal stem cells overexpressing the IL-33 antagonist Sst2
		Autoimmune diseases	C4BP(b-): a therapeutic anti-inflammatory and immune-modulatory agent in autoimmunity
IdiPAZ	IDIPAZ Madrid	Colorectal cancer	Test for the prediction of prognosis and response in colorectal cancer patients
		Inflammation	New therapeutic agents with efficacy in the treatment of inflammatory disorders characterized by high levels of TNF- α
idis	IDIS Galicia	Acute ischemia	Repositioning of the drug CBG000592 for treatment of ischemic stroke
IKERCHEM	IKERCHEM Basque Country	Liver cancer	IKH02: Inhibitor of HDAC with excellent pharmacokinetics properties as monotherapy for liver cancer

	IMMUNOVATIVE Catalonia	Sepsis	CombPath6.0: new biological drug for the treatment of sepsis
	INST. ARAGONÉS DE CIENCIAS DE LA SALUD Aragón	Oncology	Nanocoat. Formulations for the coating and transfer of different elements towards tumours
	I. NEUROCIENCIAS U. A. BARCELONA Catalonia	Neurodegenerative diseases	ASS234: a new multipotent cholinesterase/monoamine oxidase inhibitors with antioxidant properties and anti-Aβ aggregating profile for the therapeutic use in Alzheimer's disease
	INSTITUTO GERMANS TRIAS I PUJOL Catalonia	Brain ischemia	Apotransferrin to treat stroke: a new indication to cover an unmet medical need
	JANUS DEV. Catalonia	Glioblastoma	JAN0908, tumor iniciating stem cell modifier for the treatment of solid tumors
	LIFELENGTH Madrid	Telomeric analyis	Telomere Analysis Technologies: a fit-for-purpose biomarker
	LIPOPHARMA Balearic Islands	Glioma	Minerval® for the treatment of glioma and other types of cancer
		Glioma	Minerval for the treatment of glioma and other solid tumors
	LYKERA BIOMED Catalonia	Metastasis	LK-3: anti-S100P monoclonal antibodies for anti-cancer and anti-metastasis therapy
	NANODRUGS Castile-La Mancha	Oncology	Antitumor therapy using dendrimer-delivered siRNA
	NANOIMMUNOTECH Madrid	Drug delivery	NIT-zipper®, a nanometric systems multifunctionalization strategy for drug deliver
	NEURON BIO Andalusia	Epilepsy	NST0037, a novel statin with an improved neuroprotective profile
		Central nervous system	NST0037: a novel statin with high neuroprotective activity
	NEUROSCIENCE Catalonia	Pain	Microneurography: an opportunity for translational drug development in neuropathic pain
	NEUROTEC PHARMA Catalonia	Sclerosis	NT-KO-OO3: a new oral treatment for Multiple Sclerosis based on a novel mechanism of action
	ONCOMATRIX BIOPHARMA Basque Country	Breast cancer	Recombinant human Cystatin-C for the treatment of invasive triple negative breast cancers
		Invasive tumors	New treatments against invasive tumors based on Cystatin-C human protein
	ORYZON Catalonia	Alzheimer's disease	LSD1/MAOB Inhibitors as Disease Modifying Drugs for Alzheimer's and Huntington's Diseases
		Prostate	LSD1, an epigenetic target member of a transcriptional complex that plays an important role in regulating the expression of crucial genes involved in the onset and progression of cancer
		Prostate cancer	Fully human monoclonal antibodies targeting several novel internalizing proteins suitable for the treatment of Prostate Cancer

		Neurodegeneration	Inhibitors of Lysine specific demethylase 1, a novel target in neurodegenerative disease
	PALAU PHARMA Catalonia	Inflammation and asthma	UR-63325 for the treatment of asthma and rhinitis
		Inflammation	UR-67767 for the treatment of inflammatory diseases
	PROTEIN TARGETS UNIVERSIDAD DE ZARAGOZA Aragón	H. pylori infection	Three novel bactericidal compounds specific against Helicobacter pylori
	SANIFIT Balearic Islands	Kidney failure	SNF 472, a new approach to calcification related disease and health problems
	SOM BIOTECH Catalonia	Glioblastoma	SOM-0777, a new chemical entity as αvβ3/αvβ5 integrin inhibitor for the treatment of glioblastoma
	SPHERIUM BIOMED Catalonia	Central nervous system	Oxaloacetate donors as new neuroprotective agents
	UNIVERSIDAD DE BARCELONA Catalonia	Multiresistant infections	Antibacterial Polymyxin B analogs
		Antitumor agent	Novel proapoptotic compounds for cancer treatment
		Alzheimer's disease	New family of Alzheimer's disease-modifying agents that hit multiple biological targets
	UNIVERSIDAD DE VIGO Galicia	Oncology	UVI5008, a multiple epigenetic modulator for the treatment of cancer
	UNIVERSIDAD POMPEU FABRA Catalonia	Fragile X syndrome	New pharmacological target for fragile x syndrome and related disorders
	VCN BIOSCIENCES Catalonia	Oncology	VCN-01: a highly selective and efficient virus specifically designed to treat refractory tumors
	VIVIA BIOTECH Castile-León	Non-Hodgkin's lymphoma	Vivia-009 for the treatment of blood cancers
	ZYRNAT BIOTHERAPEUTICS Catalonia	Transplants	ZY-11 – A Specific CD40-siRNA Immune Co-stimulatory Blocker in Autoimmune Disorders and organ Transplantation

3.2 Advances in projects presented

To provide a perspective more oriented to the development of the product presented, it may be interesting to rearrange the information by grouping the projects by **therapeutic area** concerned and specifying their **stage of development** as of January 2015, which is when the latest information on the projects was collected.

It is not intended to be extremely accurate about the stage of development, since the dynamics of a development itself cause a continuous change in the information over time. It was thus chosen to consider five basic segments where each product could be broadly placed:

a) nonregulatory initial preclinical tests;

b) completing regulatory preclinical trials;

c) preparing to start clinical trials;

d) the product is in clinical trials;

e) the product is available for marketing or is already on the market.

An additional category was added to place projects for which updated information could not be obtained or which are known to have been discontinued, either because clinical trials were unfavorable or due to lack of funding. All these categories are shown in the table with a color code to facilitate an overview of the projects.

It should be taken into account that this table does not include all the projects presented. As noted before, several correspond to products similar or identical to other previously presented products but which were repeated to assess whether the progress made would increase the interest of the audience to undertake new contacts toward a potential collaboration.

In general, it was found that the vast majority of the products that have participated in the Pharma-Biotech program were still active and progressing, despite the severe funding problems seen in recent years. But there are also some small start-up companies that have had to stop work or even in some cases initiate liquidation proceedings as a result of not obtaining the necessary funding to go ahead with the required preclinical or clinical trials.

Public research centers have also slowed down or completely halted some of projects presented in the past because they had reached the maximum level of trials and tests that the institution could fund with its own resources and the only way to continue is through a cooperation agreement with the pharmaceutical industry or by transfer of the product rights to an intermediate company or a venture capital fund.

PROJECTS PRESENTED AT THE MEETING BY THERAPEUTIC AREA

DEGREE OF DEVELOPMENT AND CURRENT STATUS

		Progress from date of presentation (1) to January 2015 (2)				Graphical visualization of **current state** of development					
Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E

X Discontinued or unknown | A Preclinical tests | B Completing preclinical trials | C Preparing for clinical trials | D Product in clinical trials | E Product available on market

ONCOLOGY

Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E
Vivia-009 for the treatment of blood cancers	VIVIA BIOTECH	May 2011	Nonregulatory preclinical testing for an intravenous formulation	Change of formulation and demonstrated efficacy	Progressing at good rate since some months ago						
Novel Berberine derivatives as antitumor agents for cancer	AROMICS	Apr 2011	initial preclinical development	Efficacy demonstrated in vivo in malignant mesothelioma, progress in	Significant progress						
LK-3: anti-S100P monoclonal antibodies for anti-cancer and anti-metastasis therapy	LYKERA BIOMED	Jul 2012	In vitro tests	Humanized antibody ready for in vivo tests	Project slowdown pending funding						
Anticancer therapy based on tumor self degradation	BIONCOTECH	Apr 2011	Regulatory preclinical	Preparing approval of clinical studies (IND phase)	Yes, according to expectations						
Antitumor therapy using dendrimer-delivered siRNA	NANODRUGS	May 2011	Preclinical trials	More advanced preclinical trials	Moderate progress						
Novel proapoptotic compounds for cancer treatment	UNIVERSIDAD DE BARCELONA	May 2013	Scientific bases and experimental verification established	Mechanism of action better established	Moderate progress						
ENAX003: Preclinical development of an oral wide spectrum antitumoral drug for pancreatic cancer	ARGON PHARMA	Jul 2012	Regulatory preclinical	Project canceled	Activity canceled due to lack of investment						
miColon* - Non-invasive screening test for Advanced Adenomas and Colorectal Cancer in blood	AMADIX	Jul 2014	Testing of diagnostic test for initial validation	Clinical trial ongoing in nine hospitals	Significant progress						
Selected miRNAs as biomarkers for Advanced Colorectal Cancer (CRC) Response to Chemotherapy	HOSPITAL VIRGEN DEL ROCÍO UNIVERSIDAD DE SEVILLA	Jul 2014	Preliminary validation in two patient cohorts	Research project requested for multicenter validation	Pending granting of requested project						

		Progress from date of presentation (1) to January 2015 (2)				Graphical visualization of **current state** of development					
Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E
Test for the prediction of prognosis and response in colorectal cancer patients	IDIPAZ	Jul 2014	Genetic signature identified and predictive capacity validated	Gene conferring poor prognosis identified	Significant progress						
ABTL0812: an oral, safe mTORC1/C2 and DHFR inhibitor in phase I/Ib in lung and pancreatic cancer	ABILITY PHARMACEUTICALS	May 2011	Regulatory preclinical trials	Clinical phase I/IIb	Significant progress						
IKH02: Inhibitor of HDAC with excellent pharmacokinetics properties as monotherapy for liver cancer	IKERCHEM	Jul 2012	Preclinical phase completed	Unknown	Project discontinued Company under review						
Recombinant human Cystatin-C for the treatment of invasive triple negative breast cancers	ONCOMATRIX BIOPHARMA	Jul 2012	Preclinical trials	Working on new applications related to ocular diseases	Change of therapeutic target Moderate progress						
First-in-class epigenetic antitumor agent against a histone demethylase (LSD1)	ORYZON	Feb 2011	Preclinical trials	Clinical phase I/IIb	World leader at time of current development						
SOM-0777, a new chemical entity as αvβ3/αvβ5 integrin inhibitor for the treatment of glioblastoma	SOM BIOTECH	May 2011	Compound identified	Licensed to another country in preclinical phase	Project out of company after licensing						
Minerval for the treatment of glioma and other solid tumors	LIPOPHARMA	Apr 2011	Phase I/IIa clinical trials in solid tumors including malignant glioma	Preparing phase IIB clinical study for glioblastoma	Very significant progress						
Cannabinoid agents for the treatment of multiple myeloma and related conditions	HOSPITAL VIRGEN DEL ROCÍO UNIVERSIDAD DE SEVILLA	Sept 2014	Proof of concept completed in multiple myeloma	Proof of concept completed in myeloblastic leukemia	A significant advance						
Advanced PI3K inhibitors	CNIO	May 2011	Candidates identified in phase of optimization	New indication identified for these compounds	Pending demonstration of application to new therapeutic area						
EC 70124, a kinase inhibitor of NF-kB pathway, targets initiating cancer cells (cancer stem cells)	ENTRECHEM	Jul 2012	Preclinical trials	Unknown	Unknown						
Nielix: New antitumoural drug for leukaemia, melanoma, colon and ovarian cancer	FAES FARMA	May 2013	Preclinical toxicology initiated	Preclinical toxicology completed	Moderate progress						
ATH001- Acadra (Acadesine) is a small molecule, in development for the treatment of leukemia and lymphoma of B-cell origin	ADVANCELL	Apr 2011	Clinical trials IIa	Unknown	Project discontinued Company under review						
New epigenetic agents: therapeutic approach in cancer	CIMA	Jul 2014	Efficacy and safety demonstrated in in vivo models	Preclinical trials	Short interval since presentation						

		Progress from date of presentation (1) to January 2015 (2)				Graphical visualization of **current state** of development					
Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E
Nanocoat. Formulations for the coating and transfer of different elements towards tumours	INSITUTO ARAGONÉS DE CIENCIAS DE LA SALUD	Jun 2012	Patented	Formulation is being improved	Only one marketed product, with 60% less efficacy						
UVI5008, a multiple epigenetic modulator for the treatment of cancer	UNIVERSIDAD DE VIGO	Sept 2014	Natural product derivative validated in vivo tests	Status unchanged	Presented only four months earlier						
VCN-01: a highly selective and efficient virus specifically designed to treat refractory tumors	VCN BIOSCIENCES	Apr 2011	Preclinical proof of concept	Patent approved Clinical phase I in 12 patients	Very significant progress						

AUTOIMMUNE DISEASES

Early diagnosis and prognosis of rheumatoid arthritis based on citrullinated peptides	IQAC-CSIC	Nov 2013	Diagnostic test validated in over 1000 patients	Granted European and U.S. patent	Improves current diagnostic systems						
Development of Novel Anti-Calcineurin Drugs for the Treatment of Inflammatory and Autoimmune Diseases	CNIC	Mar 2012	Calcineurin inhibitory activity demonstrated	Specificity demonstrated and working on other similar peptides	Significant progress						
VIP serum levels as prognostic biomarker in patients with rheumatoid arthritis	HOSPITAL UNIVERSITARIO LA PRINCESA UNIV. COMPLUTENSE	Nov 2013	PCT phase of patent initiated	PCT phase granted	Reasonable progress						
A therapeutic anti-inflammatory and immune-modulatory agent in autoimmunity	IDIBELL	Mar 2012	European patent requested Licensed to Janus Dev.	Preclinical trials in animals	If the results are positive, it will be a very important advance						
Neuroprotective BN201 for multiple sclerosis and orphan CNS indications	BIONURE	Feb 2011	Preclinical phase completed	Starting regulatory toxicology	Restarted after a certain delay due to financial constraints						
Methylthioadenosine: immunomodulation and neuroprotection for the multiple sclerosis treatment	DIGNA BIOTECH	Feb 2011	Preclinical trials	Unknown	Unknown						
NT-KO-OO3: a new oral treatment for Multiple Sclerosis based on a novel mechanism of action	NEUROTEC PHARMA	Feb 2011	Reprofiling Clinical phase IIa	Unknown	Project discontinued Company under review						

CARDIOVASCULAR

Usage of the calcineurin variant CnAβ1 with gene therapy to treat heart failure	CNIC	Jul 2014	Proof of concept in mice	Working on new virus	No significant progress made						
Soluble protein AXL as a Heart Failure biomarker	CLINIC Coporació Sanitària IDIBAPS	Nov 2013	Specificity tests for different diseases	New data confirm specificity	Significant progress						

		Progress from date of presentation (1) to January 2015 (2)				Graphical visualization of **current state** of development					
Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E
NMC, a new antithrombotic candidate aimed to a multibilion dollar market	ENEMCE PHARMA	Nov 2013	Nonregulatory preclinical tests started	Nonregulatory preclinical tests completed	Significant progress according to expectations						
Repositioning of the drug CBG000592 for treatment of ischemic stroke	IDIS	Sept 2014	Preclinical proof of concept	Approval for start of clinical phases in process	Significant progress according to expectations						
Apotransferrin to treat stroke: a new indication to cover an unmet medical need	INSTITUTO GERMANS TRIAS I PUJOL	Jul 2013	Patent in PCT phase	Progressing with preclinical development	Progress within expectations as a research institute						
Quinoline and steroidal nitrones with neuroprotective activity for the treatment of ictus	HOSPITAL RAMÓN Y CAJAL	Nov 2013	In vivo trials completed	In vivo comparison with other drugs	Reinforced previous results presented						

CENTRAL NERVOUS SYSTEM

Novel strategy for symptomatic and disease-modifying treatment of Alzheimer's Disease	CIMA	Sept 2014	Efficacy and safety demonstrated in in vivo models	Preclinical trials	Short interval since presentation						
New family of Alzheimer's disease-modifying agents that hit multiple biological targets	UNIVERSIDAD DE BARCELONA	Jul 2013	Model well established and efficacy proven in transgenic mice	Additional positive efficacy determinations have been made	The next step would be toxicity tests that are out of the reach of the GI						
ASS234: a new multipotent cholinesterase/monoamine oxidase inhibitors for the therapeutic use in Alzheimer's disease	INSTITUTO DE NEUROCIENCIAS UNIVERSIDAD AUTÓNOMA DE BARCELONA	Jul 2013	Positive results in in vitro tests	Positive results confirmed in in vivo tests	Significant progress						
NST0037: a novel statin with high neuroprotective activity	NEURON BIO	Jul 2013	Preparing to enter clinical trial phase I	New efficacy tests and pending approval to start clinical phase I	Moderate progress						
Oxaloacetate donors as new neuroprotective agents	SPHERIUM BIOMED	Jul 2014	Preclinical proof of concept demonstrated	Preclinical studies performed yielded negative results	Project stopped in view of preclinical results						

INFECTION

Antibacterial Polymyxin B analogs	UNIVERSIDAD DE BARCELONA	Mar 2012	Proof of concept in vitro	Testing in vivo toxicity	Significant progress will be when preclinical phase is completed						
CombPath6.0: new biological drug for the treatment of sepsis	IMMUNOVATIVE DEV.	Jul 2011	Preclinical phase	Unknown	Project discontinued Company under review						
Three novel bactericidal compounds specific against Helicobacter pylori	PROTEIN TARGETS UNIVERSIDAD DE ZARAGOZA	Jun 2012	Efficacy proven against H. pylori cultures	New variants with lower toxicity generated	Significant progress						

		Progress from date of presentation (1) to January 2015 (2)				Graphical visualization of **current state** of development					
Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E
INFLAMMATION											
1,2,3,5-tetrasubstituted pyrroles: new molecules with potent antiinflammatory activity in acute lung injury	CIBERES 29 ENFERMEDADES RESPIRATORIAS	Mar 2012	Preclinical trials	Work started with other compounds	No progress made with initial project						
Antibodies for the Diagnosis, Prevention and Treatment of Diseases Involving Alteration of the Inflammatory Response	HOSPITAL NUESTRA SEÑORA DE VALME UNIVERSIDAD DE SEVILLA	Jul 2014	Preclinical proof of concept completed	Status unchanged	No progress due to short interval since presentation						
New therapeutic agents with efficacy in the treatment of inflammatory disorders characterized by high levels of TNF- α	IDIPAZ	Jul 2014	Preliminary studies in mice models	Publication made with results obtained	No longer working on the project						
UR-67767 for the treatment of inflammatory diseases	PALAU PHARMA	Jul 2011	Preclinical phase completed	Unknown	Unknown						
OTHER											
Dermosome Technology®, nanomedicines for the treatment of Actinic Keratosis	*ADVANCELL*	Jul 2011	Performing preclinical phase	Unknown	Project discontinued Company under review						
Microneurography: an opportunity for translational drug development in neuropathic pain	*NEUROSCIENCE*	Feb 2011	Medical device under commercial exploitation	Still under commercial exploitation	Still on the market						
DD04107, the first peptide of a new class of long-acting analgesics	*BCN PEPTIDES*	Jul 2011	Performing preclinical phase	Unknown	Unknown						
New probiotics with novel functional effects against celiac disease and infection by Helicobacter pylori	*BIOPOLIS*	Mar 2012	Preclinical phase completed	Is being marketing internationally	Substantial progress to be put on market						
SNF 472, a new approach to calcification related disease and health problems	*SANIFIT*	Jul 2011	Preclinical trials	Clinical phase I	Significant progress						
Innovative pharmacological treatment for retinal dystrophies	*ANKAR FARMA*	Sept 2014	Preparing to start regulatory preclinical tests	Actively seeking funding	No progress due to short interval since presentation						
Allosteric inhibitors of the NS3 protease from the hepatitis C virus with a new action mechanism	*BIFI UNIVERSIDAD DE ZARAGOZA*	Jun 2012	Cell-based assays of antiviral activity	Efficacy trials in animals	If the results are positive, it will be very important advance						

		Progress from date of presentation (1) to January 2015 (2)				Graphical visualization of **current state** of development					
Product presented	Company or Entity	Date 1	State on date 1	State on date 2	Perceived progress	X	A	B	C	D	E
NIT-zipper®, a nanometric systems multifunctionalization strategy for drug deliver	*NANOIMMUNOTECH*	Jul 2011	Initial phase of R&D	Marketed	Very significant progress						
New genetic biomarkers	*AB BIOTICS*	Feb 2011	In process of completion	Marketed	Assessing overall savings in system if this biomarker is used						
Telomere Analysis Technologies: a fit-for-purpose biomarker	*LIFELENGTH*	Sept 2014	Technology available	Exploring new applications	Technology available						
Lorediplon: "best-in-class" product for insomnia treatment	*FERRER*	May 2013	Clinical phase Ib	Clinical phase II	Significant progress						
Preventing the spread of HIV / AIDS through the use of nanotechnology	*AMBIOX BIOTECH*	Jul 2011	In vitro experiments	In vivo assays	Significant progress						
CUPS. New contribution to plaque psoriasis treatment	*ASAC PHARMA*	Mar 2012	Pending start of clinical test of oral administration in phase I	Pending start of phase II clinical studies	Moderate progress						
Use of the immune-modulator Ruti® for prevention and treatment of stational rhinitis and asthma	*ARCHIVEL FARMA*	Jul 2011	Starting phase III	Abandoned for now	Remained in phase III due to lack of funding						
New pharmacological target for fragile x syndrome and related disorders	*UNIVERSIDAD POMPEU FABRA*	Mar 2012	Preclinical trials	Unknown	Unknown						
ZY-11 – A Specific CD40-siRNA Immune Co-stimulatory Blocker in Autoimmune Disorders and organ Transplantation	*ZYRNAT BIOTHERAPEUTICS*	Mar 2012	Preclinical tests	Unknown	Unknown						

3.3 Spin-offs of research centers and universities

The table below lists the companies that have participated in the Pharma-Biotech program that were created as spin-offs of universities and public research centers, specifying for each the date of creation and the institution of origin.

Probably the oldest and most consolidated company at present in the Spanish biotech panorama is ORYZON, created fifteen years ago as a spin-off of the CSIC and the University of Barcelona.

Although only companies that have participated in the Pharma-Biotech program are listed, the table is to a certain extent representative of the overall situation and allows us to become

aware, though probably insufficiently, that there are notable experiences of innovative technology-based companies that arose from public research institutions and which are slowly learning to position themselves on the international market.

Obviously, although a spin-off company has an excellent scientific capacity, for as long as it continues collaborating with the institution from which it arose, it will be unable to achieve by itself the financial effort required to take the discovery of a new molecule to the level of clinical phases and if all goes well to its placing on the market. This is precisely the reason why in 2011 FARMAINDUSTRIA launched the Pharma-Biotech program with the aim of generating a sufficient environment of information and interaction to contribute to the start of cooperation agreements that in time would lead to joint developments.

COMPANIES THAT HAVE PARTICIPATED IN THE PHARMA-BIOTECH PROGRAM

WHICH AROSE AS SPIN-OFFS OF UNIVERSITIES OR RESEARCH CENTERS

AB BIOTICS	*Spin-off of the Autonomous University of Barcelona (UAB) in 2005*
ABILITY PHARMACEUTICALS	*It was founded in November 2009 and has its headquarters in Bellaterra (Barcelona) within the campus of the Autonomous University of Barcelona. Initially known as AB Therapeutics*
ADVANCELL	*Spin-off of the University of Barcelona (UB) in 2004*
ANKAR PHARMA	*Spin-off of the CSIC in 2014*
ARGON PHARMA	*Created in 2008 as a spin-off of Santa Creu i Sant Pau Hospital of Barcelona and the University of Barcelona*
BIONCOTECH	*Bioncotech Therapeutics has its headquarters in the University of Valencia Science Park (PCUV) and arose with the support of the National Center for Cancer Research (CNIO), Genoma España and Instituto Empresa.*
BIONURE	*Bionure was founded in 2009 as a spin-off of Hospital Clínic of Barcelona – IDIBAPS and the CSIC*
BIOPOLIS	*Founded in 2003 as a spin-off of the CSIC together with three industrial partners: CAPSA (Corporación Alimentaria Peñasanta), the venture capital group Talde and Naturex España S.A.*
DIGNA BIOTECH	*It was created in 2003 by the University of Navarra and fifteen Spanish corporations and financial institutions to develop the results generated from the research carried out at the CIMA (Center for Applied Medical Research of the University of Navarra)*
ENTRECHEM SL	*Spin-off of the University of Oviedo, created in 2005 by professors from the Departments of Organic and Inorganic Chemistry and Functional Biology. The company is located in Asturias and began to operate in 2006*

IKERCHEM	*Ikerchem arose in 2005 as a spin-off of the Department of Organic Chemistry and the Faculty of Chemistry of the Gipuzkoa Campus of the University of the Basque Country (UPV/EHU)*
IMMUNNOVATIVE DEVELOPMENTS	*Arose as a spin-off of the University of Barcelona and the Hospital Clínico of Barcelona The company was founded in February 2010*
LIPOPHARMA	*Arose in 2007 as a spin-off of the University of the Balearic Islands sponsored by Dr. Pablo Escribá, Vicenç Tur and others.*
LYKERA BIOMED	*A spin-off company of the Catalonian technology center LEITAT*
NANODRUGS	*Arose as a spin-off of the University of Castile-La Mancha, specifically the research group NeuroDeath*
NEURON BIO	*It was founded in 2005 as a spin-off of the Autonomous University of Madrid (UAM) and particularly of the research group headed by Dr. Fernando Valdivieso, professor of biochemistry and molecular biology*
NEUROTEC PHARMA	*It was created in January 2006 as a spin-off of the University of Barcelona (UB) with the initial collaboration of Oryzon Genomics, the UB Center for the Transfer of Knowledge, Technology and Innovation, and the Fundació Bosch i Gimpera (FBG)*
ORYZON	*Oryzon was created in 2000 as a spin-off of the Spanish National Research Council (CSIC) and the University of Barcelona.*
SANIFIT	*Sanifit arose in 2004 as a spin-off of the University of the Balearic Islands (UIB)*
VCN BIOSCIENCES	*VCN Biosciences was created as a spin-off from the Catalan Institute of Oncology-Bellvitge Biomedical Research Institute (ICO-IDIBELL)*
VIVIA BIOTECH	*It arose in the laboratories of the Faculty of Medicine of the University of Salamanca*
ZYRNAT BIOTHERAPEUTICS	*It was established in June 2011 as a spin-off of IDIBELL and the University of Barcelona, in particular of the research group of the Nephrology Department at the Hospital of Bellvitge*

3.4 Discovery of new molecules

As seen in the preceding pages, in the 12 Pharma-Biotech meetings held so far products in development oriented to different therapeutic areas have been presented, with a clear predominance of the area of oncology.

Although from the start it was sought that the selected projects were related to specific drugs to treat disease, many of the candidate proposals received dealt with developing products in a different area from a drug strictly speaking, such as, for example, biomarkers, diagnostic kits, prediction of drug efficacy based on genetic profiles, cell therapy, encapsulation systems, mechanisms for release and targeting of active substances within the organism, and even some medical technologies or services.

Thus, though in a much smaller proportion, there have been meetings dealing with some products in development belonging to this second area of research not related to the discovery and testing of new molecules aimed at the treatment of disease.

On the other hand, drugs in development have also been presented whose origin was not a new recently discovered chemical entity but which instead belong to three distinct categories: a) research with stem cells or monoclonal antibodies; b) proteins naturally synthesized by the human body or occurring in nature; or c) reprofiling of a known old drug or one that was never used or that was used for a different indication. In both cases, protection of industrial property is achieved through formulas of use patents or the like.

After excluding all these cases, there are still quite a few new molecules that have been discovered and patented by many of the companies or institutions than have participated in Pharma-Biotech. The following table shows this information in summary form.

31 NEW MOLECULES DISCOVERED, PATENTED AND PRESENTED AT PHARMA-BIOTECH

Name	Entity presenting the project	Chemical activity	Development	Therapeutic area
Therapeutic lipid analog	ABILITY PHARMACEUT.	DHFR and mTOR inhibitor	Clinical phase I/IIb	Lung, pancreatic and endometrial cancer
VP3.15	ANKAR PHARMA	Dual inhibitor of GSK-3/PDE-7	Preclinical	Retinal dystrophy
NAX035	AROMICS	Controls TS and DHFR and is an inhibitor of Wnt	Preclinical	Oncology
BO-110	BIONCOTECH	Tumor cell autophagy inducer	Clinical phase I	Oncology
BN201	BIONURE	Neuroprotector	Regulatory preclinical	Multiple sclerosis
1,2,3,5-tetrasubstituted pyrroles	Ciberes 29	Inhibitor of TLR4-Ikβa	Preclinical	Acute lung damage
MTA (methylthiadenosine)	CIMA	Immunomodulator	Preclinical	Multiple sclerosis
EDA-HPVE7	CIMA	Therapeutic vaccine	Preclinical	Uterine cancer

Name	Entity presenting the project	Chemical activity	Development	Therapeutic area
CM-272	CIMA	Inhibitor against two classes of epigenetic targets	Preclinical proof of concept	Oncology
CM 414	CIMA	Beta-amyloid and tau level reducer	Preclinical proof of concept	Alzheimer's disease
LxVPc1 (peptide)	CNIC	Calcineurin inhibitor	Preclinical proof of concept	Autoimmune diseases
---	CNIO	P54 kinase inhibitors	Preclinical proof of concept	Oncology
ASS234	CSIC / Univ. de Barcelona	Mutlipotent MAO-A and MAO-B inhbitor	Preclinical proof of concept	Alzheimer's disease
FI0503LO1 (NIELIX)	FAES FARMA	Tumor cell apoptosis inducer	Clinical phase I/IIa	Oncology
LOREDIPLON	FERRER	Modification of GABA receptors	Clinical phase II	Insomnia
New nitrone derivatives	Hospital Ramón y Cajal	Neuroprotector and antioxidant	Preclinical proof of concept	Stroke and brain ischemia
CFFCP 1,2,3	ICAQ-CSIC	Diagnostic reagent for rheumatoid arthritis	Clinical phase	Rheumatoid arthritis
C4BP	IDIBELL	Immunomodulator	Preclinical proof of concept	Autoimmune diseases
---	IDIPAZ	TNF-α inhibitor	Preclinical proof of concept	Autoimmune diseases
---	Instituto Aragonés de Ciencias de la Salud	Allosteric inhibitor of the NS3 protease	Preclinical	Hepatitis C
VIRADUCTIN	Instituto Aragonés de Ciencias de la Salud	Adenovirus transducer agent	Preclinical proof of concept	Oncology
MINERVAL	LIPOPHARMA	Modulator of the activity of SMS	Clinical phase I/IIa	Glioblastoma
NST0037 (new statin)	NEURON BIO	Neuroprotector	Clinical phase I	Alzheimer's and Epilepsy
OMTX001	ONCOMATRIX BIOPH.	TNF-α inhibitor β	Preclinical	Oncology
ORY1001	ORYZON	LSD1 inhibitor	Clinical phase I/IIa	Oncology
ORY2001	ORYZON	LSD1 and MAO-B inhibitor	Regulatory preclinical	Neurodegeneration
SOM-0777	SOM BIOTECH	avB3 integrin inhibitor	Preclinical	Glioblastoma
Polimyxin analogs	Univ. de Barcelona	Antibiotic against multiresistant bacteria	Preclinical	Broad-sprectrum antibiotic
PG10 (fluorinated thiazoline)	Univ. de Barcelona	Anti-prohibitine	Preclinical proof of concept	Oncology
AVCRI 175	Univ. de Barcelona	Beta-amyloid level reducer	Preclinical proof of concept	Alzheimer's
---	Univ. de Zaragoza	Flavodoxin inhibitor	Preclinical	Helicobacter pylori

4 PERCEPTION ABOUT SCOPE AND RESULTS

In order to improve the service provided with the Pharma-Biotech program and optimize the resources allocated, regular surveys are made with the participating pharmaceutical companies and researchers presenting projects.

In particular, four types of monitoring and follow-up of the program have been performed:

a) Post-meeting evaluation questionnaires: Immediately after each meeting, all participants, both pharmaceutical companies and speakers, were administered the questionnaires.

b) Pharmaceutical company interviews: In February 2013 a survey directed to pharmaceutical companies that had attended one or various of the meetings held up to then was performed. Subsequently, in October 2013, a series of direct in-depth interviews were carried out with 16 participating pharmaceutical companies.

c) Final review questionnaire: From December 2014 to January 2015, an extensive questionnaire was requested from all researchers who had presented their projects with several aims, among others, to determine the degree of progress, stagnation, or cancellation of the projects.

d) Representative interviews: During the month of March 2015 a series of in-depth personal interviews were held with persons participating in the meetings, seeking a broad representativeness, so that interviewees included two general managers of start-ups, two executives from pharmaceutical companies (one national and the other multinational), a researcher from a public research center and a technology transfer manager at a hospital.

4.1 Individual evaluation of meetings

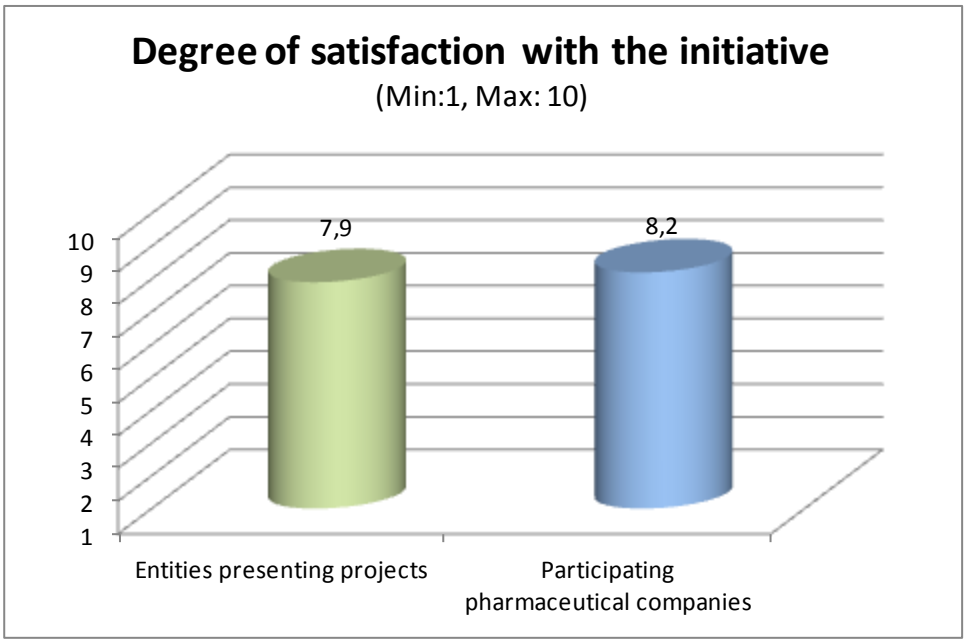
At the end of each meeting, a brief questionnaire that could be completed in five minutes was sent by email to each participant (pharmaceutical companies and speakers), except in the two meetings held in the framework of BioSpain (Bilbao in 2012 and Santiago de Compostela in 2014), which due to their open nature were not included in the overall evaluation system.

On average over the 10 remaining homogeneous meetings, 65% of pharmaceutical companies and 70% of speakers returned the completed questionnaire.

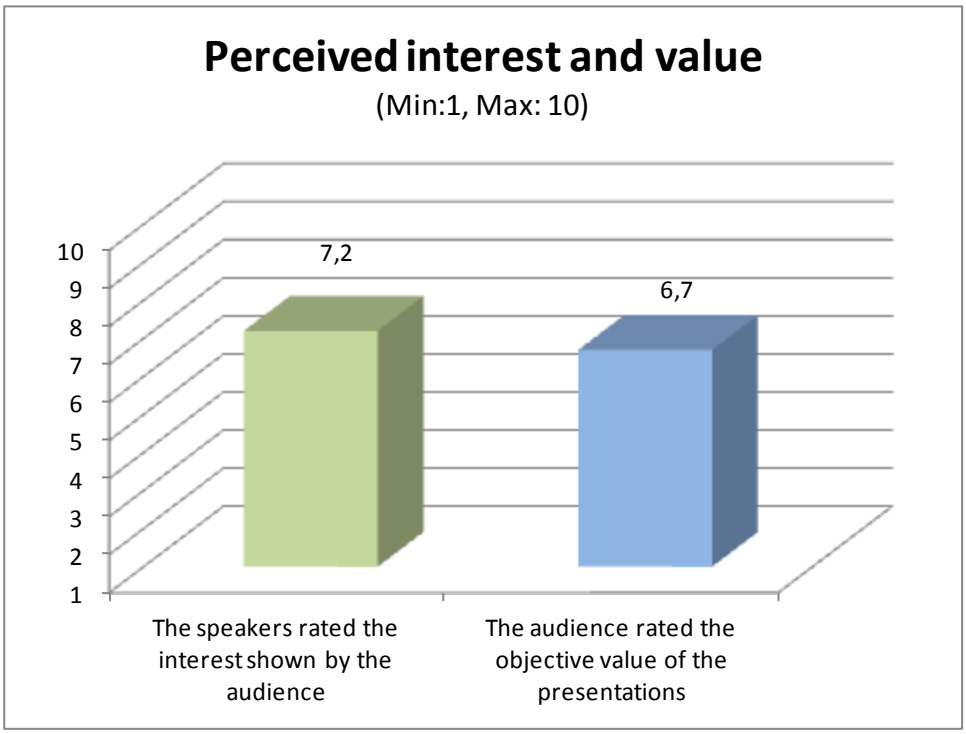
The same set of questions were always asked in this questionnaire.

- Overall degree of satisfaction with the initiative
- Perceived interest among the participants, novelty and degree of innovation of the proposals
- Main strong and weak points of the developments presented
- Preliminary contacts made and their possible evolution
- Organization, atmosphere achieved and logistics
- Suggestions for improvement

Notable as a general response was the high degree of satisfaction with the initiative, both by pharmaceutical companies and speakers.



A high overall opinion, on average, was also noted, both regarding speakers' perception of the interest shown by pharmaceutical companies in their presentations and regarding pharmaceutical companies representatives' perception of the real value of the products presented to the pharmaceutical industry. However, although this perception of the objective interest for the industry was notable (6.7/10 points on average), most of the companies responding to the evaluation questionnaire stated that at present and in the short term the product presented is not a priority for the particular pharmaceutical company.

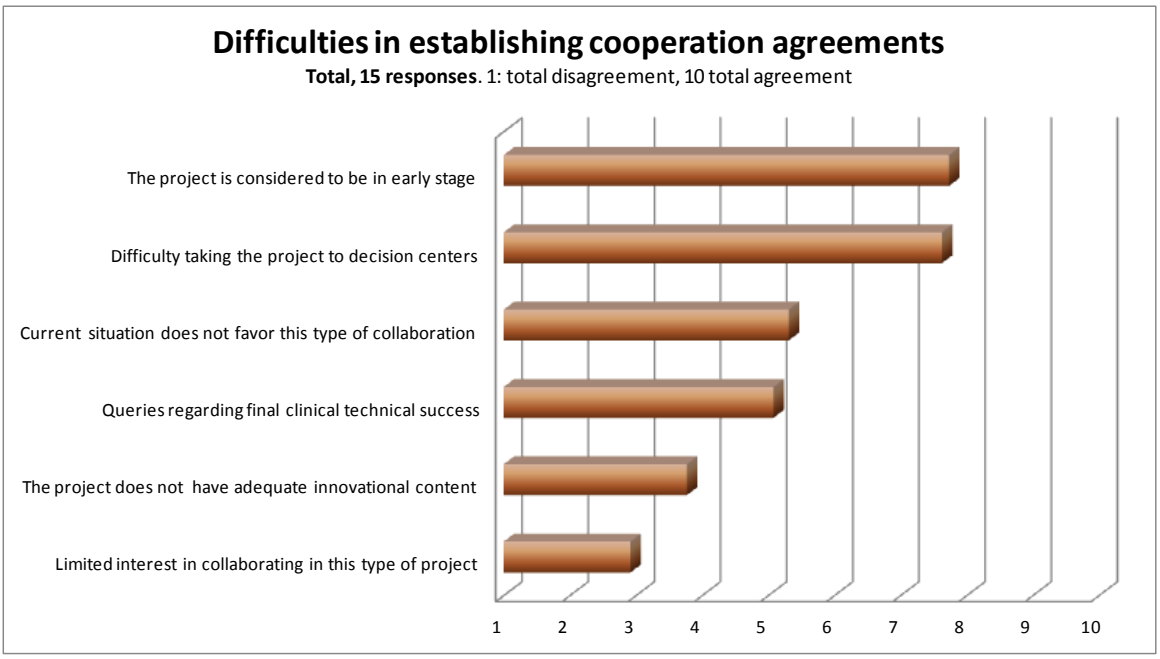


4.2 Interim assessment

In the second half of February 2013, after having held 7 meetings (four in 2011 and three in 2012) pharmaceutical companies that had participated in at least one of these meetings were requested to respond to an email survey in which they were asked about the direct contacts they had had with the speakers (number, continuity, depth, etc.) and they were also asked to rate from highest to lowest in importance a series of barriers to interaction, such as, for example, the willingness of the company to enter collaboration agreements with this type of projects, the degree of development seen in the research presented, the speaker's ability to communicate, or the degree of involvement in this type of decisions of the representative participating in the meeting. Finally, it was asked what minimum conditions, in the opinion of the pharmaceutical company surveyed, the projects presented should have to generate high interest in the pharmaceutical industry (state of development, degree of novelty, international prestige of the researchers, etc.)

Fifteen pharmaceutical companies (*Almirall, Bayer, Daiichi Sankyo, Esteve, Faes, Ferrer, Merck, MSD, Novartis, Pfizer, Pierre Fabre, Reig Jofre, Rovi, Sanofi Aventis, and Servier*) responded to the survey out of a total of 30 which had participated at the time, representing a response rate of 50%.

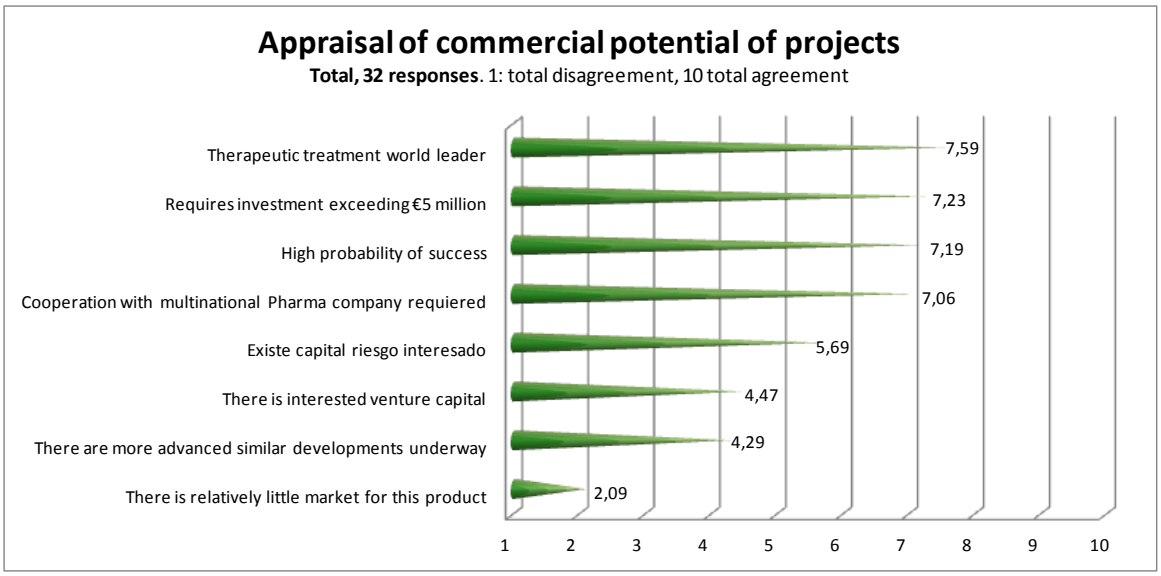
It may be interesting, as shown in the following chart, to see the degree of agreement or disagreement that the interlocutors showed with regard to which difficulties they considered were the most obvious barriers to the achievement of cooperation agreements between the pharmaceutical companies and the entities researching new drugs that presented their proposals at the meetings organized by Pharma-Biotech.



It can be seen from the responses collected in the questionnaire that the most significant barriers from the viewpoint of pharmaceutical companies are a) the fact that most of the developments presented are in early stages and b) the difficulty for the information presented at each meeting reach and be properly processed by the decision-making centers of the respective pharmaceutical companies, especially multinationals.

At the same time as the questionnaire responded by pharmaceutical companies, another questionnaire was sent **specifically directed to the 40 speakers** who had up to then presented their projects at the meetings, of whom 32 (80%) responded.

It is illustrative to see that the perception of researchers and small biotech companies regarding the business potential of the developments presented. Thus, the following chart shows the degree of agreement or disagreement of the speakers with a series of statements given in the survey for their assessment.



It was found that, on average, the speakers expressed great confidence (7.59/10) in that the drug they were working on would be a world leader if clinical tests were successfully concluded, granting it a high probability of success (7.19/10). At the same time they recognized that they need very large investments to go forward with the research and that cooperation with a multinational pharmaceutical company would be a key factor for achieving success.

On the other end of the scale, speakers' opinion grants on average rating of 2/10 points to the statement that the market for the product presented is relatively small and therefore would not justify the investment required.

To complete the information received in the survey done in February 2013 and to attempt to validate some suggestions received to improve the efficiency of the Pharma-Biotech program, during the first two weeks of October of the year 15 direct personal interviews were carried out with the representatives of the pharmaceutical companies that had attended one or various of the ten meetings organized up to then. The aim was to confirm their perception of the added value represented by the organization and participation in the Pharma-Biotech program.

Representative from the following companies participated in these interviews: *Abbvie, Astrazeneca, Bayer, Boehringher, Esteve, Faes, Ferrer, GSK, Janssen-Cilag, MSD, Pierre Fabre, Reig Jofré, Rubió, Salvat and Servier*.

Once all the opinions and suggestions were processed, the following conclusions could be drawn:

- The interviewees considered the initiative to be highly valuable, emphasizing three positive effects: **Initial filtering of projects**, which saves a lot of time, the **catalyzing effect** it produces, and the **good image** conveyed by Farmaindustria.
- The interviewees expressed their desire for the initiative to be continued at a frequency of **two annual meetings**.
- Regarding the degree of development of the projects presented, the interviewees were divided into two large groups of roughly 50% each: a) those who thought that companies normally require that projects have a **degree of development** of at least clinical phase IIb to be interested in a cooperation agreement; b) those who think that **projects in early stages** may even be more interesting because of their more beneficial opportunity cost.
- Nonetheless, it was generally found that pharmaceutical companies assessed higher than other criteria the fact the projects have a high degree of **innovation and differentiation** relative to other developments available internationally.
- The vast majority of the interviewees wished to expressly underline that a program of these characteristics should not set as a realistic objective the achievement of **cooperation agreements** in the short term as an indicator of the program's success. The function performed by the program should be focused on: a) provide verified information on the state of scientific knowledge and drug development; b) ensure a process of screening and selection based on robust criteria; c) generate trust on both sides, pharmaceutical laboratories and developers; y d) provide a flexible and well-organized framework for the meeting and initial interchange of first contacts.

4.3 General questionnaire for speakers

A large part of the information collected regarding the projects presented in Pharma-Biotech comes from the general survey that was requested from all speakers during the period from December 2014 to January 2015.

In total, over the twelve meeting to date, 60 speakers have presented a total of 86 projects, representing 37 companies, 17 research centers and 6 hospitals.

Of these 60 speakers, 51 responded to the questionnaire, representing 85% of the total.

The survey was formed by three well-differentiated parts:

a) Name of the entity, name of project presented, state of development of the project when presented and at present, and expectations of interesting the pharmaceutical industry again in the near future, either with same product in a more advanced state or a different product. It was also asked if the company or entity had maintained, increased or decreased its capacity and effort in R&D&I.

b) Perception about the Pharma-Biotech program, and particularly about the criteria for selecting projects, way of convening and conducting each meeting, number of pharmaceutical companies attending and overall format of each meeting.

c) The results obtained up to now, specifically the number and quality of the contacts made during the meeting, how many continued at a later date, degree of interest raised by the presentation in the audience and main obstacles perceived that could be managed better in future editions.

The information collected served as the basis for writing this document, so it is not necessary to repeat here again the results of the survey. Nevertheless, some points on which most of the speakers agreed should be highlighted:

- The perception that the **selection process** for proposals is adequate is practically unanimous and the guidelines supplied to tailor the content and form of the presentation to the representatives of the participating pharmaceutical companies was considered highly useful.
- There was also a high consensus regarding the **format** given to the meetings, assessing positively its **originality** versus other events also aimed at fostering technology transfer. In this regard, it was stressed that open meetings generally tend to be less operational precisely because they are open and have less control over the persons participating in them.
- Opinions were divided as to the **ideal number of participants** at each meeting. While the format of six to eight presentations with a duration of 30 minutes each was considered optimum, in contrast, some thought the number of representatives of pharmaceutical companies should be increased, especially in meetings where there were fewer than ten. Others, however, stated that it is not the number of representatives attending by rather their suitability that is important.
- With regard to the suitability of the **representatives of pharmaceutical companies** participating in the meetings, some of those surveyed noted that it was important that projects at first glance suitable for some of the attending pharmaceutical companies reach effectively the person or persons in charge of looking for new business opportunities.
- It was suggested in this respect if it would be possible to optimize the identification of the **final recipient of the prior information** that is sent to pharmaceutical companies before convening the agenda of each meeting, to facilitate as far as possible the best internal dissemination within each company.
- Nonetheless, most of the surveyed stated that they had the opportunity, and took advantage of it, to make **initial contacts** with many of the attending representatives, and that a reasonable percentage of the contacts continued days later, though very few actually culminated in specific cooperation agreements. There was a fairly general consensus about this being a slow and complex process and that it is necessary to persist in their efforts in order to close specific contracts.
- Finally, the surveyed were practically unanimous in their desire **to continue participating** in the Pharma-Biotech program with the same product when it is in a more advanced stage or with new products they are also developing.

4.4 Personal interviews

As a final action of follow-up and monitoring of the program, personal interviews of six participants were carried out, each of which fulfills the circumstance of representing a specific area of interest: public research centers, national health system hospital, multinational pharmaceutical laboratory, national pharmaceutical laboratory, small spin-off company from a university and small start-up company in an international setting.

This aimed to provide an overview of what has been done so far from the perspective of the users of the program, in any of its forms, placing the emphasis on their specific experience, without seeking to make a generalization from it but **an immediate and direct vision** of its protagonists.

Below are included the **extracts of the interviews** performed of the following persons:

Rocío Arroyo	*Chief Executive Officer (CEO)*	**AMADIX**
Vicenç Tur	*Cofounder and General Manager*	**LIPOPHARMA**
Lola Pérez Garre	*Technology Transfer Technician*	**IdiPAZ**
Juan Miguel Redondo	*Research Group Head*	**CNIC**
Andrés G. Fernández	*Director of Advanced Therapies and Business Development*	**FERRER**
Antonio Gómez	*Liaison for Spain of J&J Innovation Centers*	**JANSSEN-CILAG**

"For a pharma to show interest in a new drug there must be at least a well-established proof of concept"

Rocío Arroyo, CEO of **AMADIX** has 15 years of experience in the pharmaceutical and biotechnological sector, and her previous posts include executive positions at Bionostra and Eli Lilly.

AMADIX is a small biotech company located in Valladolid and dedicated to research, development and marketing of innovative biomarkers for cancer diagnosis, particularly colon, lung, and prostate cancer. It was created in June 2010 as a spin-off of TCD Pharma (*Translation Cancer Discovery*) which arose in Spain to develop and market patents from the CSIC aimed at the treatment by new targets of cancer patients.

In December 2012 AMADIX acquired the company TRANSBIOMED, a spin-off of the Research Institute of Vall d'Hebron Hospital of Barcelona, to join forces for better diagnosis and treatment of cancer patients.

AMADIX participated in the 9th meeting of the Pharma-Biotech program of FARMAINDUSTRIA presenting an innovative *noninvasive test for the diagnosis of advanced adenomas and colorectal cancer in blood*, which is currently in the clinical phase in 9 hospitals.

After presentation of the project, AMADIX was able to contact various attending pharmaceutical companies, such as, for example, MSD, Ferrer or Pierre Fabre, with whom it maintained contacts subsequent to the forum.

For Rocío Arroyo, the Pharma-Biotech initiative is important because it fosters contacts of small companies and research groups with the pharmaceutical industry, particularly in those cases when they do not have networks of international contacts, though this is not the case of AMADIX, which has a network of contacts with diagnostic companies worldwide.

It should also be taken into account that there are considerable differences in the pharmaceutical industry between the areas of research in therapeutics and diagnostics. Pharmaceutical companies oriented to the development of drugs are not always willing to incorporate diagnostic biomarkers in their portfolio.

There are numerous research groups in our country, belonging to both research centers and universities and the network of hospitals of the national health system, whose results could serve as the scientific basis for the creation of numerous spin-offs or be licensed to international pharmaceutical and diagnostics companies.

AMADIX bases its business model on this availability of knowledge, looking for patents that create synergies with its own lines of development and negotiates with centers to establish agreements of mutual interest. But it needs to find the necessary funding for the first years of research until completing the preclinical phase or at least until a well-established proof of concept is demonstrated.

In this scenario, cooperation with pharmaceutical companies can be crucial, not only because this cooperation allows the development to be oriented and accelerated, but also because it can be a point of reference for the entry of venture capital. Cooperation between pharmaceutical companies, research groups and spin-off companies, as promoted by the Pharma-Biotech program, can be genuinely useful to orient and accelerate the development of these projects, generating an environment of trust that facilitates collaboration and subsequent materialization in specific agreements.

"One never knows where opportunity will arise; that's why it is essential to participate in programs that foster interaction and mutual knowledge between different players."

Vicenç Tur is co-founder and General Manager of **LIPOPHARMA**, a small highly innovative company created in 2007 as a spin-off of the University of the Balearic Islands and located in Majorca. Their most advanced product is Minerval, a drug whose activity is based on regulating the lipid structure of the cell membrane inducing autophagy of tumor cells, and which has proven in the laboratory and in living organisms its therapeutic potential to reduce and eliminate solid tumors including malignant glioma.

Lipopharma first presented Minerval at Pharma-Biotech in April 2011 in Barcelona and subsequently presented it again in Madrid in May 2013 to explain the advances achieved in research since then, which has currently reached a phase I/IIa clinical study in which 25 patients have already been treated with very promising results, and which is expected to be completed over the course of 2015.

As a result of this, various contacts have been established, among others, with the pharmaceutical company Janssen-Cilag, with whom it has held exploratory meetings, independently of other contacts with other pharmaceutical companies that Lipopharma has initiated through other routes, since it is a company that is regularly present in various forums and international congresses.

For Vicenç Tur, the big advantage of the Pharma-Biotech program is that it facilitates "being inside" the sector, opening interaction that may not yield concrete results immediately, but which help the industry to become aware of the existence of small start-up companies like Lipopharma, and in turn allow these small companies to know better and first hand what pharmaceutical companies are looking for at each moment. To be able to present a project in development like Minerval and obtain an initial *feedback* in real time by attending pharmaceutical companies is of great importance for a small spin-off company.

PIPELINE

PRODUCT	THERAPEUTIC AREA	DEVELOPMENT PHASE					
		RESEARCH	PRECLINICAL	PHASE I	PHASE II	PHASE III	REGIST.
Minerval	Cancer						
LP226A1	Alzheimer's Disease, CNS pathologies						
LP204A1	Inflammation						
LP10218	Cancer*						
LPA181	Spinal Cord Injury, Pain						
LP205A1	CNS, Metabolic & Cardiovascular diseases						
LP30171	Metabolic disorders, Cancer						

*partnered with Ability Pharmaceuticals

The Pharma-Biotech program is quite original in its approach and there are not many similar initiative inside or outside of Spain, because it combines simplicity and approach and provides an invaluable prior analysis of the projects that are presented to the pharmaceutical companies, which gives representatives attending each meeting valuable information and guidance about them. What is distinctive about Pharma-Biotech is its capacity to make known the advanced developments in new medicines that are carried out in Spain and the way in which it fosters direct interaction with both national and multinational pharmaceutical companies. The realistic goal should not be to close short-term agreements but to maintain the maximum interaction and growing attention of the pharmaceutical sector towards the advanced research that is carried out in research centers and small companies that arise as spin-offs of these.

As part of its intense scientific-commercial activity, the company Lipopharma is in contact with the biotechnology cluster of Massachusetts (USA), and so are well acquainted with other initiatives to promote cooperation and open innovation that are carried out in countries with a strong entrepreneurial culture. In one of the activities they participated in, for example, researchers were given access to mentors from the pharmaceutical industry who studied and discussed the most relevant aspects in terms of technical, economical and financial feasibility of their respective developments.

In the last fifteen years Spain has made considerable progress in terms of the development of an entrepreneurial culture, but it is still far from the levels of countries like the USA, Germany or the United Kingdom, where there is a scientific and industrial community that since much longer age is conscious of and oriented to the practical applicability of the results of research.

"To improve industrial exploitation ratios of research in hospitals and health research institutes, it is necessary to encourage mutual knowledge between the parties"

Lola Pérez Garre has a degree in chemical sciences and is technology transfer technician at the Innovation Unit of **IdiPAZ** (Institute for Health Research of La Paz University Hospital), a place for biomedical research that is the result of the union between La Paz University Hospital (HULP), the Autonomous University of (UAM), and the Foundation for Biomedical Research of La Paz University Hospital (FIBHULP). IdiPAZ has 48 research groups that focus their activity in six larger areas: Neurosciences, Cardiovascular, Infectious Diseases and Immunity, Large System Diseases, Cancer and Human Molecular Genetics, and finally Surgery, Transplants and Health Technologies. To date, 10 licensing agreements have been signed and 1 spin-off has been created**.**

The Pharma-Biotech program began its first meetings in 2011 for small biotech companies. In 2012 the source of projects was expanded to include to research centers and finally in 2014 it was extended to advanced research work carried out in hospitals. It is at this time when the IdiPAZ takes part in the program presenting two developments: a kit based on biomarkers predicting response to treatment with chemotherapy in colorectal cancer, and a new range of compounds effective for the treatment of inflammatory diseases with high TNF-α levels.

As a result of its participation in the program, at least three pharmaceutical laboratories showed interest in the project about cancer: Ferrer, Pierre Fabré, and GSK, though it was subsequent found that it did not conform to their technological approach. It is also interesting to highlight that not only pharmaceutical companies but also other participants were present at the meeting: small start-up companies, research centers and other hospitals, which is another opportunity to know the sector better or even the possibility of making unexpected contacts, as in the case of the company Amadix, a participant at the same meeting, which initially showed interest in the biomarker though it did not go further.

Participation of IdiPAZ in the Pharma-Biotech program has allowed us, thanks to the dialogue established, to know better what the industry is looking for and what are the key factors for presenting them our research so that they find it more relevant and more interesting for their objectives. We have attended many meetings of this type, but the attractive format of this one, so special, and the ability through it to contact openly with the organization of FARMAINDUSTRIA was of great value for us.

It is very interesting that the Pharma-Biotech program encourages the entry of developments made in hospitals, though it should be taken into account that a large part of the technological offering of the hospitals consists of biomarkers and medical devices, for which, unfortunately, pharmaceutical companies participating in the meeting do not show special interest.

A peculiar situation occurs in hospitals as, though contacts with national and multinational pharmaceutical companies are normally fluid and daily due to the clinical research carried out, this does not usually extend to the area of basic or preclinical research. The reality is that a large part of the knowledge generated in hospitals is unknown by the pharmaceutical industry and to take advantage of it would require improving the channels of communication between both.

The bottleneck in terms of effective exploitation of the results of research conducted in hospital, therefore, is that they correspond to products that are far from what most pharmaceutical companies are looking for or the research work is in early phases that do not seem to offer sufficient confidence for a company to commit to cofunding and acceleration of the research. As a result, it is difficult to move from the scientific/medical area to the business/industrial area. Increasing information and mutual knowledge would undoubtedly help to improve expectations.

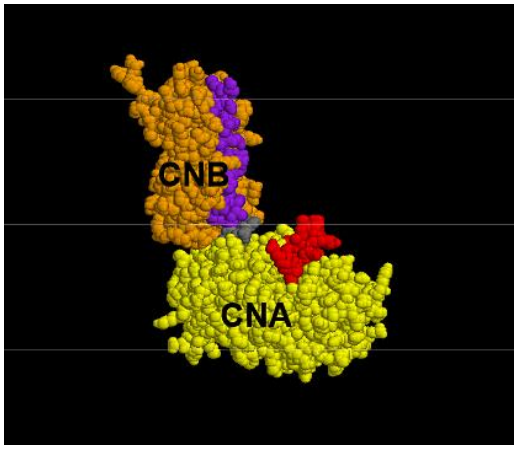
"We have worldwide pioneering lines of research that could be better taken advantage of by the pharmaceutical industry if they decided to cooperate in earlier stages."

Juan Miguel Redondo holds a Ph.D in science and is a renowned expert in the area of immunology and inflammation. In 2001 he joined the **CNIC**, where he does research in the Department of Vascular Biology and Inflammation. A large part of his work has focused on study of the regulation and function of the calcineurin/NFAT signaling pathway.

The CNIC (National Cardiovascular Research Center) has presented various projects to the pharmaceutical industry within the Pharma-Biotech program. Specifically, the last project presented in Madrid, in July 2014, was related to the use of peptide inhibitors of calcineurin for the treatment of inflammatory and autoimmune diseases. He is currently working with three families of cell-permeable inhibitors and with peptide inhibitors expressed by lentiviral vectors that serve as a vehicle to the interior of the target cell.

This same project had been previously presented in Barcelona in March 2012 in a less advanced stage. It was then when companies such as Novartis and chiefly Ferrer showed a strong interest in the project, holding several subsequent meetings, though, finally, it did not conclude in specific cooperation agreement for joint development. Two main reasons explain the situation: firstly, the *economic and financial crisis* made many pharmaceutical companies reconsider and reduce their R&D budgets, concentrating their investments and narrowing the focus of their explorations; and secondly, *the manner in which contact is initiated* does not always meet the optimal conditions for one or the other party to understand the key issues in the project presented.

For public research centers is it fundamental to reach agreements of financial and technical cooperation with the pharmaceutical industry because it is difficult, other than by this means, to continue the research beyond a preclinical proof of concept. For instance, in the case of calcineurin, the approaches used in the CNIC are completely original, protected by patent and differentiated from what other prominent laboratories are doing in other countries, so it makes sense for pharmaceutical companies working in the therapeutic areas concerned, both national and international, show interest here in Spain after knowing the scientific results obtained, and for this purpose, the Pharma-Biotech program plays a significant role.



Obviously the CNIC takes part in wide range of forums to make its developments known, including periodic presentations in its own facilities to pharmaceutical companies, on their own initiative or by invitation of the center. The Pharma-Biotech program is complementary initiative whose principal originality and added values is prior filtering by FARMAINDUSTRIA to ensure that the projects presented fulfill the conditions to generate the interest of the attending pharmaceutical companies, and this gives credibility and solidity to each meeting, clearly differentiating it from other *partnering* events which take place inside or outside of Spain.

It is true that sometimes the developments made in research centers may be overvalued by their own researchers in terms of their potential therapeutic benefits or the actual degree of innovation in comparison with what is being researched in other places. Precisely because of this, their presentation at meetings like Pharma-Biotech allows their contrast against the perspective of pharmaceutical companies, and this may represent a reality check and a high added value for the research group. But also, reciprocally, it helps pharmaceutical companies to perceive and know scientific advances that are being carried out in many public centers and that they are not always aware of, due sometimes to prejudices that only interaction and adequate information will be able to overcome.

"Place more emphasis on collaboration with small innovative companies and reputed academic groups rather than supporting a classic research center"

Andrés G. Fernández is director of Ferrer Advanced Biotherapeutics (FAB), the collaborative research area of Ferrer. The company **Ferrer** was founded in 1959 in Barcelona and today is one of the large Spanish pharmaceutical companies, with a turnover exceeding 800 million euros, and is present in over 90 countries.

As a consequence of the evolution in R&D models and the impact of the recent economic and financial crisis in the sector, Ferrer first decided to reorganize its internal R&D department in four areas: Ferrer HealthTech, Corporate Product Development, FAB and Clinical Development, encompassing from high technological barrier generics to disruptive projects in the area of advanced therapies, and, second, to expand its participation in biotech companies. Thus, the already existing investments in Diater, Gendiag and Oryzon Genomics were joined by the creation of Spherium Biomed, the transformation of Janus Developments, dedicated to identifying and promoting new drug development opportunities originating in public research centers, and the entry in Venter Pharma and Genmedica.

Andrés G. Fernández has participated very actively in nine of the twelve meetings carried out since 2011 and is thus an excellent observer from the perspective of the national pharmaceutical industry. The Pharma-Biotech program has been offering over these four years a quite accurate picture of the real offer that biomedical research in Spain is in a position to offer the pharmaceutical industry and which, in relative terms, is reasonably similar to the worldwide panorama, with most of the projects focused on oncology, followed by those related to the central nervous system.

National and multinational pharmaceutical companies often share a similar search spectrum and in this regard the Pharma-Biotech program can be equally useful for either one, though the greater proximity and availability in Spain of their main staff supports a more direct contact with national companies. As has been shown in the meeting held up to now, there are real opportunities in Spain to promote developments of interest and for the national pharmaceutical industry it is the closest and most cost-effective option, although they also come to seek opportunities in the rest of Europe.

Within the framework of its participation in the program, Ferrer has initiated contacts with at least two or three projects at each of the meetings, and has always found, thanks to the strict prior selection performed by FARMAINDUSTRIA, a state of development and reliability in the developments that has justified the company's interest in them, as the preclinical proof of concept required as a rule to present a project is usually sufficient to demonstrate the minimum maturity to warrant their attention.

It is worth noting a very positive experience for Ferrer and **Vivia Biotech**, since both companies as a result of participation in the program closed a collaboration agreement for codevelopment of a product in the oncohematological area. For Ferrer it was the entry in a project of opportunity where Vivia Biotech is providing a strong dynamics and high motivation, which enhances and accelerates the performance of the project. The preclinical phase is currently being completed, after several months of negotiations, where a cooperation model satisfactory for all had to be designed. In parallel to the initial preclinical tests, a redirecting of the priority indications of the drug was carried out in order to adapt to the changes occurring in the competitive scenario. The future drug could start clinical trials in the beginning of 2016.

The project with Vivia Biotech went ahead because it is clinically and commercially attractive, sufficient mutual trust was generated, the costs of development were reasonable, and the experience of the small biotech company is very good, with a wide knowledge of both the Spanish and international environment.

"Farming vs Fishing: The processes of cooperation should be seen more as a long-distance race than as a sprint"

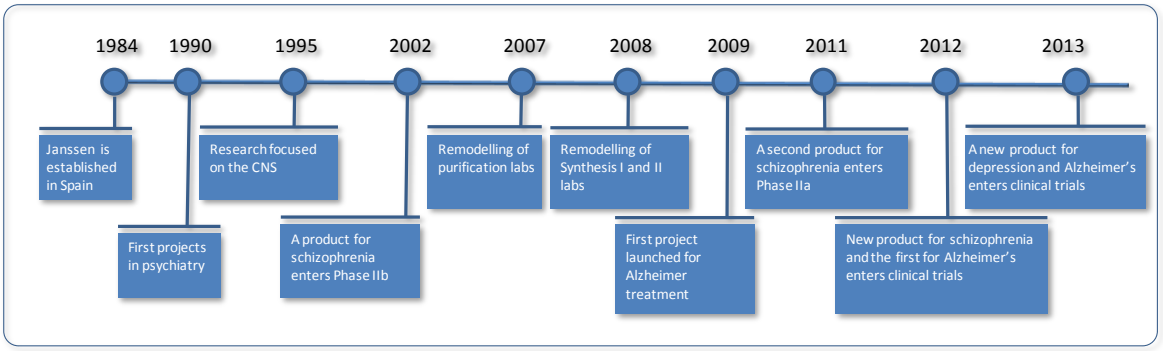
Antonio Gómez, a great expert in new paradigms in open innovation, is liaison for Spain of J&J Innovation Centers, a position he performs from the **Janssen-Cilag** Basic Research Center in Toledo.

In 1989 Janssen set up a Basic Research Center in Toledo, which is one of the five drug discovery centers belonging to Johnson & Johnson Pharmaceutical Research and Development (two in the USA and three in Europe) and one of the few centers of this type existing in Spain.

Janssen has been one of the most active multinational pharmaceutical companies in terms of its participation in the Pharma-Biotech program, having taken part in eight of the twelve meetings, so its knowledge of the program from perspective of the pharmaceutical industry is very extensive.

For Antonio Gómez, one of the most relevant aspects of Pharma-Biotech is that in this initiative all of the projects presented have been previously analyzed in depth to ensure a reasonable degree of maturity with respect to the criteria of interest to the pharmaceutical industry. This quality of the program ensures participating pharmaceutical industry a efficient use of the information distributed prior to the meetings as well as use of the meeting time itself.

On the other hand, the task of comprehensive searching and selection carried out by the team of FARMAINDUSTRIA grants high credibility and confidence to the projects presented, which in all cases generated high interest. However, a direct correlation does not necessarily exist between the interest in the project presented and the immediate options of cooperation, as it depends above all on whether the area of the project coincides or not with the strategic research objectives that at any given moment the participating pharmaceutical companies may have.



While the signing of a collaboration agreement anywhere in the world is always complex and usually a lengthy process, in the setting of the Spanish Pharma-Biotech program sponsored by FARMAINDUSTRIA it is even more difficult, because multinational laboratories operate in a global environment, where offers may occur in various countries and where in addition the centers of analysis and decision making on the development of projects and the strategies for new drugs are precisely often in those countries. In this regard, Janssen is somewhat different since after the recent creation of its four ***Open Innovation Centers*** (Shanghai, London, San Francisco and Boston), a worldwide network is working effectively for which precisely Antonio Gómez is the liaison for Spain.

Thanks to this, some of the projects presented at the Pharma-Biotech meetings in which Janssen could have interest because they fit in principle in its product pipeline, have been contacted as a result of the Pharma-Biotech meetings. Most notable among these are **NeuronBio** which presented an interesting development in neuroprotection, **Ability Pharmaceuticals** with a dual action anticancer drug, **Lipopharma** with an advanced antitumor development, **Ankar Farma** which presented an innovative treatment in retinal dystrophies, or Professor Rodolfo Lavilla from the **University of Barcelona** who described a very promising development in the fight against cancer by means of the use of fluorinated thiazoles. In fact, meetings have already been organized between some of the speakers and representatives of the Johnson & Johnson Innovation Center in London, thus demonstrating that although the processes of cooperation are slow and difficult, the road can be smoothed by initiatives where the agents involved start to contact and know each other better, which often is a usually pleasant surprise for all.