



Agenzia nazionale per l'attrazione
degli investimenti e lo sviluppo d'impresa SpA

Investment Opportunities

Life Sciences

Invitalia is the Italian national agency for inward investments and economic development. Its mission is to promote the country competitiveness – in particular in the Southern Regions – and support growth in strategic sectors.

Its main objectives are:

- Supporting inward investments*
- Boosting innovation and growth*
- Improving the economic opportunities in the country.*

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Presentation

Italy is one of the world leaders in Life Sciences market, being the **third largest** industry in **Europe** after **Germany and France** (Source: IMS 2011), both in terms of turnover and number of employees. Italy's companies cover the whole market spectrum including Pharmaceuticals, Biotechnology, Biomedical applications, Bioinformatics, Biomechanics and Nanobiotechnology, integrated with traditionally strong Italian sectors such as Agro-Food, Chemicals and Textiles.

On a world scale, the Italian pharmaceuticals market ranks **fifth** for total sales (pharmacies + hospitals), thus providing a relevant driver for biotech development in the Country. Furthermore, in line with other western European countries, healthcare provision in Italy proves advanced and ensures universal access. The population size ensures that the Italian pharmaceuticals market remains quite relevant and attractive. More specifically, whilst the overall population is declining, the over-65 ratio has already attained 20.4% and is set to further rise with a corresponding increase in chronic and long-term medical conditions, which will inevitably raise demand for pharmaceuticals (Source: *Espicom 2010*).

Italy also runs the supremacy on scientific publications by researchers at worldwide level accounting for 44.1%, compared to publications in UK (35.4%), France (25.2%), Germany (22.5%) and Japan (9%).

Italy's Pharmaceuticals: Facts & Figures

- **Third highest turnover** in Europe amounting to € 23.3 billion
- **Substantial R&D** spending at over € 1.2 million per year
- **70,000 employees** with a further 200,000 engaged in hundreds of industry-related businesses
- **Some 100 foreign companies** operating in the sector, including all major multinational players
- **Strong export orientation** with € 12.2 billion exports yearly

(Source: *Farmindustria, Istat*)

1. Focus on Biotech

Italy's Biotech is a dynamic sector composed of 375 companies (2011) investing in Research and Development Biotech Sector. Among these, 221 are the so called "pure biotech" (59% of total amount).

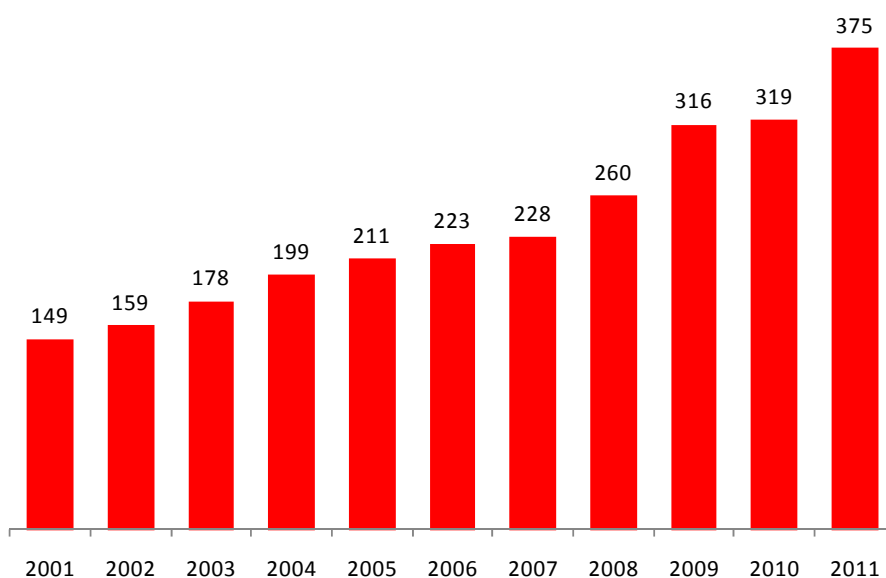
Biotech Industry in Italy

	Total	Pure Biotech
Companies	+1.6%	+2.7%
Biotech turnover	+2.7%	+12.1%
R&D Investments	+ 3%	+10%
Employees	+0.8%	+2.5%

Source: E&Y 2010 versus 2011

An overall turnover of € 23,3 billion, namely about € 7.4 billion euro, is generated from the biotech segment and approximately € 1.76 billion in R&D biotechnological investments.

Biotech Companies in Italy: Development over time



Source: E&Y 2011

Italian biotech companies spring as start-up (53%) and as academical spin-off (24%) .

Throughout the Country, over 40,000 employees, operate in the sector (approximately 9,000 in R&D), with a +36% year-on-year increase (Source: Blossom Report 2009).

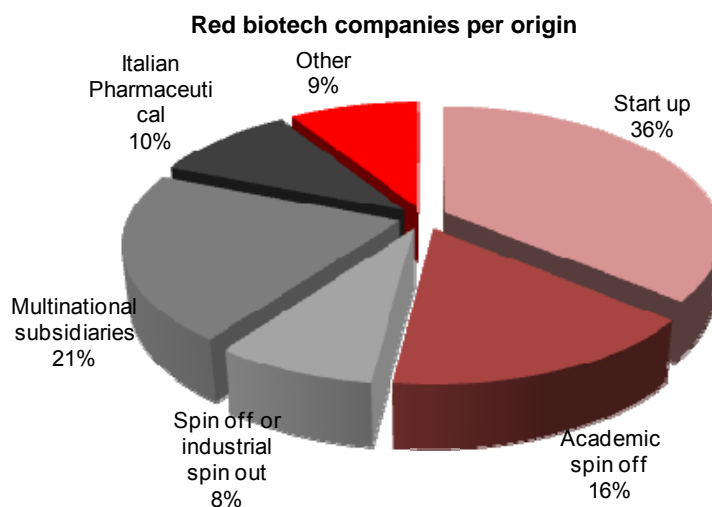
The analysis of the companies' geographical location shows how 75% is concentrated in 6 regions: Lombardy (129), Piedmont (37), Tuscany (30), Veneto (31), Lazio (30), and Emilia Romagna (26) alongside the main Italian scientific parks. On a territorial level, the biggest concentration is in the Milan area, which hosts 26% of the Italian companies which belong to this category.

RED Biotech

A breakdown of the analysis by application area reveals absolute predominance of the healthcare biotechnology sector: 246 companies work in the healthcare segment ("Red Biotech Companies"). They represent the 96% of sector turnover, with 5.587 employees dedicated to the research activities and 305 products in development phase.

Red biotech companies are located mostly in Lombardy (40%). Lombardy and Lazio are the main destination region where multinational established their business (72%). Piedmont and Sardinia shows their vocation to attract Science&Technology Parks and business incubator (80% of local companies were set up in that favourable situation).

The majority (36%) of red biotech companies proceeded from start up. Over the last year there was a small increase of red companies originating from academic spin off.



Source: BioItaly Report 2011

Over the last few years (2005-2009) six Italian Biotech companies were listed on the stock exchange of foreign markets – i.e. Gentium, NicOx, BioXell, Newron Pharmaceuticals, Cosmo Pharmaceuticals, and Molmed (Source: Assobiotech 2009).

Over 2010, the Biotechnology sector recoded strong signals of consolidation and growth by innovative companies operating in the field. Data confirm the sector development and a large number of new companies investing in the field of life sciences, environmental and agro-food sciences (Source: www.biotechitaly.com).

The sector is undergoing evident transformation placing great emphasis on innovative offshoots connected with biotechnological developments in the healthcare field.

R&D spending is on the rise as well as the number of new biotechnology ventures, mainly as spin-offs of academic work and foreign companies.

The process – supported by research centres with proven track record of excellence in Healthcare Research and ever stronger ties between the academic and business world – has already given life to several **Biotechnology segments**, some specialised in Diagnostics and Therapeutic Trials. Recent applications – notably in Biomedical, Bioinformatics, Biomechanics, and Nanobiotechnology sectors– are strongly appealing investors' interest. The opportunities offered by Clinical Trials, mainly carried out by foreign companies, are likewise encouraging, featuring cutting edge set-ups in the development of a wide range of therapeutic areas (i.e. Oncology, Neurosciences, Cardiology, and Vascular Diseases, and Immunology).

Assets

1. Human talent and excellence in R&D

Human capital is one of the chief strongholds for Life Sciences investors. By investing in Italy, companies gain access to a highly-qualified labour pool, directly stemming from a school and university system providing education and research developed consistently with market needs. Italy offers companies a modern and dynamic business environment in which to invest with an average of over 12,000 PhD scholars annually registered, as well as 200,000 students and **45,000 graduates every year in Biotechnology, Pharmacy and Medicine**, combining a traditional flair for creativity together with high productivity levels (*Source: MIUR*).

- **Long standing excellence in applied medical research** in the fields of Vaccines, Oncology, Gene Therapy, Neurosciences, Immunology, and Cardiovascular and Infectious Diseases
- **Huge number of universities, hospitals and research centres** providing ideal business setting for innovative investment projects
- **7 universities** among the Top 65 in Europe in terms of impact factor in Life Sciences sector
- **40 universities** running specialist Biotechnology degree courses
- **14 specialised Science and Technology Parks** offering technology transfer services.

2. Public and Private Excellence in R&D

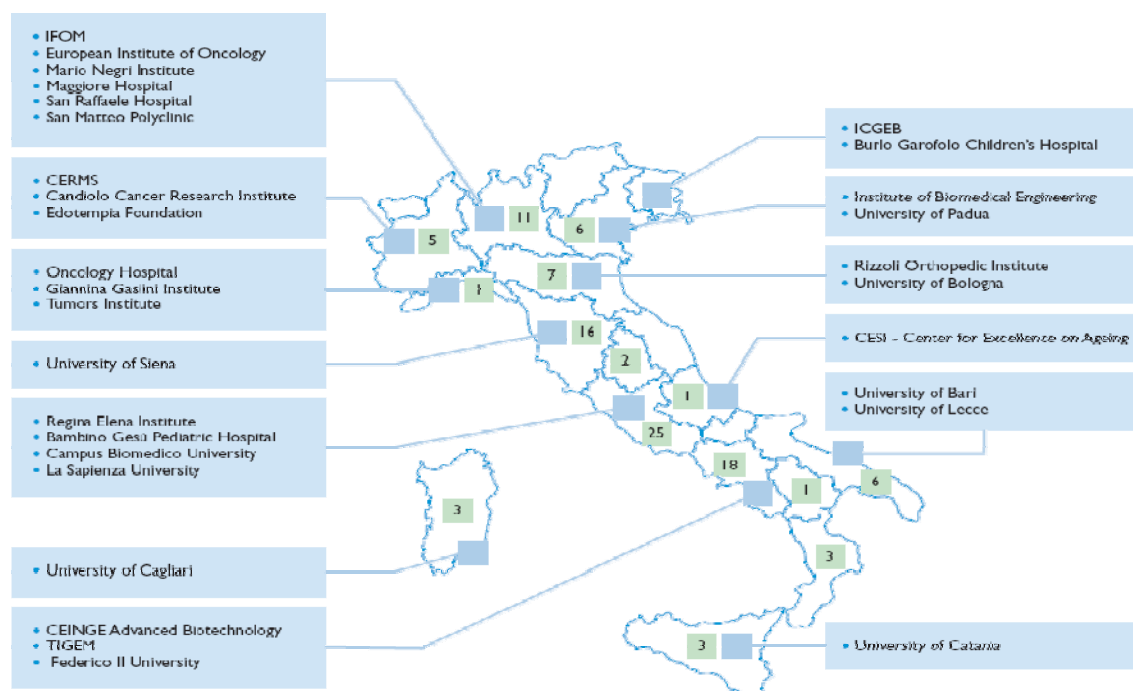
Life Sciences research in Italy is underpinned by an extensive network of dedicated centres, some of which internationally renowned. Numerous specialised **university degree courses**, are available, as well as committed research centres, and both public and private institutes.

Among top public and private centres:

- San Raffaele Hospital (Milan), a world leader in Gene Therapy and Neurosciences; and the National Institute for Research and Treatment of Tumours (*Istituto Nazionale per lo Studio e la Cura dei Tumori*), Milan
- European Institute of Oncology (*Istituto Europeo di Oncologia - IEO*), Milan

- National Cancer Research Institute (*Istituto Nazionale per la Ricerca sul Cancro*), Genoa
- *Regina Elena* Institute for Research and Treatment of Tumors (*Istituto Regina Elena per lo Studio e la Cura dei Tumori*), Rome
- *Giovanni Pascale* National Institute for Research and Treatment of Tumors (*Istituto Nazionale per lo Studio e la Cura dei Tumori "Giovanni Pascale"*), Naples
- Mario Negri Institute for Pharmacological Research (*Istituto di Ricerche Farmacologiche "Mario Negri"*), Milan
- National Research Council (CNR - *Consiglio Nazionale delle Ricerche*), Rome – operating throughout Italy
- Italian National Agency for New Technologies, Energy and Sustainable Economic Development (*ENEA - Ente Nazionale per l'Energia e l'Ambiente*) operating throughout Italy

Selected Institutes and Research Centres



3. Science and Technology Parks

Closer ties between the academic and business world have strongly contributed to accelerating innovation in the sector, thanks to recent legislative developments and Italy's long-standing focus on applied sciences. Most universities and research institutes cooperate on a regular basis with companies operating in Italy. Among main technologies currently in use and shared in Italian research centres are Molecular Biology and Monoclonal Antibodies.

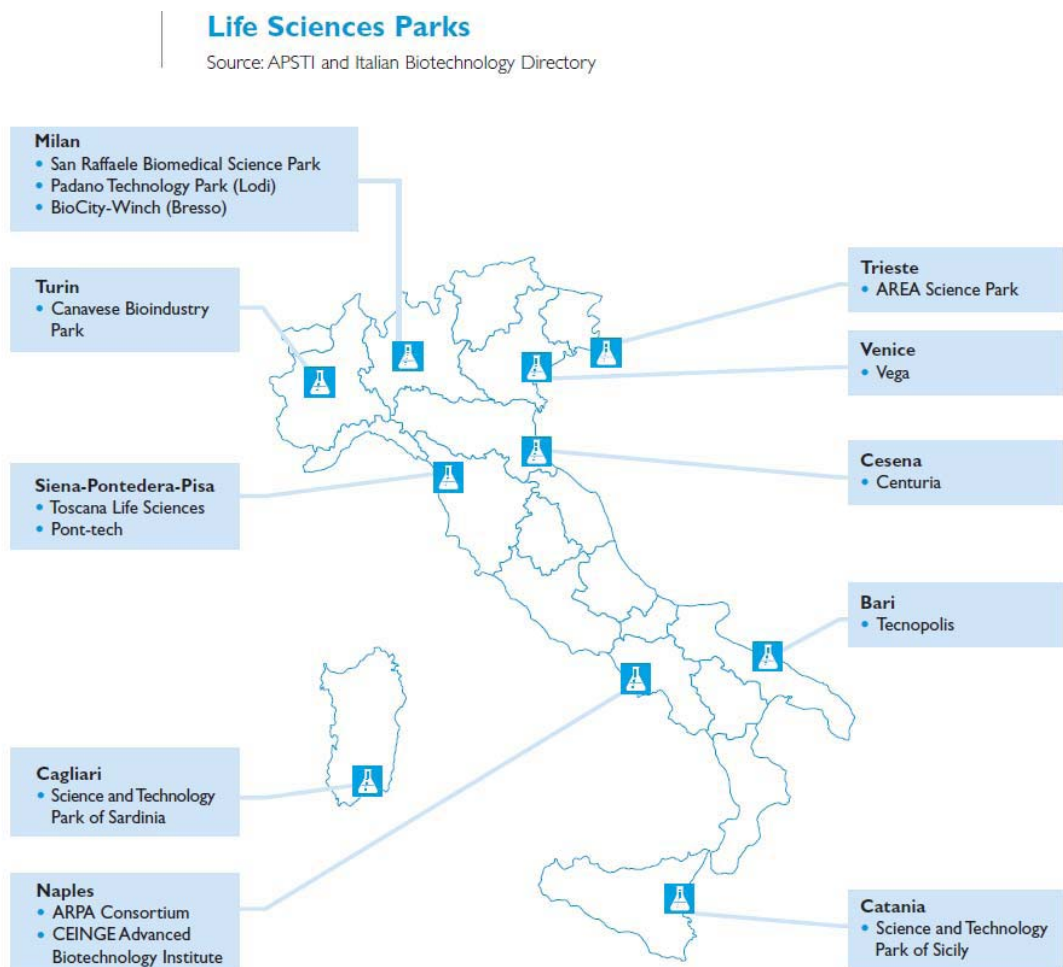
Bioinformatics is assuming ever growing importance within Genomics and Proteomics:

Bioinformatics units, involved in the integration of databases compiled during the Mapping of the Human Genome and other organisms, have greatly reduced research timing.

In-Vitro Testing, Transgenic Animals, Enzymatic Biocatalysis and use of growth regulators are only some of the new research strands most commonly employed in Italy.

Start-ups and new business initiatives in the most innovative sectors can count on the support of a network of 40 science parks and business incubators that has contributed to creating a growth-oriented business environment, thanks to dynamic interaction among companies, research centres, finance institutions and authorities. Such centres, encompassing companies, venture capitalists, universities, laboratories and research centres, can offer a wide range of services such as premises provision, technology transfers, patenting, marketing and commercialising products.

Life Science Parks



Several parks specialised in Life Sciences. Among them, notably:

- **San Raffaele Biomedical Science Park** in Milan – one of the largest in Europe specialised in Biotechnology and Biomedical technology. Linked to San Raffaele Hospital, the Park hosts numerous research centres (e.g. DIBIT, *Vita-Salute* San Raffaele University) and is notably active in technology transfer to locally-situated businesses (e.g. Axxam, BioXell, Bracco, Schering-Plough, TelBios, MolMed).

- **Canavese Bioindustry Park** in Turin (owner of the Laboratories for Advanced Methodologies - LIMA) – provides state-of-the-art services and performs exploitation of scientific results in the fields of Chemistry, Molecular Biology, Proteomics and Bioinformatics. Furthermore, a University Centre in Imaging Technologies (CEIP) managed by University of Turin focuses on the use of different technologies (MRI, Ultrasound, X-ray, etc.) in order to identify new solutions in diagnosis and assessment of drugs efficacy/efficiency.
- **Toscana Life Sciences Park** – located in Siena's *Torre Fiorentina* historic area, where Novartis Vaccines and Diagnostics has today concentrated its R&D activities and part of its vaccine manufacturing facilities. Since 2002 the area has also hosted Senabiotech. and the Molecular Biology Department of Siena University. Besides the equipped labs and office rental, the TLS Science Park provides incubated companies with full packages of services.
- **Science and Technology Park of Sardinia** in Cagliari – equipped with Technology Platforms comprising equipment and know-how available for use by companies such as: Bioinformatics Platform, Genotyping and Gene Expression Profiling Platform, Pharmacology Platform, High Throughput Screening Platform, Prototyping and Medical Devices Platform, Innovative Food Technology Platform, Proteomic Biotechnology Platform (located at the Alghero branch), NMR Spectrometry and Analytical Chemistry Platform, Microbial Biotechnology Platform.
- **AREA Science Park** in Trieste – one of the main multisectoral science parks in Europe with institutes and centres of excellence in the fields of Biotechnology, Diagnostics, Chemicals and Biomedical Technology. Among the leading park initiatives is the Regional Technology District of Molecular Biomedicine (TDMB), established within AREA end-2003.

Incentives

For detailed information on incentives to Life Sciences sector, please read the following sections (Chapter 6: Incentive Programmes) in Invitalia's Investment Guide - Doing Business in Italy: (<http://www.invitalia.it/on-line/eng/Home/BusinessEnvironment/Incentives.html>).

Opportunities

The main business opportunities in the Italian biotech industry lie in the **Red Biotech segment**, (i.e. R&D), and primarily in the areas of top specialisation and prestige of Italian research such as Biomedicine, Oncology, Diagnostics, and Neuroscience.

Prospective investment typologies include:

- Spin-off by research or company
- Multifunction R&D centres
- Research Partnership between foreign company and R&D Italian centres
- Research Partnership between foreign company and Italian company
- Venture Capital Funding.

The small and flexible structure of Italian companies encourages B2B–B2R technological partnering in the Red Biotech segment. Furthermore the opportunity, for Italian small enterprises with turnover below 10 million euro to increase research activities thanks to Venture Capital funds, provides relevant perspectives for development.

Italy offers plenty of scope for opportunities in the field of **Clinical Trials**. In recent years changes to regulatory procedures, now compliant with European rules, have decentralised decision-making to special Ethics Committees.

In May 2009, *Assobiotec* (Italian Association for Biotechnology Development), *AIFA* (National Medicines Agency) and the *ISS* (National institute of Public Health, *Istituto Superiore di Sanità*) signed the agreement aimed at fostering early-phase clinical trials for new drugs in Italy.

Thanks to the Agreement, timing for evaluation of **Clinical Trial applications was reduced from 100 days in 2005 to 45 days in 2009.**

Such a major result, combined with the presence of an extensive network of over 170 competent centres (including hospitals, IRCCS institutes and universities), led to a drastic reduction in terms of market costs and timing, thus making Italy one of the most appealing locations for carrying out clinical trials.

TOP Clinical Trials

Year	CT	%
2000	562	8,3
2001	610	9.00
2002	571	8.04
2003	579	8.05
2004	623	9.02
2005	663	9.08
2006	777	11.04
2007	791	11.07
2008	869	12.08
2009	742	10.09

Total **6,787** **100**

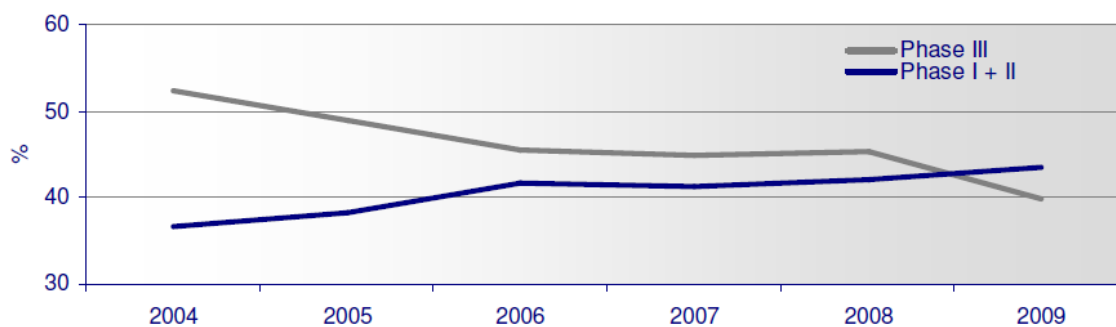
(Source: National Medicines Agency- AIFA 2010)

Total clinical trials performed in the 2000-2009 period amounted to 6,787.

Primarily concentrated on Phase II and Phase III, clinical trials are routinely conducted in Italy compliantly with the internationally recognised clinical protocol and quality control standards.

In 2009 Phase III studies, for the first time, are below 40% whilst Phase I and Phase II trials are still growing: in the last year they reached combined 43.5% of the total. In 2004 -2009, 159 Phase I studies were entered into OsSC (3.6% of total clinical trials). They are mainly multicentre and international and sponsored by pharmaceuticals companies. Nearly 26% of them (41) are *first in human trials*.

Phase III versus Phase I + II clinical trials



(Source: National Medicines Agency- AIFA 2010)

Oncology is the most investigated therapeutic branch (29.4%), followed by Cardiology/Vascular Diseases (9.6%), Neurology (8.9%) and Immunology and Infectious Diseases (8.4%).

The main objects of studies include Gemcitabine Therapy, Acetylcarnitine, Erythropoietin (EPO), Levocarnitine, and Influenza Antigens.

In the years 2004-2009, about 260 studies were carried out with “orphan drugs”, medicinal products that can potentially be of significant benefit to those affected by a “rare disease”. Their number in OsSC noticeably increased since 2008. They are multicentre, international, Phase I and II clinical trials, for the most part; pharmaceuticals companies fund about 80% of studies with orphan drugs.

Top 5 clinical trial by Therapeutic Branch

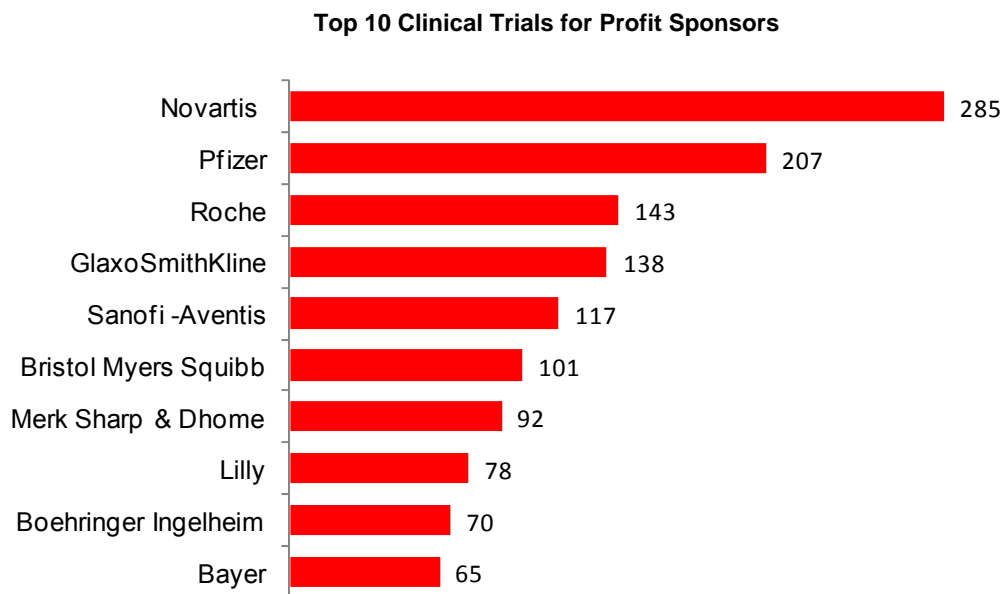
Total CT's 4,465 – of which 4,444 (99,5%) with specified therapeutic branch

Therapeutic branch	CT	%
Oncology	1,314	29.4
Cardiology/Vascular Diseases	428	9.6
Neurology	396	8.9
Immunology and Infectious Diseases	376	8.4
Gastroenterology	231	5.2

(Source: National Medicines Agency – AIFA 2010)

Pharmaceutical companies are the prime players in the area of Clinical Trials. Over 350 businesses are responsible for testing primarily on Antineoplastic and Immunomodulatory Medicines, drugs for nervous system treatment, and Antimicrobials.

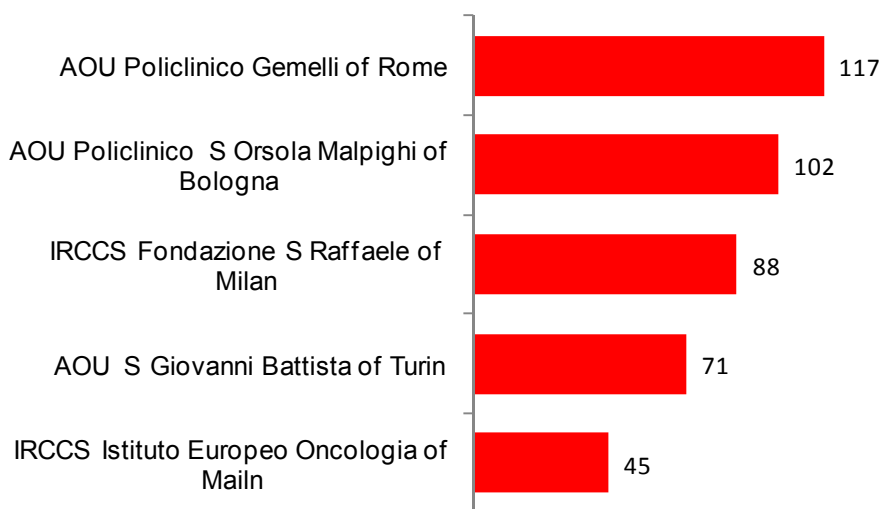
The first 26 out of 360 pharmaceutical companies sponsor 66% of clinical trials.



(Source: National Medicines Agency – AIFA 2010)

Among several important no-profit organizations carrying out Clinical Trials, *Gemelli University Hospital of Rome*, *Suor Orsola Malpighi Hospital of Bologna*, *San Raffaele Hospital of Milan*, *S. Giovanni Battista University Hospital of Turin*, and the *European Institute of Oncology (IRCCS) of Milan* are all leaders in the field.

Top 5 Clinical Trial for No-Profit Sponsors



Already in Italy

Among the factors encouraging continued foreign investment interest in Italy's Life Sciences industry, two stand out, and namely: its highly prolific Research and Innovation annually funded by private R&D investments, and its long-standing production tradition, directly involving approximately 600 companies, as well as hundreds of industry-related businesses, most of which multinational companies.

Pharma foreign companies in Italy by Region



(Source: Reprint 2011)

- Italy hosts 140 Pharma **foreign companies** and R&D foreign centres, with over 43,000 employees and € 18,839 million overall turnover.
- **USA** accounts for the first foreign investor with 44 companies, 17,108 employees and € 6,720 million turnover

Top 15 Foreign Pharma Companies in Italy

Company	Region	Employees	Turnover (mn. €)	Country
SANOFI-AVENTIS SPA	Lombardy	2.579	1.401,859	France
PFIZER ITALIA SRL	Lazio	2.260	1.251,234	USA
ABBOTT SRL	Lazio	2.039	1.139,392	USA
MERCK SERONO SPA	Lazio	621	1.101,987	Germany
GLAXOSMITHKLINE SPA	Veneto	1.956	1.101,243	UK
ROCHE SPA	Lombardy	1.182	1.047,885	Switzerland
NOVARTIS FARMA SPA NOVARTIS VACCINES AND DIAGNOSTICS SRL	Lombardy	1.716	914,574	Switzerland
	Tuscany	1.584	814,063	Switzerland
WYETH LEDERLE SPA	Lazio	1.709	730,998	USA
ASTRAZENECA SPA	Lombardy	965	699,278	UK
BRISTOL-MYERS SQUIBB SRL	Lazio	2.283	574,403	USA
ELI LILLY ITALIA SPA	Tuscany	1.005	561,917	USA
JANSSEN CILAG SPA	Lombardy	969	493,257	USA
MERCK SHARP & DOHME ITALIA SPA	Lazio	1.364	491,955	USA
BAYER HEALTHCARE MANUFACTURING SRL	Lombardy	284	458,156	Germany
SCHERING-PLOUGH SPA	Lombardy	841	457,856	USA

(Source: Reprint 2011)