

*Research, Innovation and
Industry alliances @ CNIO*

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Spanish National Cancer Research Centre



~450 People: Research (~ 90%)and admin (~10%)

~40% of the Research force is non-spanish

International Ranking 2015 (cancer centers)

(out of 4840 institutions (99 Spain) Scimago July 2010-2015)



CNIO Position in the International Ranking Cancer Centers

Excellence with Leadership

Rank	Cancer Research Centers	Country		EwL
14	Memorial Sloan-Kettering Cancer Center	USA	Health	57.88
20	Institute of Cancer Research	GBR	Health	53.85
25	Dana Farber Cancer Institute	USA	Health	49.22
27	Centro Nacional de Investigaciones Oncologicas	ESP	Health	48.96
31	University of Texas M.D. Anderson Cancer Center	USA	Health	48.01
37	National Cancer Institute (NIH)	USA	Health	45.92
48	Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospita	NLD	Health	44.09
74	Fred Hutchinson Cancer Research Center	USA	Health	39.54
82	Istituto Europeo di Oncologia	ITA	Health	38.13
83	H. Lee Moffitt Cancer Center and Research Institute	USA	Health	38.09
109	Peter Maccallum Cancer Centre	AUS	Health	35.85
148	Roswell Park Cancer Institute	USA	Health	32.36
243	National Cancer Center	JPN	Health	26.47
247	Tom Baker Cancer Centre	CAN	Health	26.36
253	National Cancer Center	KOR	Health	25.75
359	National Cancer Centre	SGP	Health	22.22
394	Cross Cancer Institute	CAN	Health	20.51
409	Istituto Nazionale dei Tumori Fondazione Giovanni Pascale IRCCS	ITA	Health	20.24
445	Aichi Cancer Center Research	JPN	Health	18.72

%Ewl: Excellence with Leadership: The amount (in %) of an institution's scientific output that is included into the set of the 10% of the most cited papers in their respective scientific fields in which the institution is the main contributor. **This is a size-independent indicator.**

International Ranking 2015 (cancer centers)

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CNIO Position in the International Ranking Cancer Centers

Parameter Q1

Rank	Cancer Research Centers	Country		Q1
19	Fred Hutchinson Cancer Research Center	USA	Health	91.15
24	Centro Nacional de Investigaciones Oncologicas	ESP	Health	90.45
29	Dana Farber Cancer Institute	USA	Health	89.20
45	Institute of Cancer Research	GBR	Health	87.42
46	National Cancer Institute (NIH)	USA	Health	87.20
52	Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital	NLD	Health	86.68
79	Memorial Sloan-Kettering Cancer Center	USA	Health	83.08
165	Institut Catala d'Oncologia, Hospitalet de Llobregat	ESP	Health	76.66
265	National Cancer Centre	SGP	Health	70.18
272	Cross Cancer Institute	CAN	Health	69.98
295	Tom Baker Cancer Centre	CAN	Health	69.28
313	Istituto Nazionale dei Tumori Fondazione Giovanni Pascale IRCCS	ITA	Health	68.25
417	National Cancer Center	KOR	Health	62.76
469	National Cancer Center	JPN	Health	59.27
573	Osaka Medical Center for Cancer and Cardiovascular Diseases	JPN	Health	51.75
574	Hospital do Cancer A.C. Camargo	BRA	Health	51.15
644	Sun Yat-sen University Cancer Center	CHN	Health	44.97
663	Shizuoka Cancer Center	JPN	Health	42.73

Q1: High Quality Publications: Ratio of publications that an institution publishes in the most influential scholarly journals of the world, those ranked in the first quartile (25%) in their categories as ordered by SCImago Journal Rank (SJRII) indicator. This is a **size-independent indicator**.

Scientific Production Spanish Biomedical Institutions



2015: CNIO was for the second time distinguished with the National Excellence Award in Science “Severo Ochoa” .

Institution outputs			
Region/country	Sector	Subject/journals	Sort by
Spain	All	Life Sciences	Weighted fractic
Institution	AC	FC	WFC
1. + Spanish National Research Council (CSIC)	218	50.74	50.74
2. Pompeu Fabra University (UPF)	74	16.24	16.24
3. - Barcelona Institute of Science and Technology (BIST)	72	13.94	13.94
Centre for Genomic Regulation (CRG), BIST	52	7.08	7.08
Institute for Research in Biomedicine (IRB Barcelona), BIST	27	6.69	6.69
4. Spanish National Cancer Research Centre (CNIO)	37	11.99	11.99
5. University of Barcelona (UB)	81	11.10	11.10
6. Institute of Health Carlos III (ISCIII)	103	9.79	9.79
7. Autonomous University of Madrid (UAM)	58	8.59	8.59
8. Autonomous University of Barcelona (UAB)	40	8.17	8.17
9. National Center for Cardiovascular Research (CNIC)	25	7.42	7.42

*Nature Index ranking WFC which includes the best spanish institutions in teh life sciences. WFC measures the contribution of each institution to a scientific publication.

Basic Research

Cancer Cell Biology

4 Research Groups: **2 senior + 3 junior**



E. WAGNER

Molecular Oncology

9 Research Groups: **7 senior + 2 junior** (+ 1 Junior NUEVO!!)



M. SERRANO

Structural Biology and Biocomputing

3 Research Groups: **1 senior + 2 junior**

3 Support Units



A. VALENCIA
(Vice-Director)

Research Organization

Traslational Research

Human Cancer Genetics

4 Research Groups: **4 senior**
2 Support Units



J. BENITEZ



M. HIDALGO
(Vice-Director hasta Dec 2015)

Clinical Research (CNIO-Hospitals)

5 Clinical Research Units: **3 senior + 2 junior**
2 Support Units

Biotechnology

8 Support Units

Experimental Therapeutics

2 sections (Biology & Chemistry)
2 Eli-Lilly labs

Technology Transfer



F. PELAEZ



A. SANZ



J. PASTOR



O. FERNANDEZ-CAPETILLO
(Vice-Director
Director de Innovación)

Academic Drug Discovery at CNIO



Joaquin Pastor, Director Experimental Therapeutics Programme

Drug Discovery Portfolio



Targeted Screening Projects

In vivo PoC

PIM inhibitors / CNIO

Licensed



PIM / PI3K (mTOR) dual / triple inhibitors / CNIO

Licensed



ATR inhibitors / Collaboration Fernández-Capetillo (CNIO)

Available

PI3K α - δ inhibitors / (Obesity) Collaboration Serrano (CNIO)

Available

"Retos MINECO"

CDK-8 inhibitors / CNIO

Target-X inhibitors / Collaboration VIB

Co-development
VIB funded



Target-Y / Collaboration VIB

MASTL / HASPIN Col. Malumbres (CNIO)

CNIO currently in development

Allosteric FAK / Col. Lietha (CNIO)

Screening Projects which require Target Deconvolution

TRF1-PI3K / Collaboration Blasco (CNIO) (after Target Deconvolution)

(Unpublished Results)

TRF1 / Blasco (CNIO) (TD)

CSCs / Serrano (CNIO) (TD)

Gluconeogenesis / Serrano (TD)

Metastasis / Valiente (CNIO)

TARGET
DECONVOLUTION
(TD)

CNIO currently in development

CSCs: Cancer Stem Cells therapies

Collaboration is possible at any stage



PROJECT PHASES

PHASE I

IDEA/Proposal

JOINT Discussion
Proposing scientist
ETP-CNIO Scientists
and Innovation

Full Proposal
Including additional
Information*

Publications

Results
Positive but NOT
competitive

EXPLORATORY
PROJECT
Screening 600
or tools for validation

GO/NO
GO

PHASE II

Results
Competitive
(Patenting)

Full CNIO
e-DD PROJECT

EXIT

Licensing/ Partnering

• Criteria:

- Scientific Rationale
- Proposing Scientist Commitment
- Stage Target validation / Therapy Assay
- Druggability
- Market Opportunity (Competitive Landscape)
- Intellectual Property
- Potential Exit Route / Partners
- Funding Plan

* Evaluation Committee

How to start your project a ETP-CNIO?



Contact us:
technologytransfer@cnio.es
www.cnio.es



Overview Collaborative Research

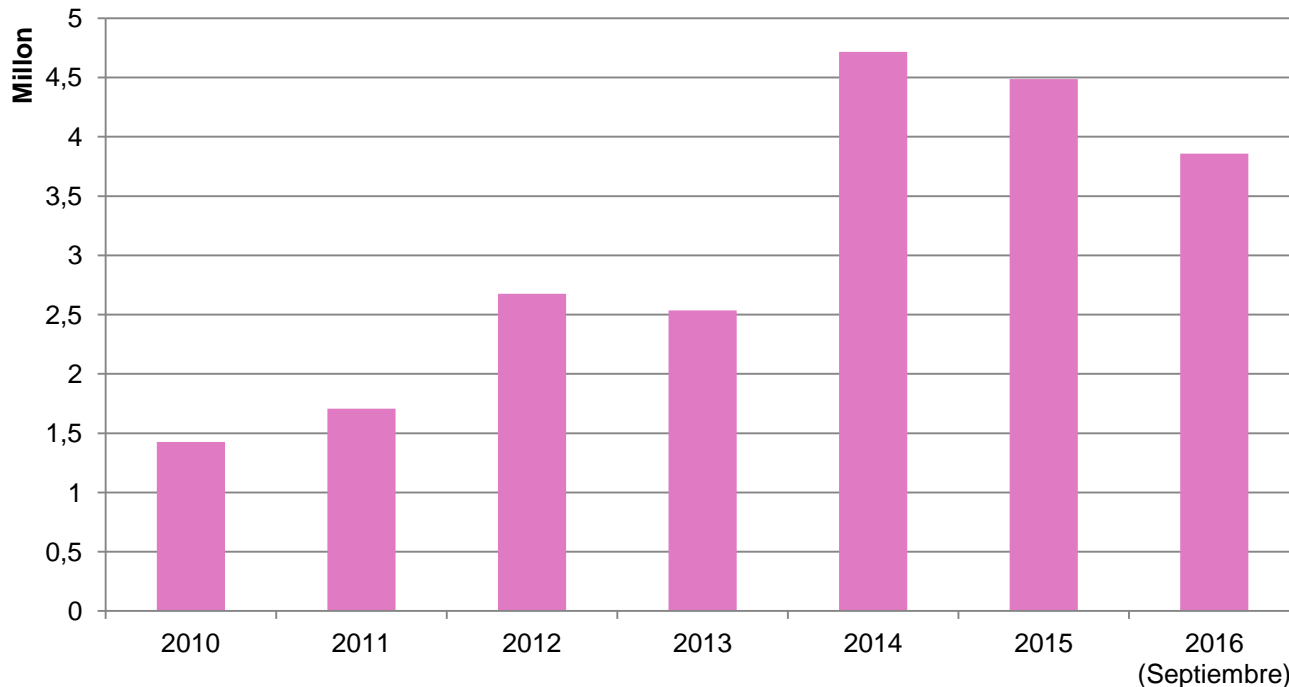


✓ 2015: Expansion of collaborative network. Significant increase (2 X) in the number of collaborative companies (from 10 to 20) (Lilly, Boehringer Ingelheim, Merck KaaG, Daiichi Sankyo...)

✓ 4.5 Mio. € secured income in contracts in 2015

✓ 2016: **3.9 Mio. €** (September)

Collaborative Research w/ Industry



Lilly



Academic partner.
Drug discovery collaboration

Classification. Type of Alliances

✓ **Strategic**

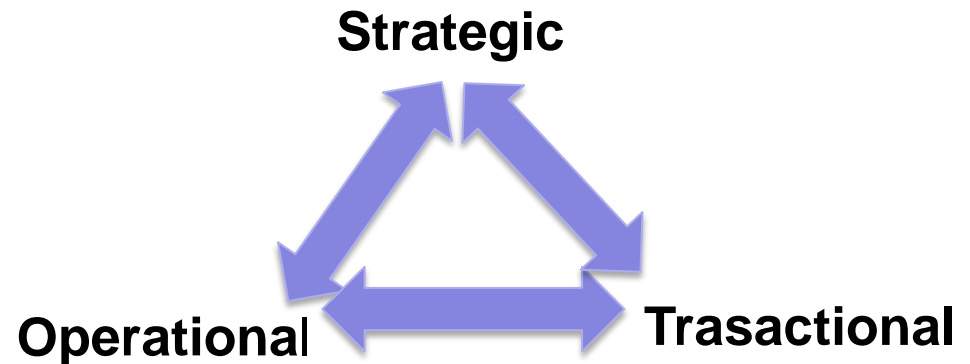
Strategic focus. Long term view.
More than 3 years
One or more projects
One or several research groups

✓ **Operational**

1-2 years
Project focus
Single research group

✓ **Trasactional**

testing/exploratory
typically involve material transactions



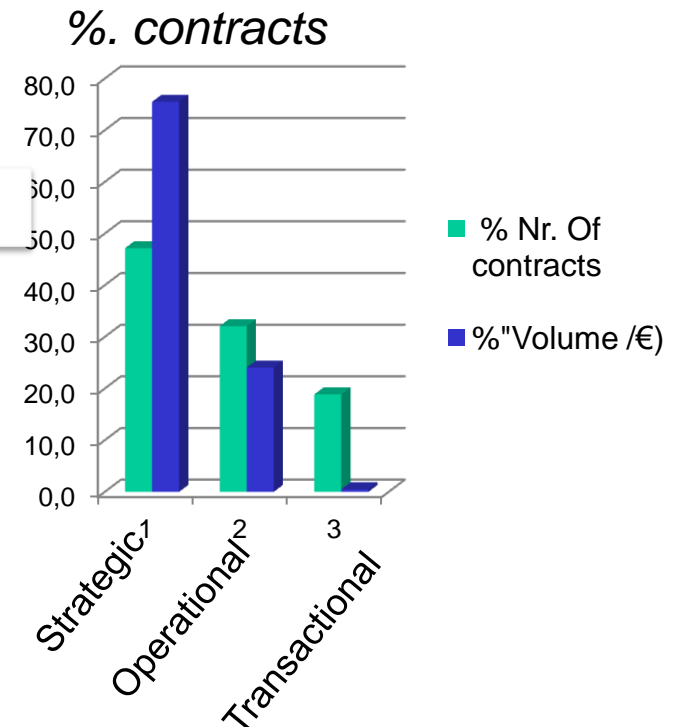
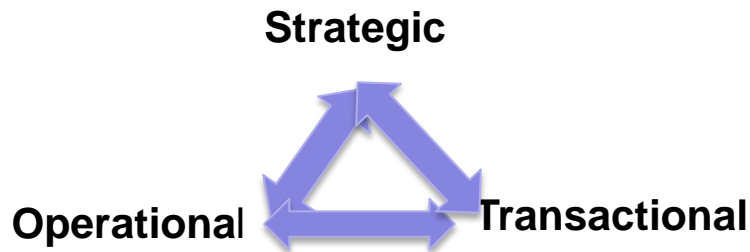
Industry Alliances CNIO Facts



2015 Classification. Type of alliances with industry

- ✓ Strategic: 48 % in Nr < - > 75% Income
- ✓ Operational: 32 % < - -> 24 % income
- ✓ Transactional: 20 % < - -> .0.1 % income

✓ **Strategic** alliances contribute **75% of the income**



Take Home messages

1. Build strategic alliances
2. Don't disregard Transaccional/Operational alliances .Not every alliance is strategic; but It may become strategic

Tale and history

2010: preclinical evaluation of a combination of drugs proprietary to the company

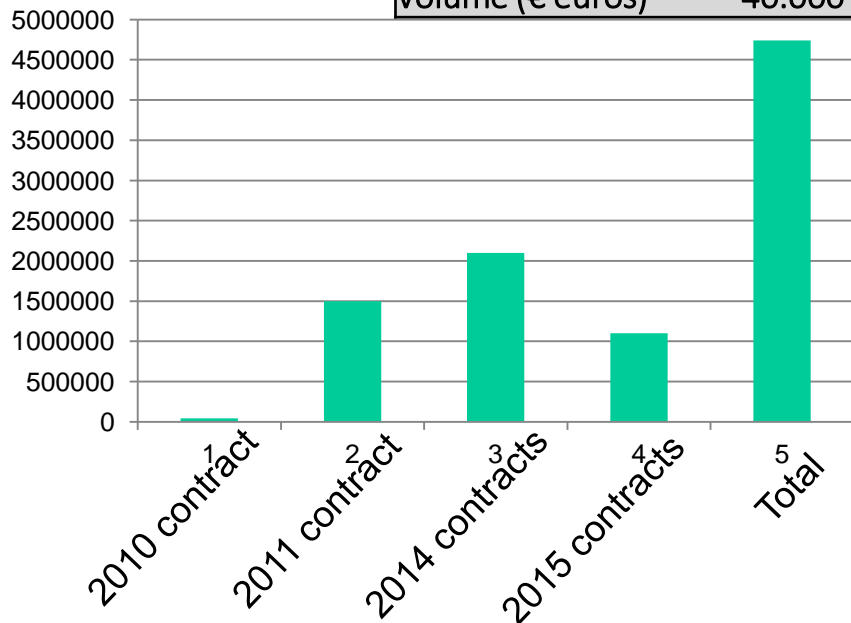
2011: identify and validate new target//perform preclinical trials with compounds modulating newly validated targets.

2014: Mechanistic studies of a company's proprietary drug

2015: Develop supportive biology packages for putative novel anticancer targets

2015: Efficacy assessment of drug combinatorial studies

Overview strategic collaboration				
Timeline	2010	2011	2014	2015
Nr. Of Research Groups	1	3	2	2+2
Duration of contract	1 year	3 years	2 years	2 years
Volume (€ euros)	40.000 €	1.5 Mio \$	2.1 Mio \$	1.1 Mio \$



✓ An strategic alliance grows from 40.000 € to 4.5 Mio in 6 years time

✓ In total 6 CNIO Research groups involved

Lessons learned



- ✓ Engagement of top leadership is essential.
- ✓ Communication of clear **goals and benefits** for each party. including for the researcher is essential
- ✓ Start with a shared vision and to create a **communication environment**:
Researchers need access to company management senior enough for opportunities to emerge.
- ✓ Having **the right people in the right place** is essential;
 - ✓ A champion that can understand both cultures: company & research centre (Academic centres need people with a CV beyond a research pedigree)
 - ✓ Companies need to devote time & people to the collaboration
- ✓ For a Researcher a key motivation is to access new **funding** streams.
But also to access companies expertise. Additionally creating an impact by bringing a solution to the market is very important
- ✓ Providing **Incentives and management resources** can push-up the collaboration
Next to funding for Researches it may be very valuable to get to other companies expertise: technical, business etc

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Lessons learned



A few Don'ts

- ✓ Don't start before the plan is drawn and clear to all stakeholders
- ✓ Avoid to get hang up on ownership and IP issues
- ✓ Avoid inequalities & make sure the plan contemplates everybody interest
- ✓ Don't close the communication channels beyond the project once the contract is signed. Reiterated circles of interactions is essential to cross-fertilize ideas and opportunities to emerge

To Conclude:

You only partner with whom you know and a partnership starts with a dialogue.

Ensuring an open dialogue between research centres and industry is essential.
The Farma-Biotech initiative of Farmaindustria is a great forum contributing to foster
Public-private collaborations

THANKS

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Back up slides

ETP-Biology (9 FTEs)

Screening / Biological Characterization of ETP and Reference compounds.

HTS and automated platform for DD assay.

- Development of biochemical and cell based assays in HTS / automated format.
- Off-target selectivity primary assays.
- Full selectivity panels done externally.
- In vitro ADMET assays in place:
 - Solubility / PAMPA / PPB
 - Microsomal stability (h,m,r)
 - CYP inhibition
 - hERG binding ...



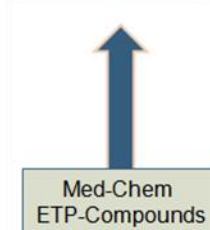
Biomek FX Dual Span 8



Biomek FX



EnVision



Med-Chem
ETP-Compounds



Assay Development

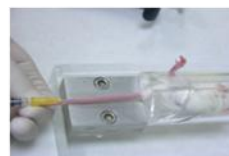


High Content Screening plate reader

Selected Compounds

Cell & in vivo Pharmacology:

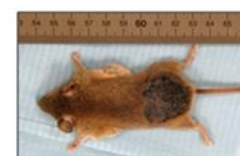
- Cell target validation and mechanistic studies: genetic inhibition, biomarkers, cycle analysis...
- Cell anti-proliferation including combinations.
- Colony Formation and Migration...
- In vivo pharmacokinetics (mouse):
 - Formulation.
 - Full PK studies.
- Anti-tumour activity & PK/PD (MoA) in xenografts, including "avatar", allografts and GEM models.
- Validation of molecular targets in GEM tumor models.



Pharmacokinetics

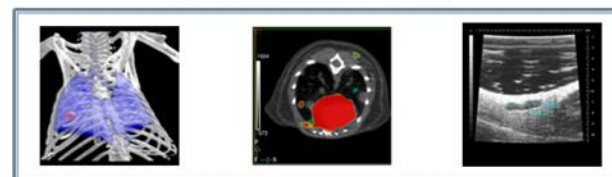


Colony Generation
and Maintenance
Xeno/Allografts and GEM



Target Validation (PoC)
PK/PD
Efficacy

CNIO-BT Molecular Imagin Unit



ETP-CNIO: Organization & Capabilities



ETP- Medicinal Chemistry (9 FTEs)

**Responsibility over ETP-Library,
Design / Synthesis of ETP compounds, and
Data Management .**

ETP-Library: 50 K single compounds.

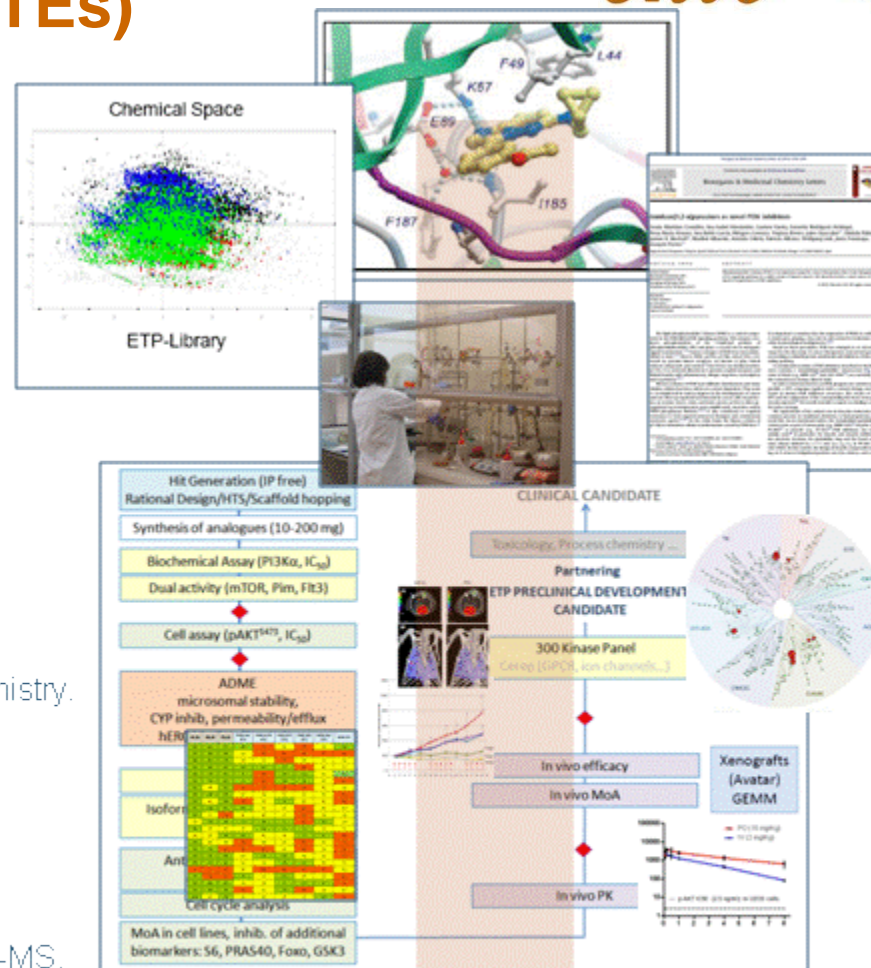
- Kinase focused & chemical diversity
- Presence of diverse fragments (MW < 300)
- Compliance with druglikeness rules.
- About 10% ETPs from internal DD projects.
- FDA approved drugs library (1.5K) for repositioning
- ETP-Antitumorals Library.

Hit generation / HitL and LO:

- Guided selection of HTS sets by computational chemistry.
- Rational design: Med-Chem expertise and Computational Chemistry.
- Crystallography guided optimization.
- Multi-factorial optimization (Potency/selectivity/ADMET)
- Early In vitro-In vivo correlations.
- Modern synthetic methodologies: SB and Parallel, MW...
- Analytical and purification systems to meet standard "Pharma requirements" for ETP compounds: >95% pure by NMR and LC-MS.

Crystallography Unit:

- 3D Crystal Structures
- SxSs (small angle X-ray scattering) and other structural techniques



Laboratory and Equipment

- ✓ ~300 m² of Laboratory Space.
- ✓ 22 Full equipped fume hoods (expansion capacity)
- ✓ 1 Microwave Biotage Sixty
- ✓ 1 Microwave CEM Discover
- ✓ Hydrogenation: H-cube™ ThalesNano
- ✓ Hydrogen Gas Generator, Parker
- ✓ High pressure synthesis (Parr)
- ✓ Parallel Synthesis: Bodham
- ✓ 7 automated purification Biotage System (SP4, Isolera one)
- ✓ 1 NMR, Bruker 300 MHz
- ✓ 1 NMR, Bruker 700 MHz
- ✓ 2 Analytical LC/MS Agilent Technologies
- ✓ 1 Preparative LC/MS Agilent Tech. 1100 Series
- ✓ FT-IR, Varian 1100 Series



Operational Model – project portfolio based



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Full Proposal
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