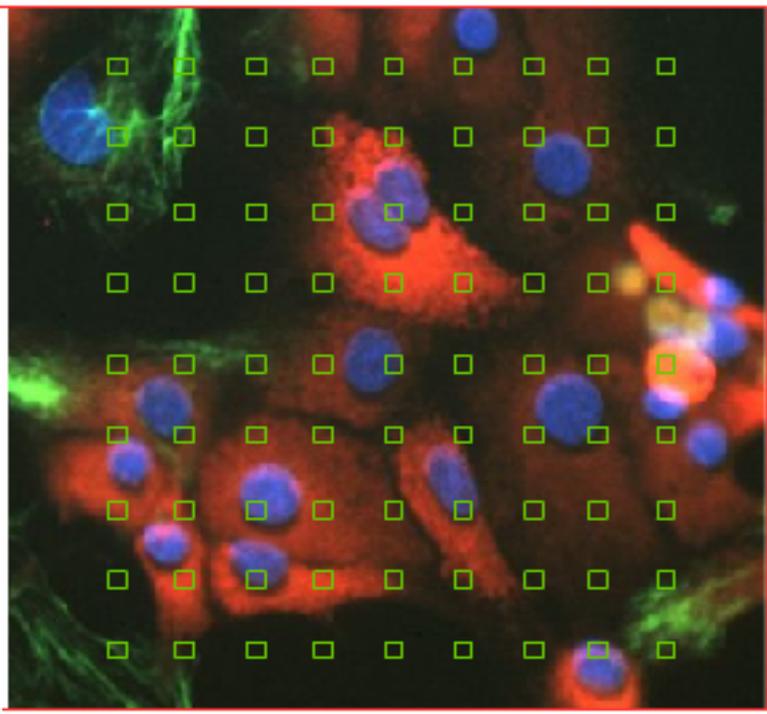


*"In vitro" models, reprofiling and nanomedicine  
for unmet medical needs*

# The Spanish biotech sector Case: ADVANCELL

**SPAIN-LUXEMBURG ECONOMIC SEMINAR  
April 18th, 2007**



BUSINESS



LE GOUVERNEMENT  
DU GRAND-DUCHÉ DE LUXEMBOURG  
Ministère de l'Économie  
et du Commerce extérieur



SECRETARÍA DE ESTADO  
DE TURISMO Y COMERCIO



# ELEVATOR PITCH

Product oriented, low burn-rate company addressing unmet therapeutical needs by *reprofiling* validated compounds.

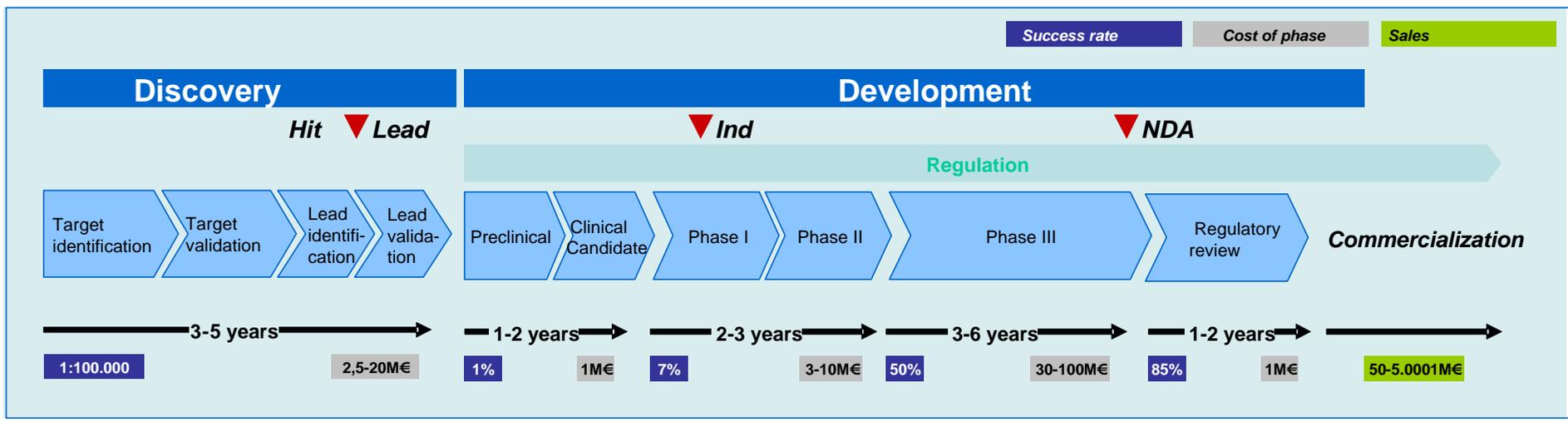
*Reprofiling* strategies are based on licensing from an extense academic network and on proprietary, broad-spectrum nanomedicine technologies which are used as cost-effective pipeline generators.

All selected developments address clearly defined unmet needs and have lower-than-average cost/time to relevant proof of principle and lower-than-average development risk.

# SUMMARY

- Privately owned, founded by University researchers in 2001
- Leading position in nanomedicine
- Strategic approach to reduce risk, cost and development time
- Board and Management with strong academic roots, financial and pharmaceutical experience
- Raised 4.6M€ since inception in 2001 (last financing event: 3M€ A round in November 2005)
- Revenues through self-sustaining Services and Reagents division and occasional licenses (total 2.4 M€ in 2006, up 50% from 2005)
- Clinical stage, balanced pipeline addressing unmet needs with cost and risk-effective reprofiling strategies
- Strong and fast pipeline generation capabilities based on proprietary drug delivery technologies and continuous access to academic innovation
- Broad intellectual property base

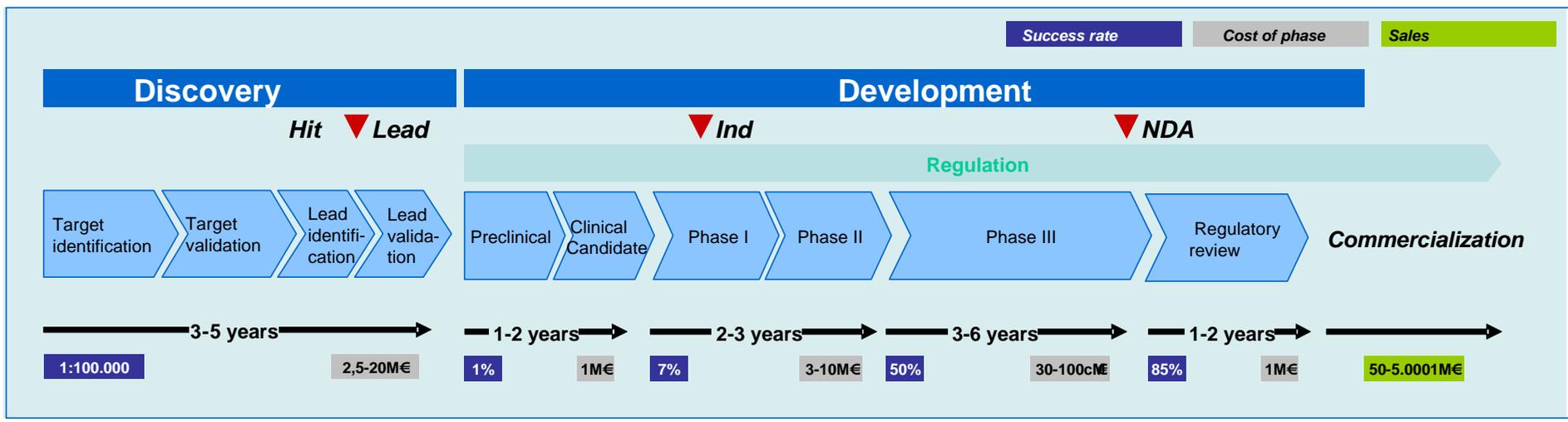
# ADVANCELL IN THE VALUE CHAIN



Services and Reagents  
("in vitro" cellular models)

Pharma developments  
(reprofiling, nanomedicine and outsourcing)

# ADVANCELL APRIL 2007



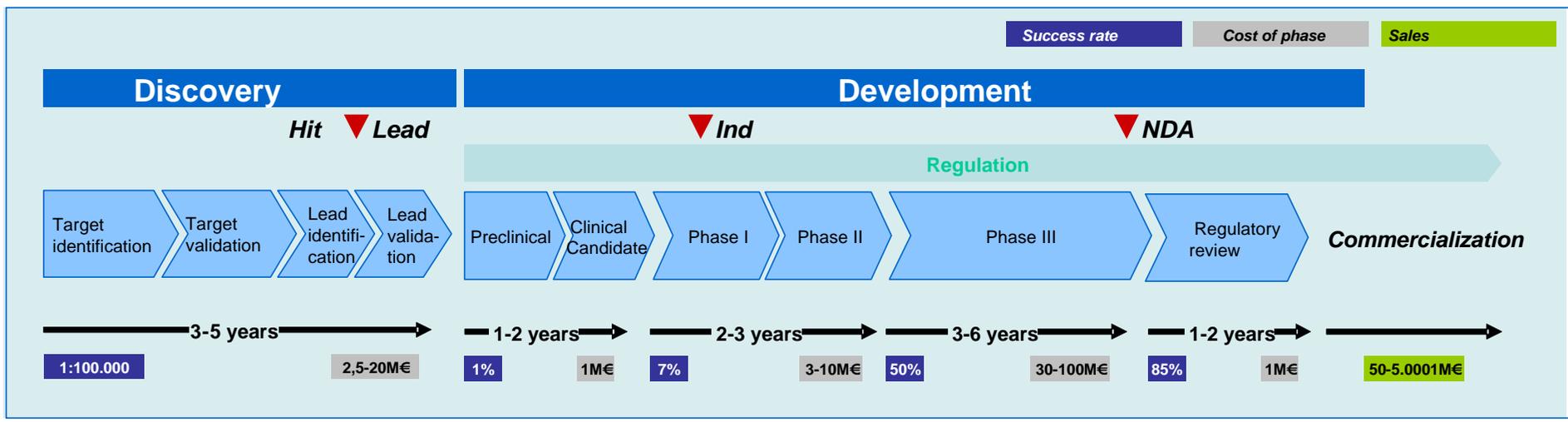
Services and Reagents  
("in vitro" cellular models)

Pharma developments  
(reprofiling, nanomedicine and outsourcing)

- 650+ research projects for 3rd parties
- > 50% success rate
- Cellular kits marketed ww
- Positive financial results in 2007
- 2 proprietary platform technologies to sustain reagent development

- 1 Phase II project
- 2 projects entering phase Ib (1 orphan)
- 2 preclinical projects
- 2 feasibility projects for third parties
- 3 research programs
- 11 nanomedicine patent families

# PIPELINE BY YEAR END 2007



Ophthalmic program  
 Nucleic acid program  
 Vaccine program

Oral Insulin  
 Oral Heparin  
 CTL6

CTL13 DT™

Cyclosporine DT™ (psoriasis)

Acadesine (B-CLL, orphan)

ADVP8 (depression)

# REPROFILING (*repurposing, repositioning*)

## Alternative uses to compounds with extensive clinical exposure

- New found mechanism of action opens space for new IP and fast clinical proof of concept (Acadesine in B-CLL)
- De-prioritized compounds amenable to risk-sharing, success-driven strategies involving academic collaborators (ADV-P8 in depression)
- Proprietary technologies enabling new delivery routes for validated compounds (Oral insuline, heparin, CTL6; Cyclosporine and CTL13 DT™ + research-stage pipeline)

# VALUE DRIVERS: ADV-P1 (ACADESINE) FOR CHRONIC LYMPHOCYTIC LEUKEMIA OF B CELLS

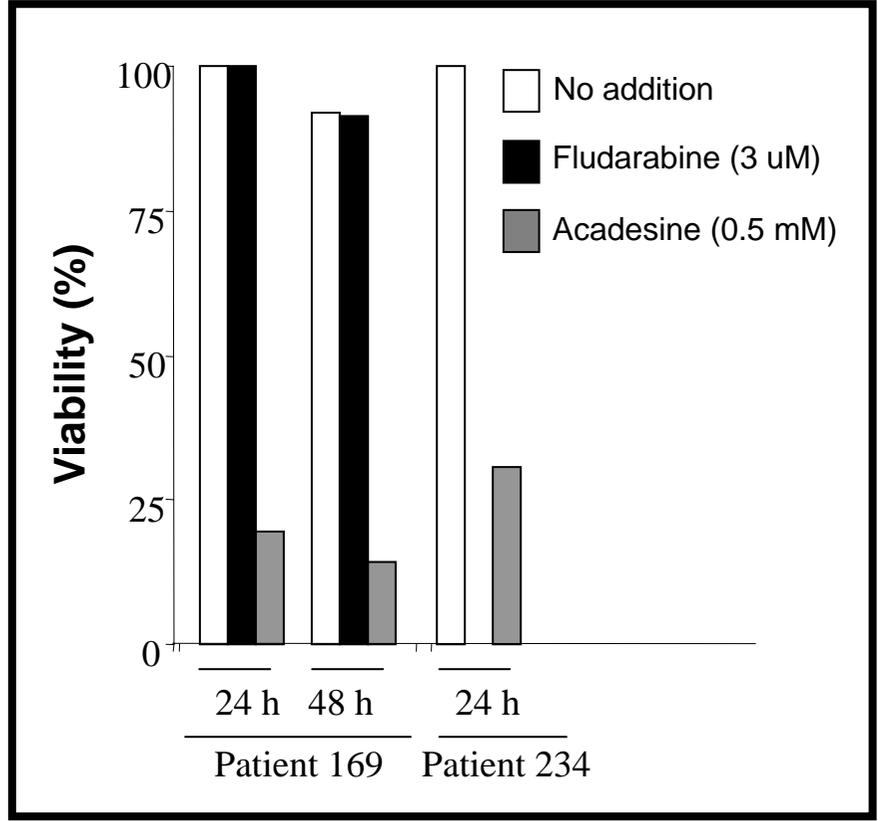
- Chronic accumulation of monoclonal CD5+ B lymphocytes in peripheral blood, ganglia and bone marrow. Cells do not proliferate in peripheral blood, apoptosis inhibited.
- Prevalence: 250,000 patients EU + US
- Patients treated: 50%
- Two groups of patients regarding prognosis: IgH unmutated, CD38+, ZAP70+ and IgH mutated, CD38-, ZAP70-. Survival from months to decades.
- Current treatment: induction of cell death (apoptosis) in B-CLL cells
  - chemotherapy (fludarabine, chlorambucil, cyclophosphamide, mitoxantrone)
  - monoclonal antibodies: rituximab, campath
  - combinations: FCM, R-FCM
- Problems with current treatment:
  - **lack of selectivity produces toxicity (immunodeficiency, infections, anemia)**
  - **resistance: ATM mutations (20%), p53 mutations (at least 5%)**

**Physicians tend to “wait and see” before treating!!**

# VALUE DRIVERS: ADV-P1 (ACADESINE) FOR CHRONIC LYMPHOCYTIC LEUKEMIA OF B CELLS

## Product profile

- ✓ **Safe** (previous clinical experience in 2000 patients for CARDIOPROTECTION!)
- ✓ **B-Cell specific**
- ✓ **Novel mechanism of action**
- ✓ **Independent of p53 or ATM mutations**
- ✓ **Effective “ex vivo” in more than 300 samples from B-CLL patients**



ATM mutated

# VALUE DRIVERS: ADV-P1 (ACADESINE) FOR CHRONIC LYMPHOCYTTIC LEUKEMIA OF B CELLS

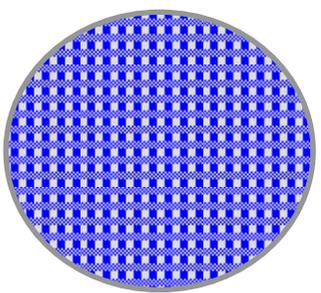


*On December 6th Advancell and Protherics Plc agreed to codevelop Acadesine for B-CLL, in a deal worth up to 29 M€ in development milestones*

*The deal reduces Acadesine financial risk to virtually “0” for Advancell while keeping a high potential value in a double digit royalty stream upon commercialization*

# VALUE DRIVERS: NANOMEDICINE PLATFORM

## PLGA-based nanosystems

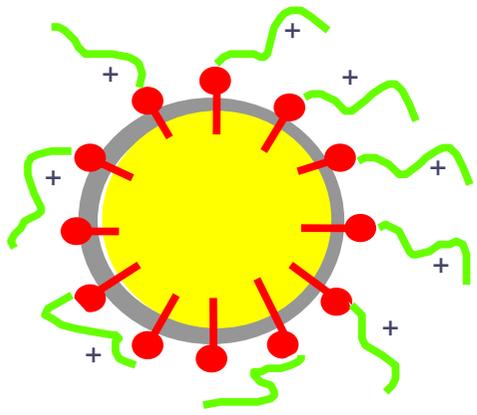


PLGA-PEO derivative  
blend nanoparticles



*Parenteral applications (feasibility)*

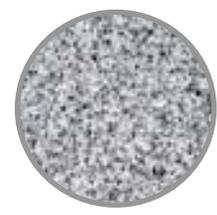
## Chitosan-based nanosystems



Chitosan-coated  
Nanocapsules



*Topical applications  
(preclinical)  
Dermosome Technology™  
(entering clinical pop)*



Chitosan  
Poloxamer  
Hialuronic acid  
glucomanan  
Nanoparticles



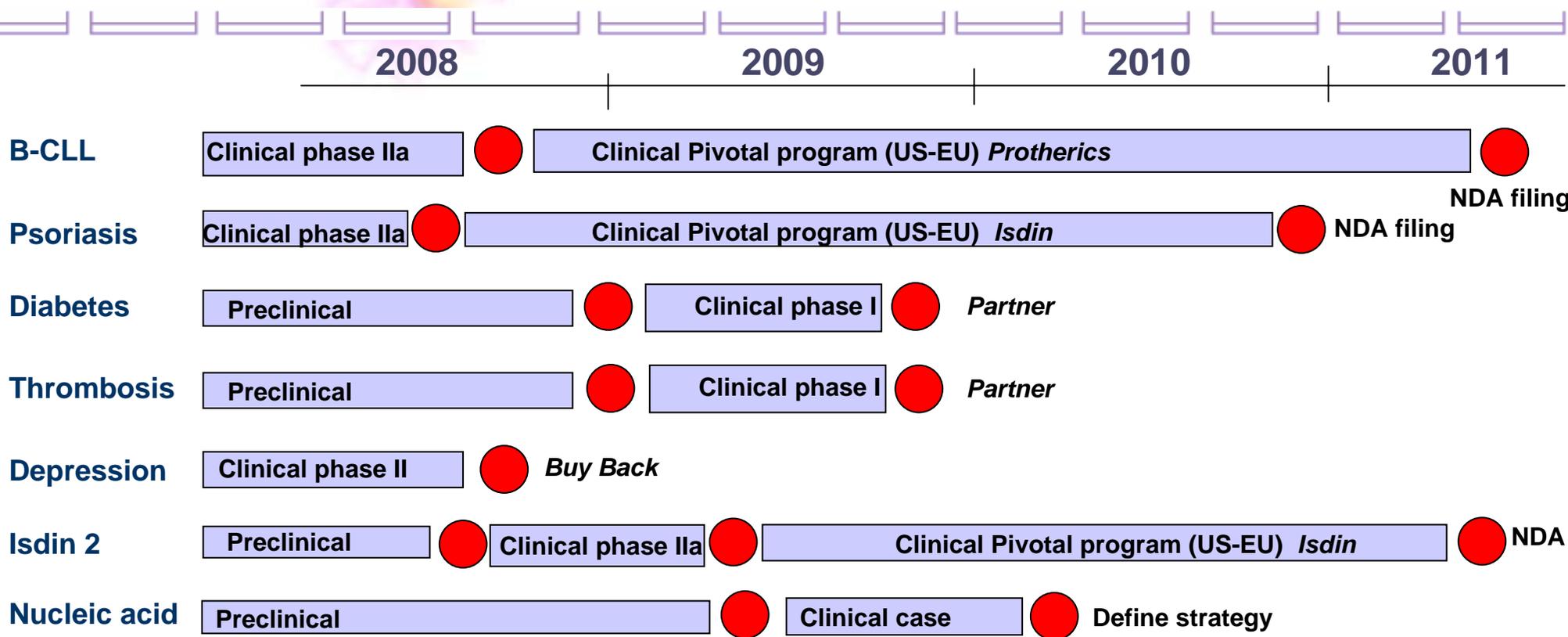
*Oral applications (preclinical)  
Ocular applications (Feasibility)  
Topical nucleic acids (Feasibility)*

# VALUE DRIVERS: NANOMEDICINE PLATFORM

***On September 15th Advancell and ISDIN, the leading dermatological company in Spain, signed a framework agreement to develop at least 3 Advancell's proprietary Dermosome Technology products. Cyclosporine DT may be the first one to enter clinical trials by the end of 2007.***

***Advancell's cost-effective approach to pipeline generation, through reprofiling is a result of the broad spectrum of applications offered by its nanomedicine platform***

# PHARMA: expected milestones 2008-2010



**Oral peptides:** 2 new own candidates in the period, entering phase IIa in 2009-2010

**Ophtalmic field:** 3 new own candidates in the period, entering phase IIa in 2008-2009

**Needle free vaccines:** pending 2007 milestone

**3rd party:** up to 6 projects expected in the period, entering phase I in 2009

# VISION 2008

## ➤ SIGNIFICANT FUNDING WILL BE NEEDED DURING 2008 TO:

- Advance clinical pipeline of proprietary and partnered projects
- Advance preclinical projects into clinicals
- Maximize nanomedicine platform potential

## PROSPECTIVE COMPANY PROFILE:

**Clinical portfolio, major codevelopments or licensing deals signed**

**Balanced pipeline: preclinical candidates, research platforms and backups**

**Small central overheads, virtual pharma business model**

**Revenue generation through profitable BU Services and Reagents (*sales in the 2-3M€ range with 15-20% annual growth*)**