Programa Cooperación Farma-Biotech

Jornada IIb: **Oncología**

JAN0908, tumor initiating stem cell modifier for the treatment of solid tumors

JANUS DEVELOPMENTS

Madrid, 12 de mayo de 2011

CataloniaBIO Associació catalana d'empreses de biotecnologia

MEDICAMENTOS INNOVADORES Plataforma Tecnológica Española

JANUS DEVELOPMENTS

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA E INNOVACIÓN

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Content

1. **The Company**
2. The Product
   a) Therapeutic focus
   b) Innovative mechanisms of action
   c) Differential features facing the market
   d) Current status of development
   e) IPR protection
   f) Pitfalls & Risks to be considered
3. Availability for cooperation

Janus' Mission

To turn **basic biomedical knowledge** into **social and economic value**

The gap from technology to product

- **Proof of concept experiments**
- **Efficient resource management**

Scientific result:

- Preliminary IP
- Far from market application
- No study about production
- No regulatory package

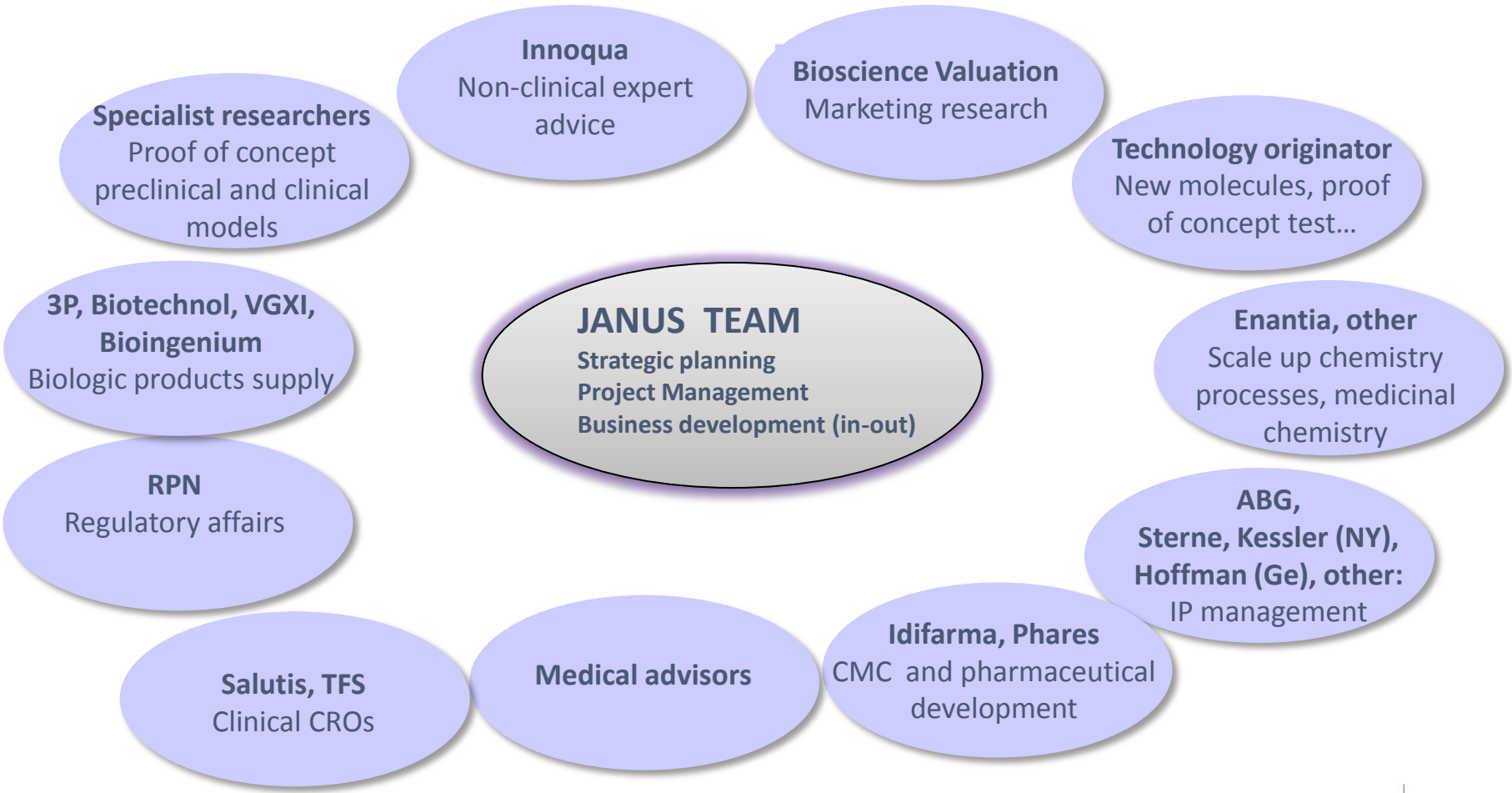
Selling package

- Solid IP
- Market oriented
- Scale-up feasibility
- Preliminary exploration of regulatory viability.

Common methodology

0. In- licensing or agreement to customer
1. GAP analysis:
   - **Market interest, unmet needs and challenges**
   - **IP protection or other barriers of entry**
   - **Evidence and robustness that supports key selling attributes**
   - **Feasibility of industrial production**
   - **Possible exit strategies: license out, spin-off, trade sale…**
2. Definition of work plan:
   - **Priorities**
   - **Activities**
   - **Budget**
   - **Project team / specialized suppliers**
3. Execution
4. License out – other exit strategy

Project team and specialized suppliers



JANUS experience to date

From its incorporation in March 2009, JANUS has achieved several goals:

- 14 in-licensed projects (3 already cancelled). Technologies coming from CSIC, CIBER-BBN, UAB, UZAR, UIB, IQS (URLl), UB, Hospitals.
- 2 of internal projects have out-licensing agreements (1 option and 1 license)
- More than 25 projects of strategic collaboration with different customers: private companies or public research centers.
- Strategic coaching and Interim management agreements:

Neurotec Pharma

Green Molecular

Transmural Biotech

Archivel farma s.l.

pasqual maragall fundació alzheimer internacional

Fundación Pedro Barrié de la Maza

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Therapeutic focus – mechanism of action

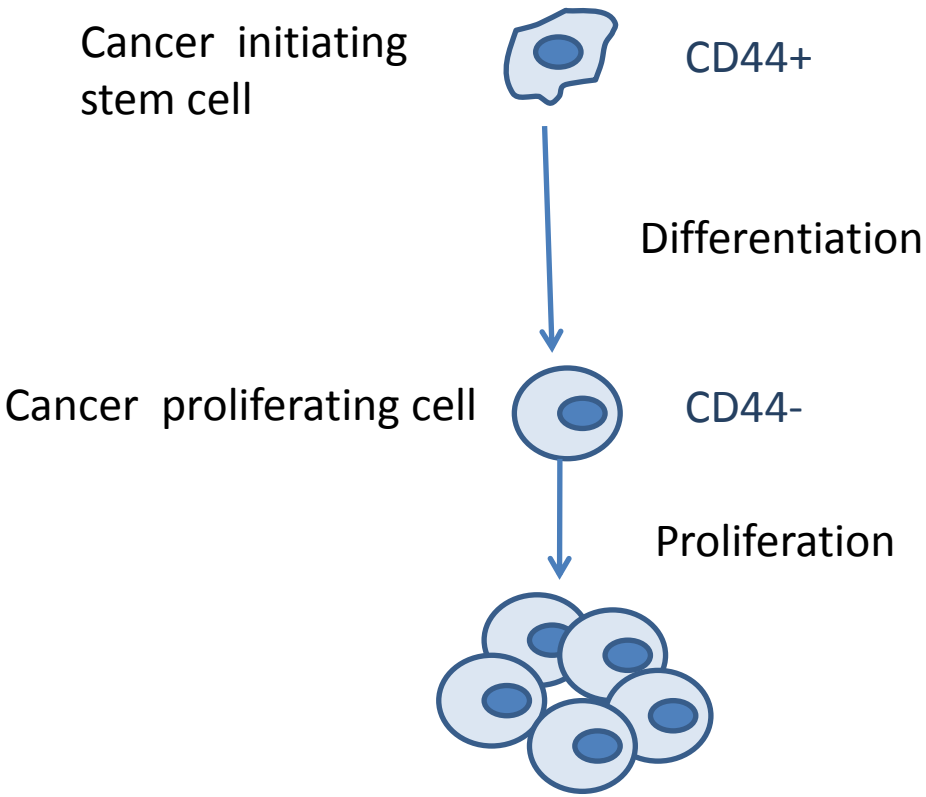
At in-license

Receptor antagonist with improved safety profile vs product tha was t cancelled in phase III for HIV (MoA confidential)

Fist steps

- Strengthen IP
- Synthesis optimization compatible with scale up and with sufficient quality
- Change the primary focus to cancer stem cell therapy (presence of this receptor in some cancers)

Therapeutic focus – mechanism of action



First question:

Potential role of our antagonist in cancer stem cell differentiation

Experiment:

Patient derived glioblastoma neurospheres. Test the effect of JAN0908 in differentiation (CD44+/CD44- ratio) and effects in glioblastoma formation

Therapeutic focus – mechanism of action

JAN0908 is able to differentiate patient-derived GBM neurospheres

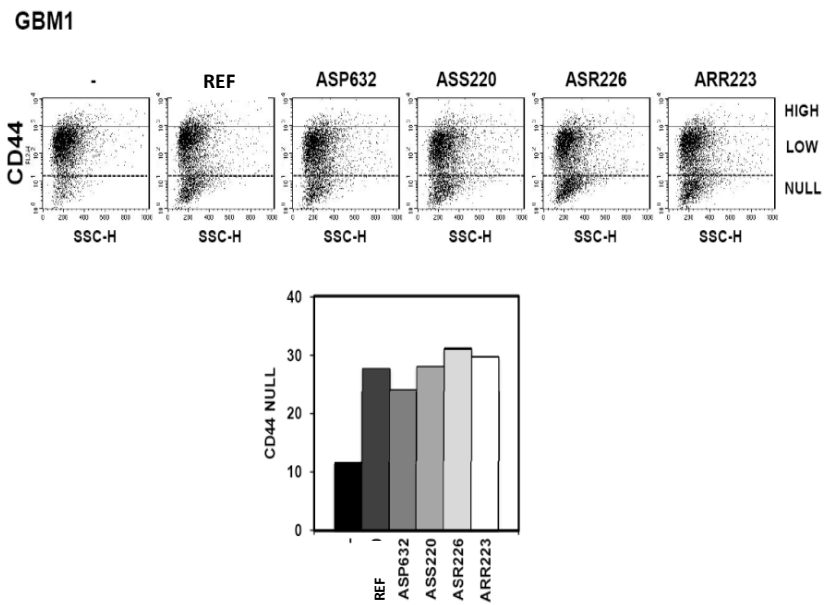


Figure 1

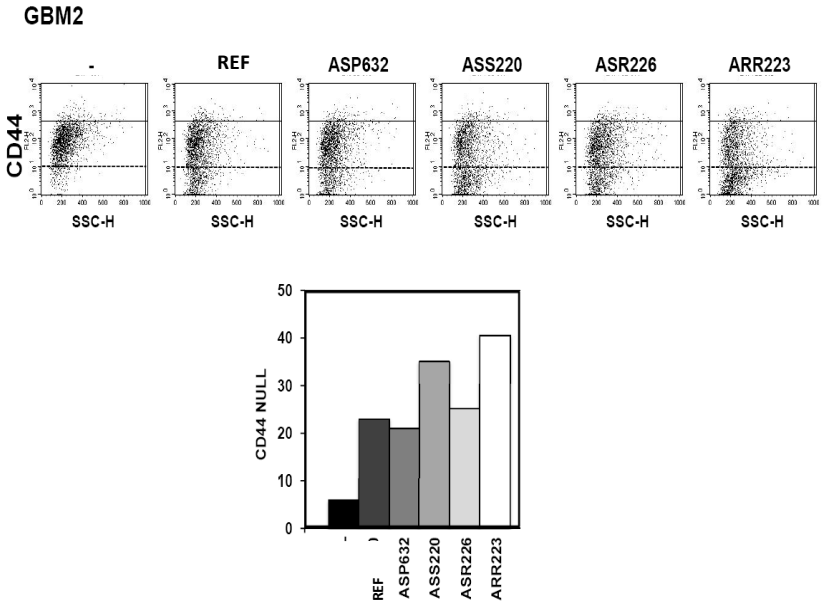


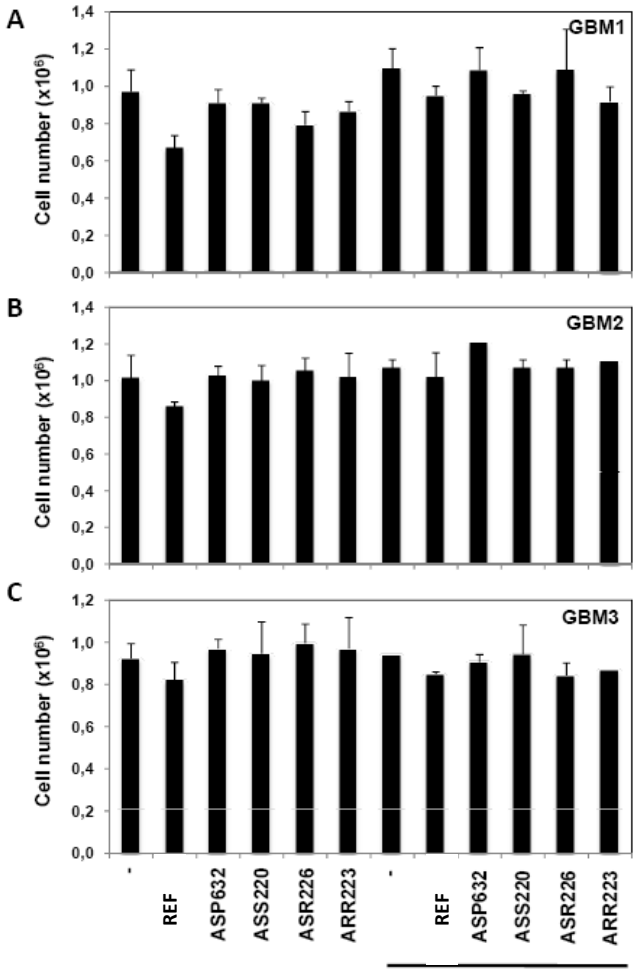
Figure 2

JAN0908 decreased the amount of glioma-initiating cells most likely inducing cell differentiation as seen per a loss of CD44+ cell population

Therapeutic focus – mechanism of action

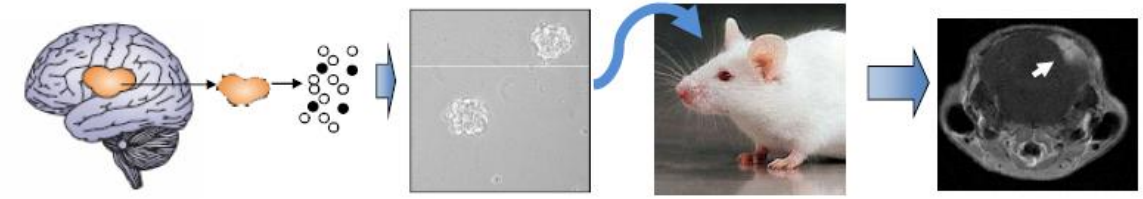
JAN0908 maintains cell viability and proliferation

Observed effect is not due to cytotoxicity



Therapeutic focus – mechanism of action

Scheme of the used mouse model for human glioblastoma.



Neurospheres (CD44+ enriched) cells from GBM patients are treated ex vivo with JAN0908 and Reference product and injected to nude mice.

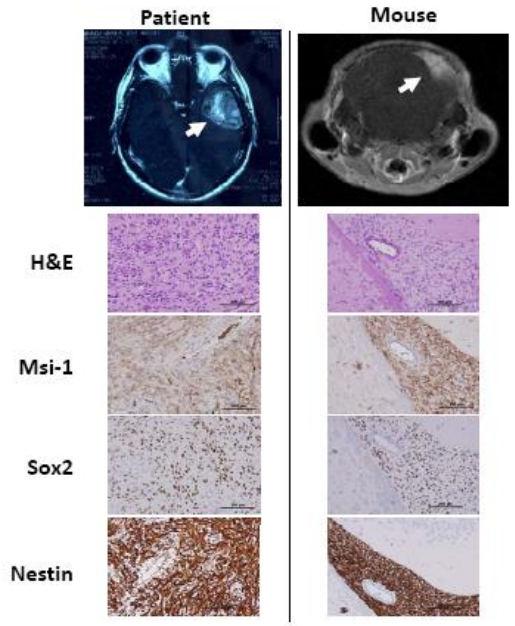
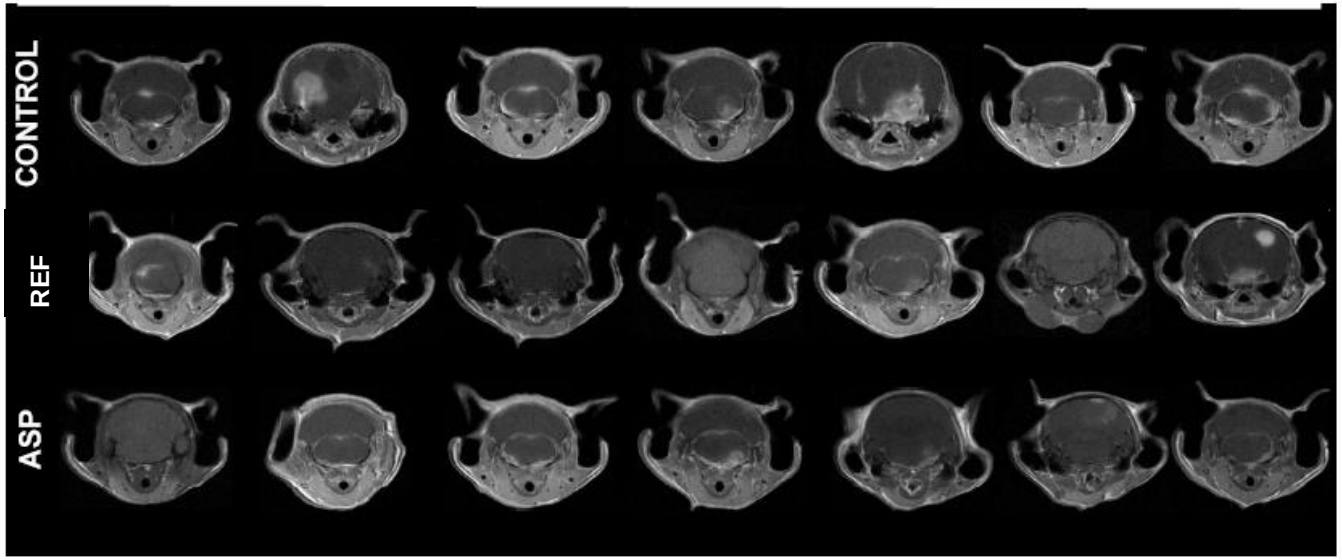


Figure 7

Therapeutic focus – mechanism of action

Preincubation with JAN0908 induces less and smaller tumors



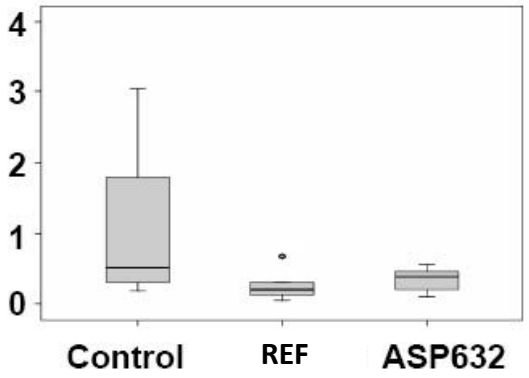
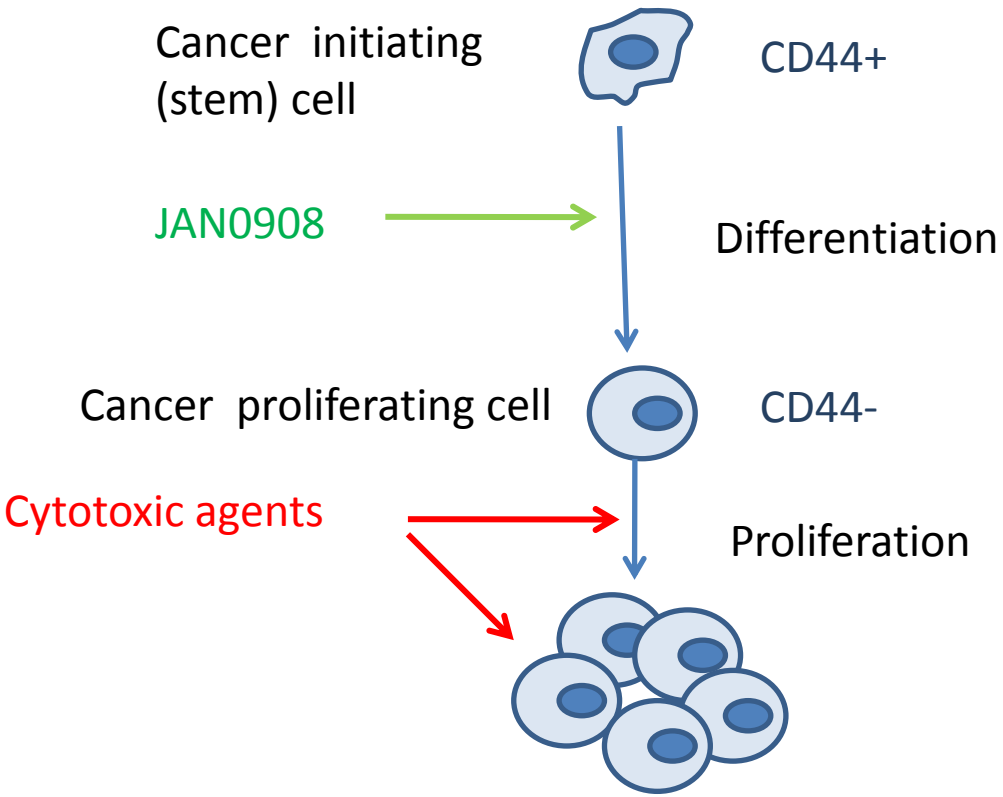


Figure 8

Therapeutic focus – mechanism of action



Our hypothesis

The exposure of JAN0908 to cancer initiating stem cells might promote their transdifferentiation (measured as a change in their CD44+/CD44- ratio) making them more sensitive to standard cytotoxic agents

Therapeutic focus – mechanism of action

Ongoing experiments in ovarian carcinoma (*ex-vivo*)

Ovarian Cancer initiating stem cell (CD44+)  + JAN0908 → Cell viability /proliferation and CD44+ marker status analysis.

Ovarian Cancer initiating stem cell (CD44+)  + JAN0908 + standard ovarian cancer chemotherapy → Cell viability /proliferation and CD44+ marker status analysis.

Therapeutic focus – mechanism of action

Planned experiments in ovarian carcinoma (*in vivo*)

MTD in mice with JAN0908 and reference product → Toxic effects comparison, dose decision for *in vivo* experiment

Ovarian Cancer initiating stem cell (CD44+) → Injection in nude mice → Survival and tumor formation analysis.

+ JAN0908
+ standard ovarian cancer chemotherapy

The product

Therapeutic focus

Cancer therapy, reduce tumor recurrence in combination with standard chemotherapy.

May be applied to tumors in which the antagonized receptor has been reported to be present (i.e. ovarian, glioblastoma, SCLC)

Innovative mechanism of action

Innovation is based on new therapeutic approach, targeting the differentiation of CSC

Differential features facing the market

New approach not reported so far. Add-on to existing treatments, may address the unmet need of cancer recurrence treatment

Current status of development

Early preclinical. Ready to start regulatory preclinical development prior to FIM by 1Q'12

Pitfalls & Risks to be considered

Need to provide sufficient evidence that this new approach makes sense. Clear differentiation needed v existing product

IP protection

Solid patent application filed as PCT in 2007 and extended to US, Canada, Japan and Europe in 2009.

Broad composition of matter claims

First Office Action received in Europe (March 2011)

Response to Final Office Action (received on February 2011) filed in US (April 2011)

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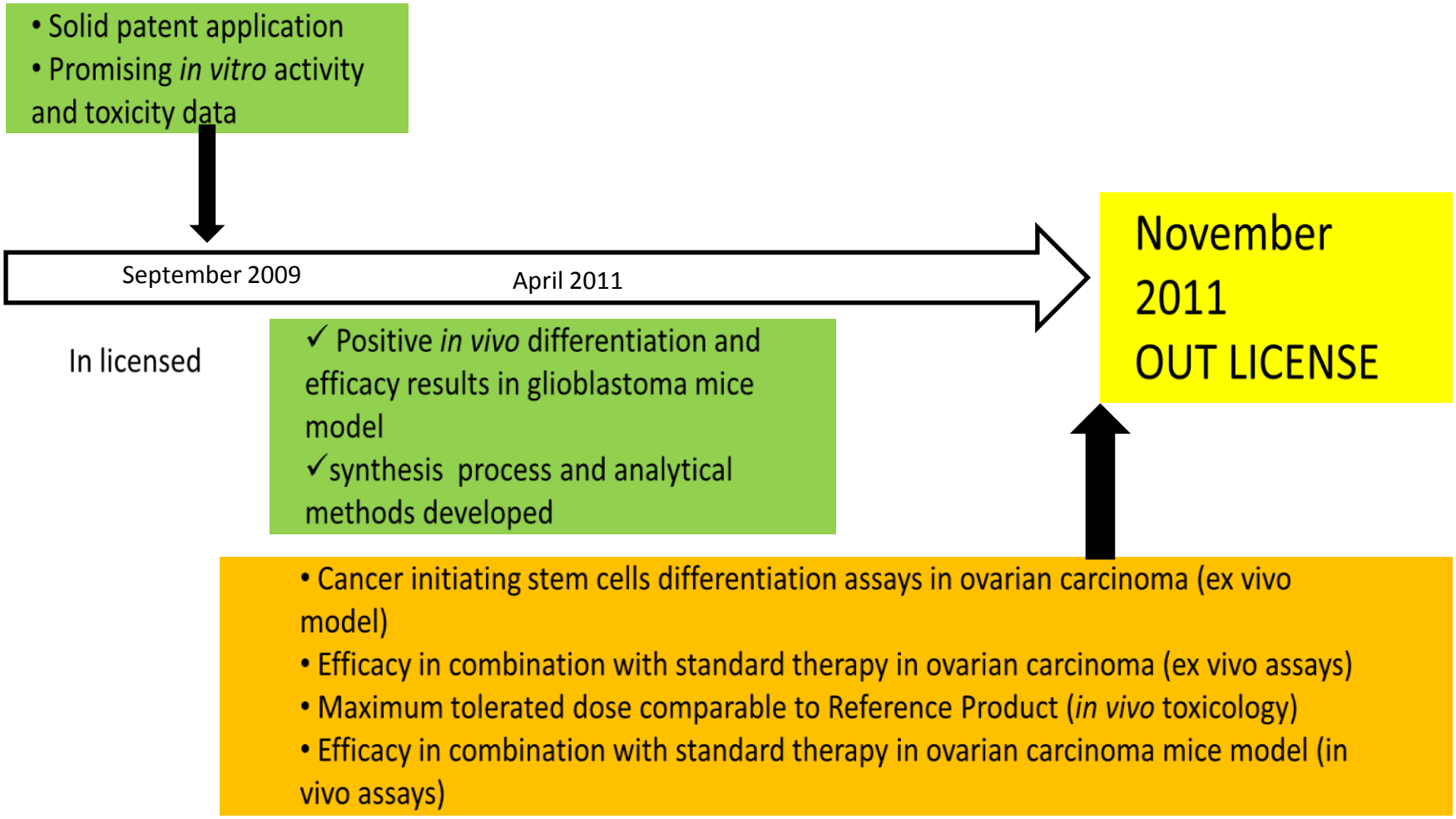
Timelines


• Solid patent application
• Promising *in vitro* activity and toxicity data
September 2009
April 2011
November 2011 OUT LICENSE
In licensed
✓ Positive *in vivo* differentiation and efficacy results in glioblastoma mice model
✓synthesis process and analytical methods developed
• Cancer initiating stem cells differentiation assays in ovarian carcinoma (ex vivo model)
• Efficacy in combination with standard therapy in ovarian carcinoma (ex vivo assays)
• Maximum tolerated dose comparable to Reference Product (*in vivo* toxicology)
• Efficacy in combination with standard therapy in ovarian carcinoma mice model (in vivo assays)

¡GRACIAS !

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