Programa Cooperación Farma-Biotech

Jornada II: **Oncología**

Anticancer therapy based on tumor self degradation

BiOncoTech Therapeutics

Barcelona, 13 de abril de 2011

CataloniaBIO
Associació catalana d'empreses de biotecnologia

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

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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

1. The Company

- **Bioncotech Therapeutics** focuses on the development of anticancer agents against aggressive tumors resistant to current radio, chemo or immunotherapy.
- **Bioncotech** emerged as the first cancer-oriented spin-off of the Spanish National Cancer Center (CNIO), one of the leading international cancer centers (5th by high impact factor publications)

The company has its laboratories at the Scientific Park of the University of Valencia (Valencia), and collaborates actively with the CNIO and other academic and clinical institutions.

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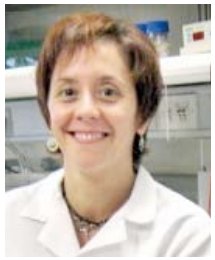
1. Bioncotech's Team

Damià Tormo, Ph.D., MBA

- Founder and CEO of Bioncotech
- Researcher at CNIO, University Michigan, Uniklinik Bonn
- Founder KR2, Biocapital Advisors



María Soengas, Ph.D.

- Founder and CSO of Bioncotech
- Scientific director at CNIO
- Professor University of Michigan, Investigator Cold Spring Harbor Laboratory

Javier Fernández, MBA

- Founder and Business Developer of Bioncotech
- Director at Bioavance, Vivia Biotech, Pevesa, Halotech
- Founder Suanfarma VC fund and IE Business School professor

Neil Collen, MBA (Livingstone Partners)

Jorge Garcia del Moral, MD (Founder and CEO of several companies in the health sector)

Jose Luis de Miguel, MBA (CEO at Onofre de Miguel Group)

Alejandro Portilla, MBA (General Excellence Manager ABBOT Europe)

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1. The Company - Collaborations

2. The Product: Therapeutic focus

BO-110

- dsRNA Nanocomplex
- Unique Mode of Action
  New concept of treatment based on tumor cell autodigestion
  (Different from Standard Therapies)
- Broad Efficacy. Orphan Disease Category
- No Detectable Secondary Toxicity in Cancer Models

Main Objectives

- Clinical Development B0-110

  Phase I/II Trials

- Pipeline

  Delivery, Reformulation

  Screening Platforms

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2. The Product: Indications

Target Tumors	Frequency (100.000)	Cases/year	Deaths
Melanoma	2,7	106,000	33,000
Pancreas Cancer	10	170,000	168,000
Bladder Cancer	4,2	269,000	115,000
Hepatic Cancer	7,7	560,000	500,000

Strong Medical Need

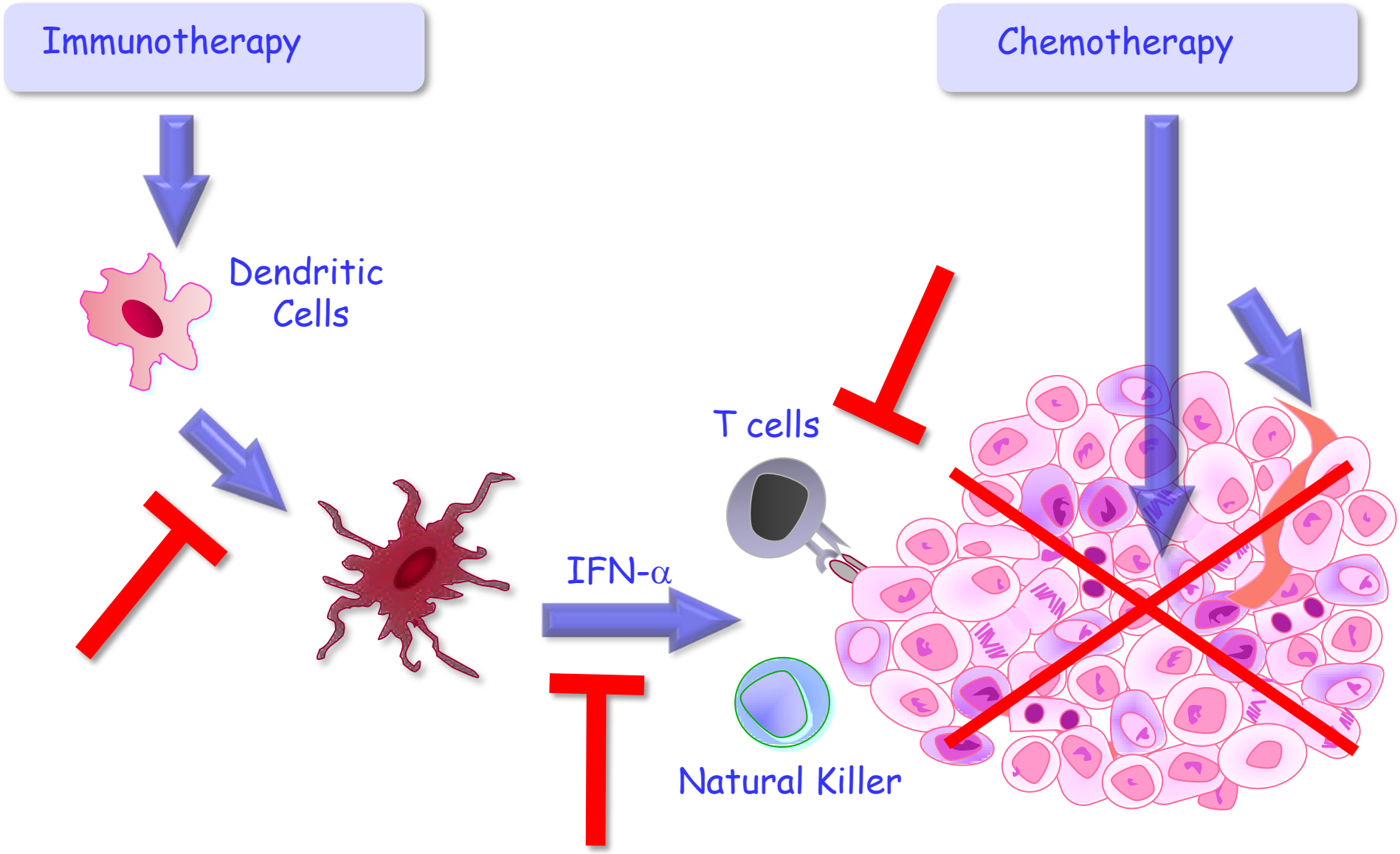
- High mortality
- No effective treatments
- High side effects
- Devastating social impact

Attractive Market

- Multi-billion expenses in medical and palliative case
- Orphan disease status (advantages for implementation and IP protection)

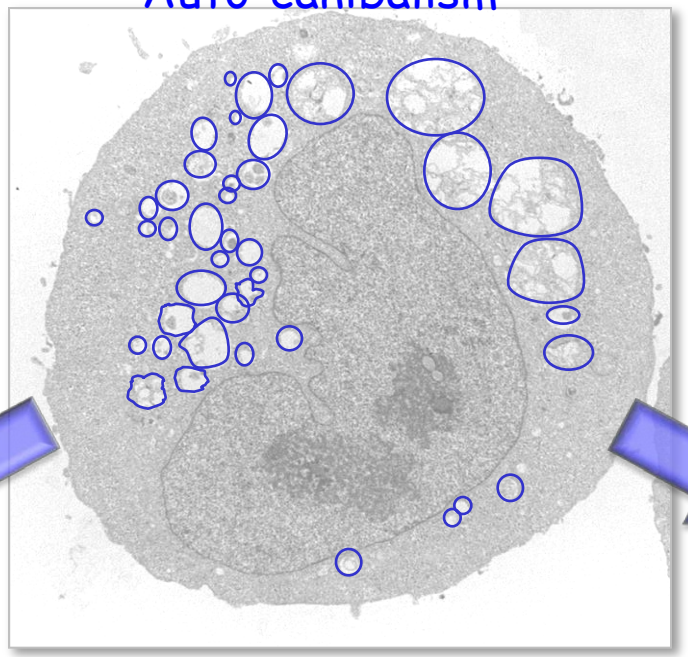
*Source: WHO

2. The Product:
Objective: Bypass Immuno- and Chemo-resistance



2. The Product:
New Mechanism. Autophagy as a double edge sword

"Auto-canibalism"



Autodegradation of celullar components for adaptation to stress conditions

Excesive autodegradation and elimination of key components

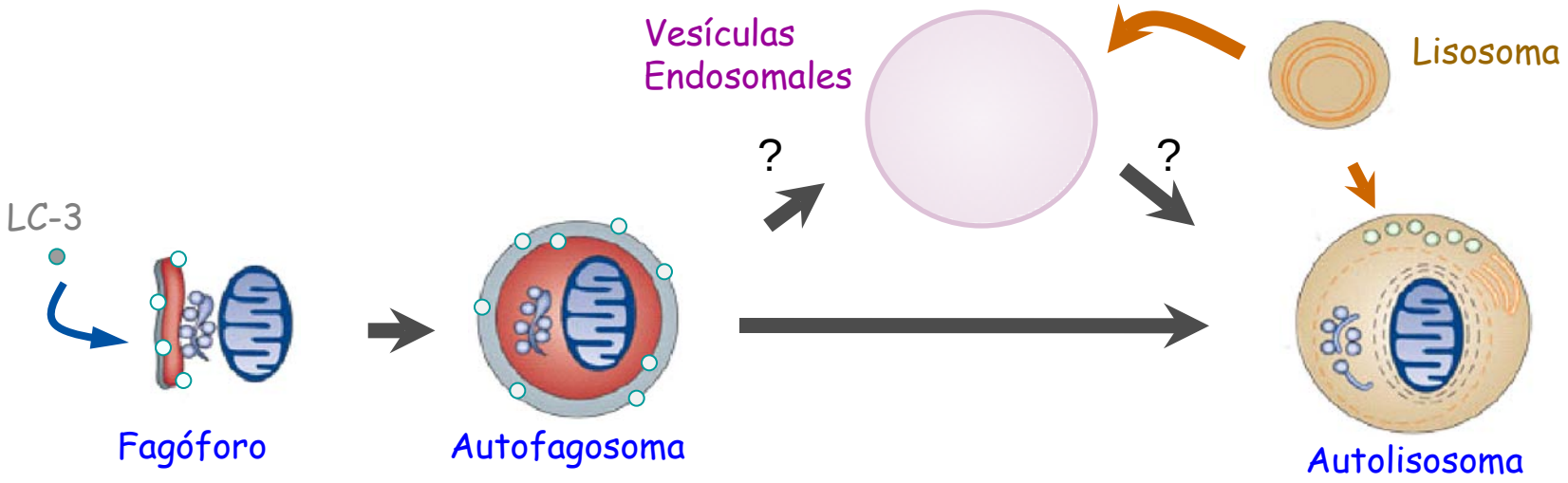
Survival

Cell Death

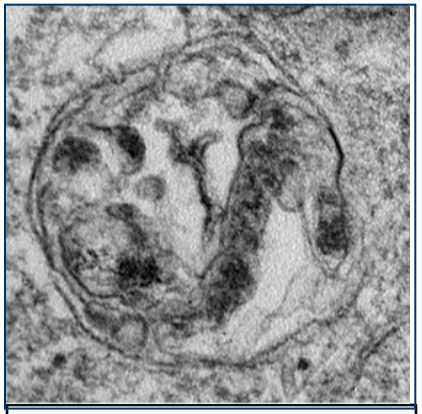
Tumor Development

Antitumor Therapy

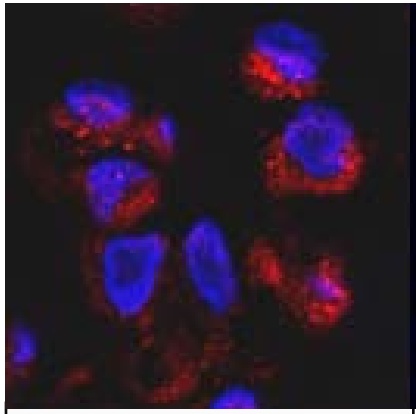
Autophagy: Mechanisms & Detection



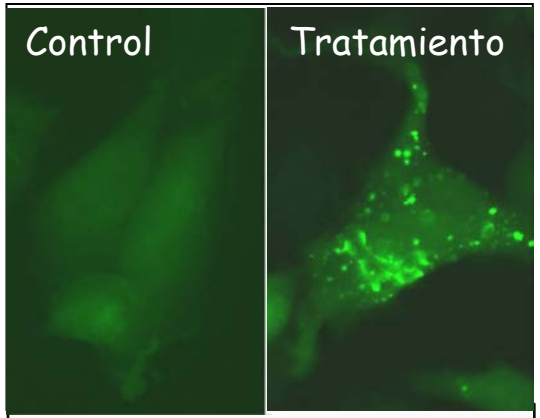
Autofagy Markers



ME alta resolución

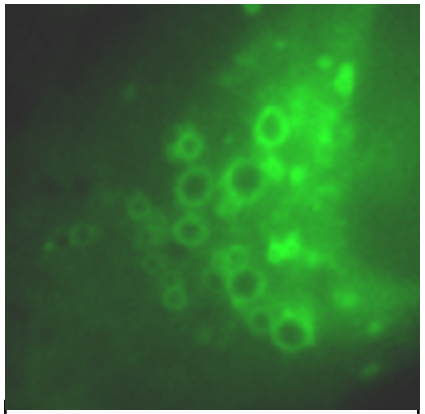


LC3 endógeno



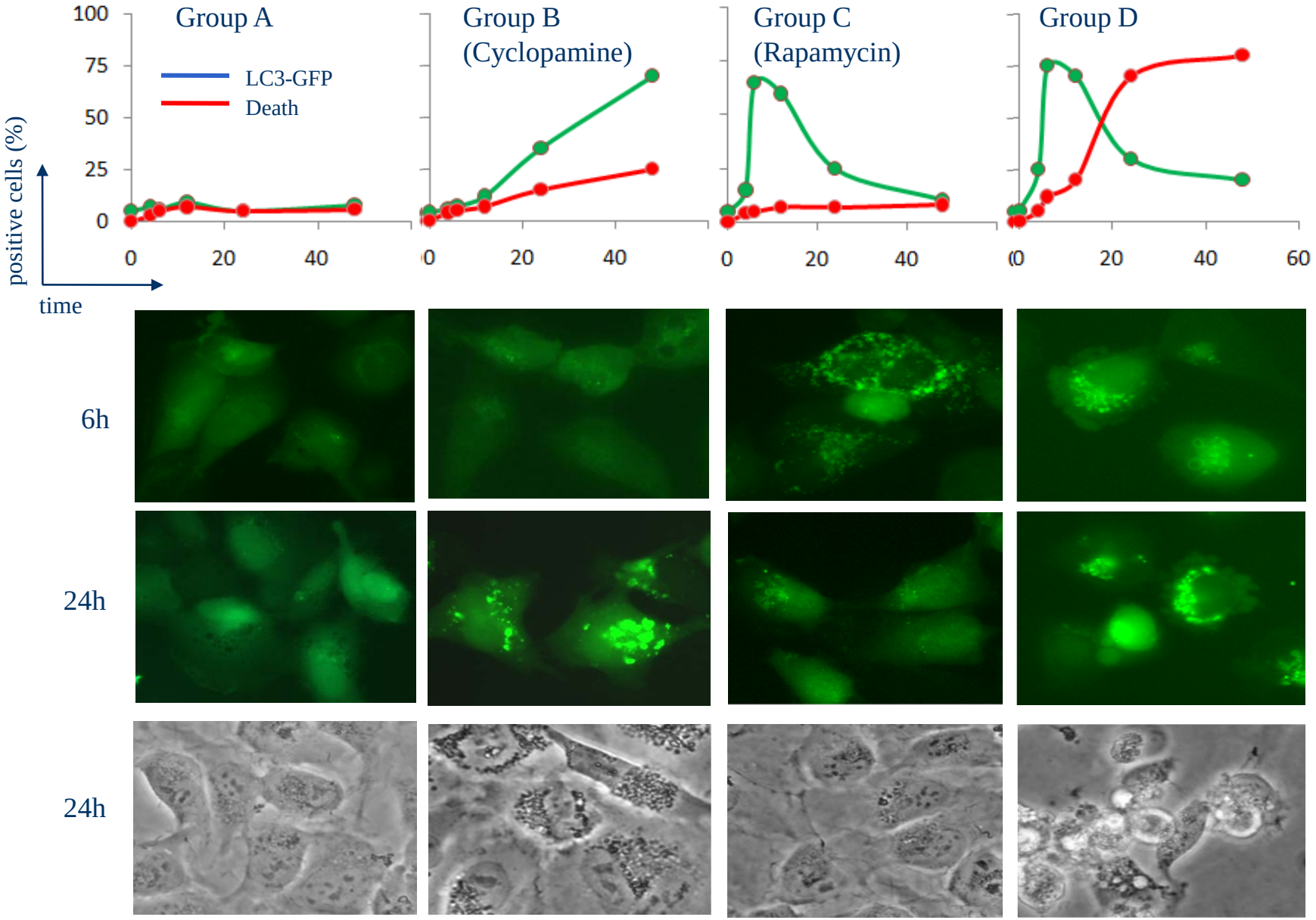
LC3 marcado fluorescente

Endosomal Markers

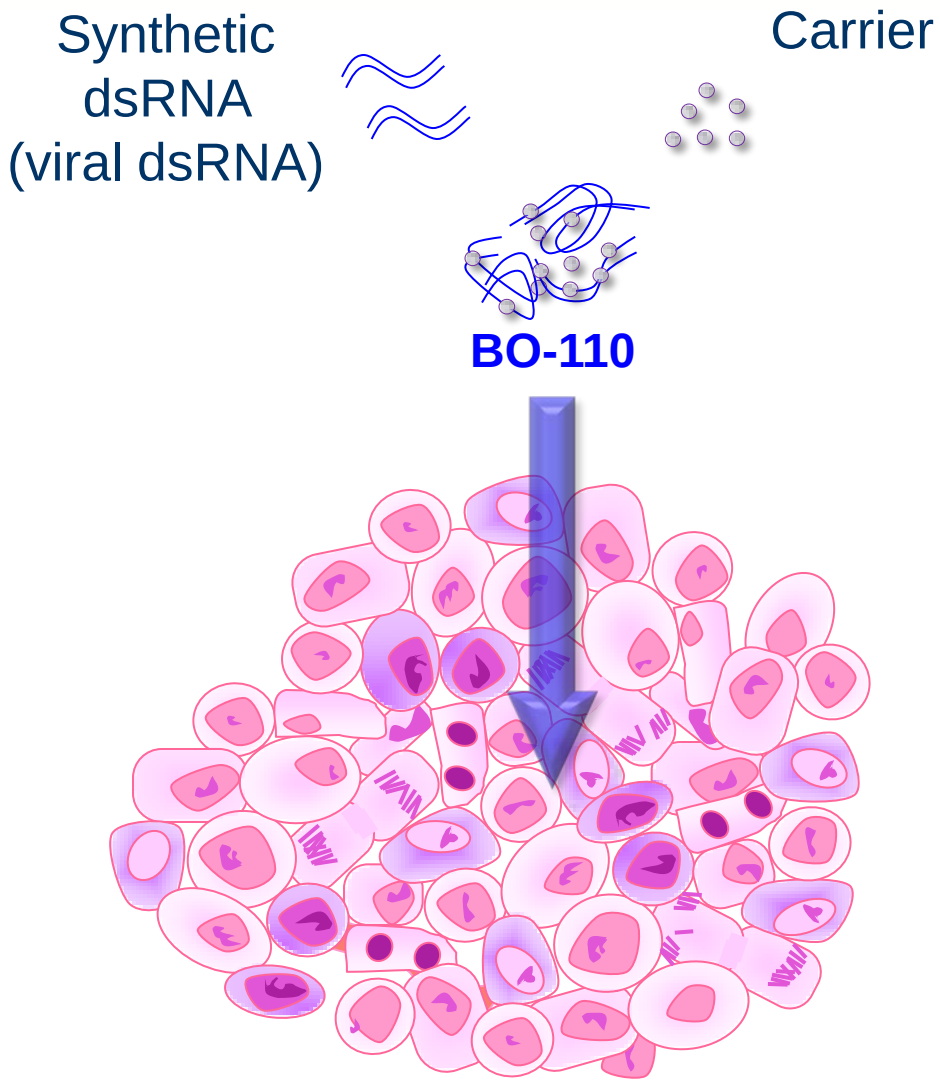


RAB7 GTPasa

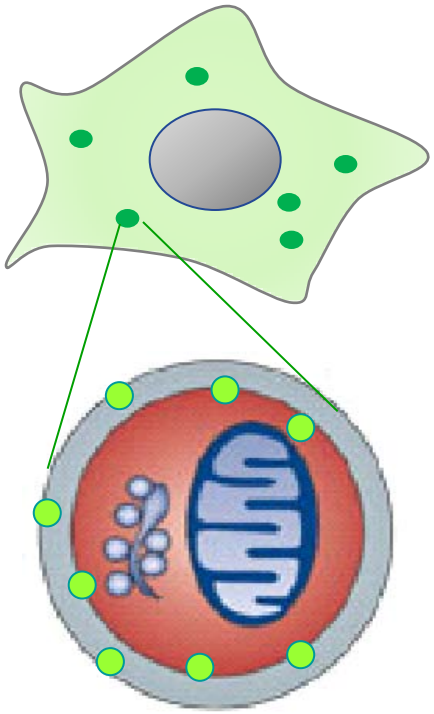
Screening for New Autophagy Inducers



3. The product: BO-110

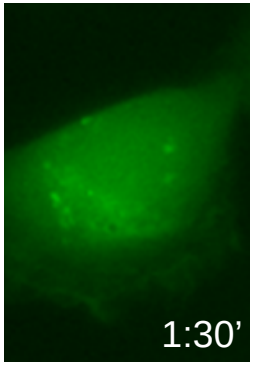


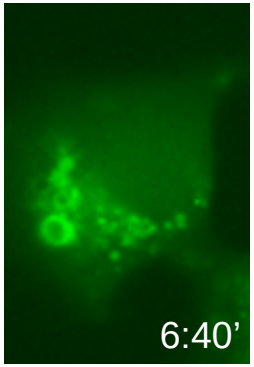
Autophagy activation by BO-110

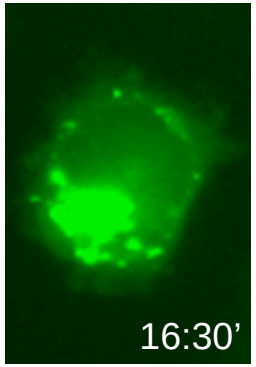


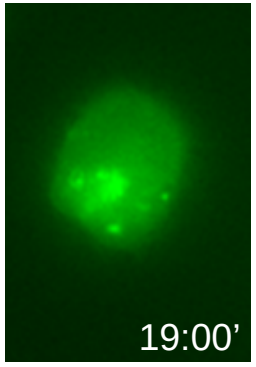
LC3-GFP

("green autophagosomes")





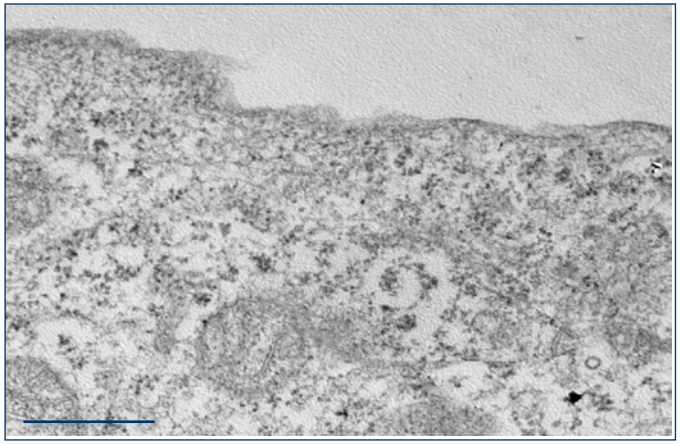




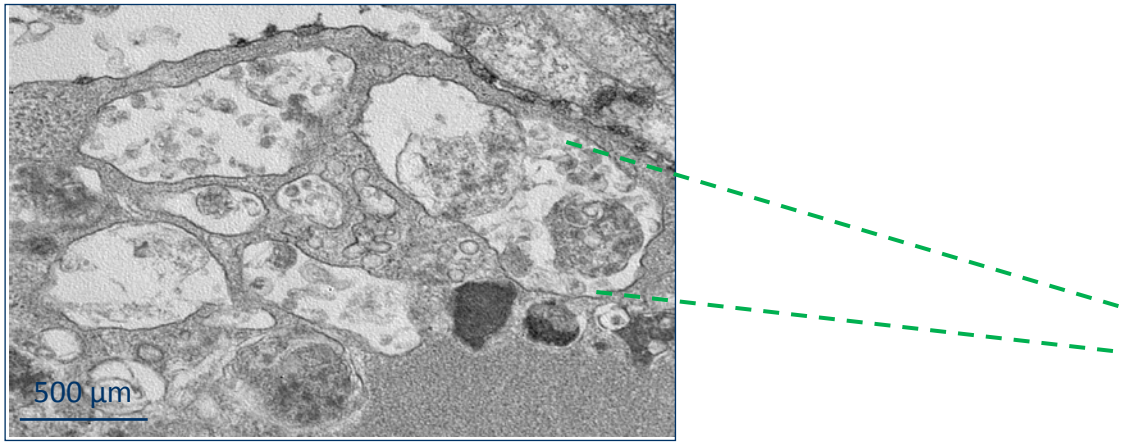
Mechanism of action

1. Massive movilization of endocytic endosomes

Control

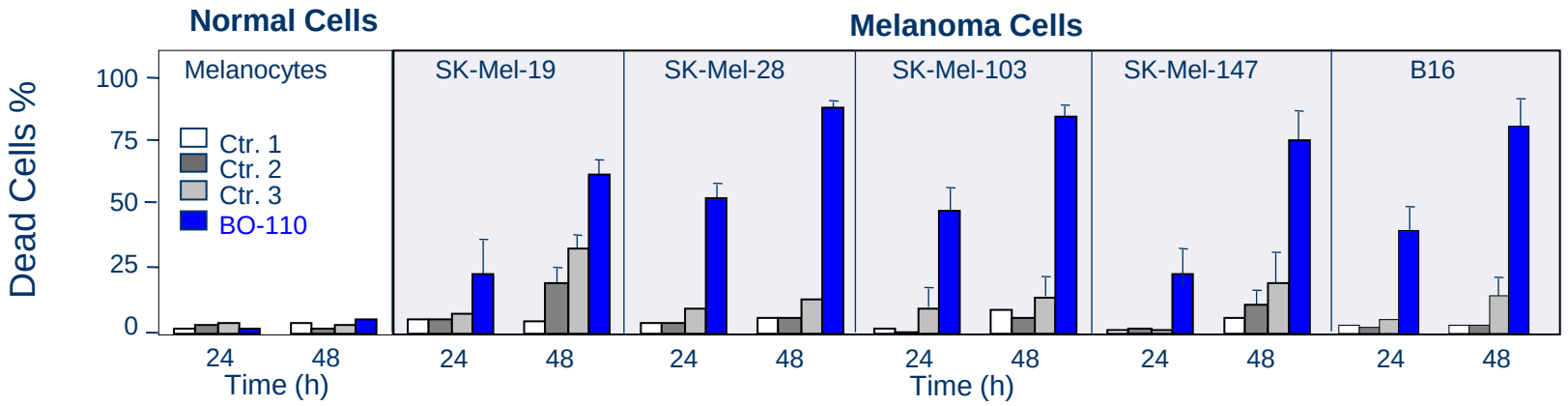


BO-110

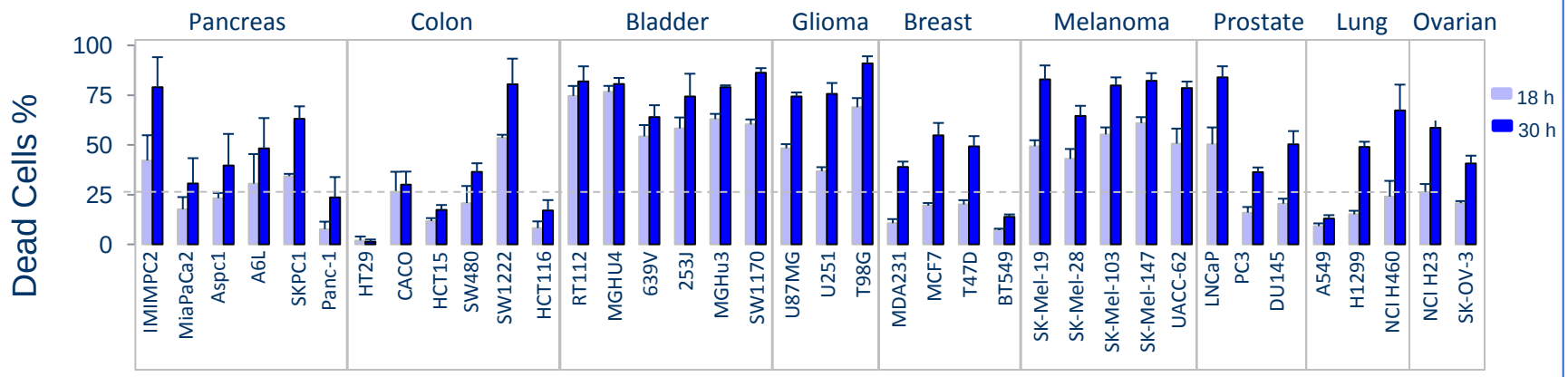


Selectivity and Efficacy of BO-110

1. BO-110 kills melanoma cells but not normal melanocytes



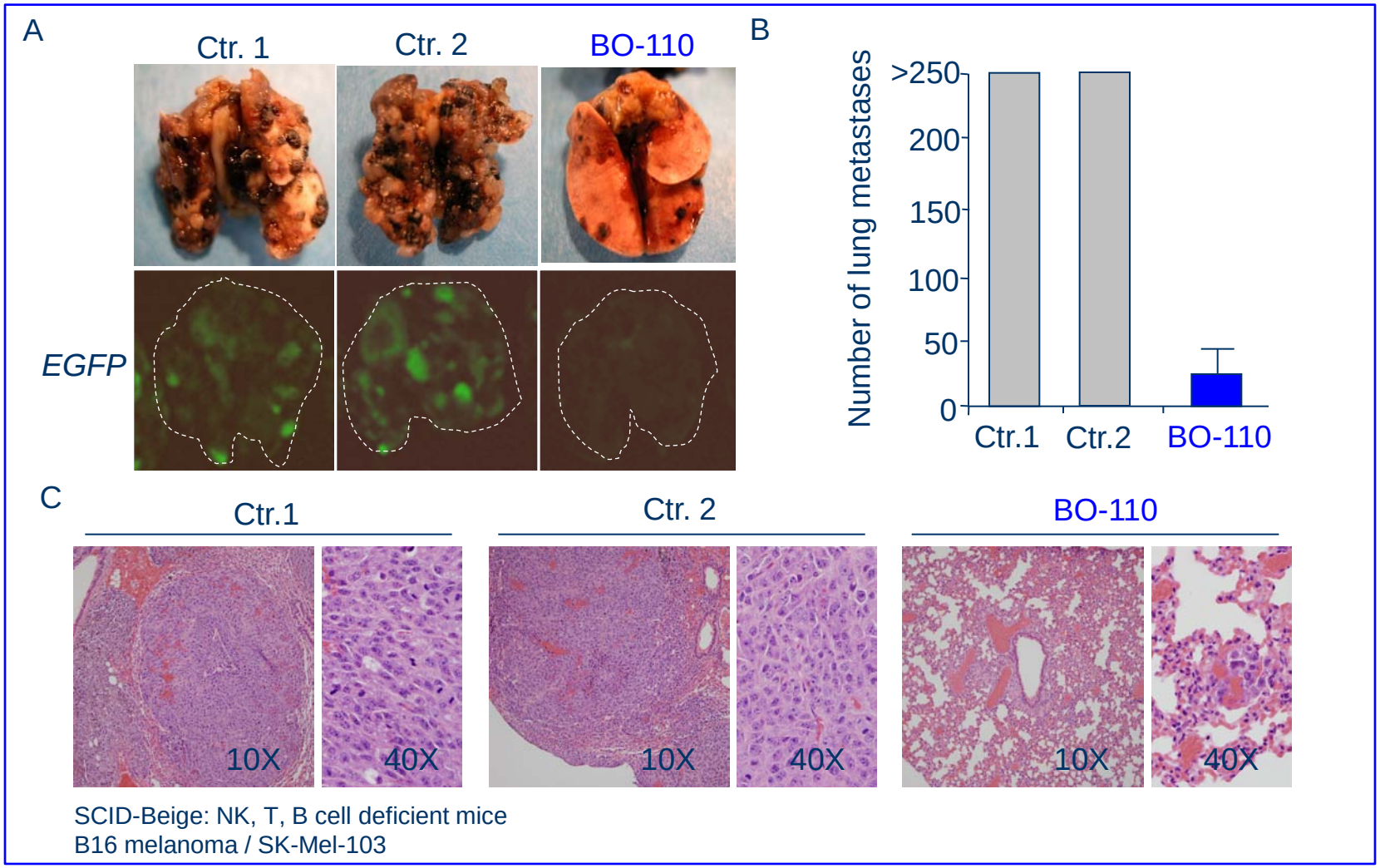
2. BO-110 has a broad-spectrum efficacy



Pre-clinical implications: animal models

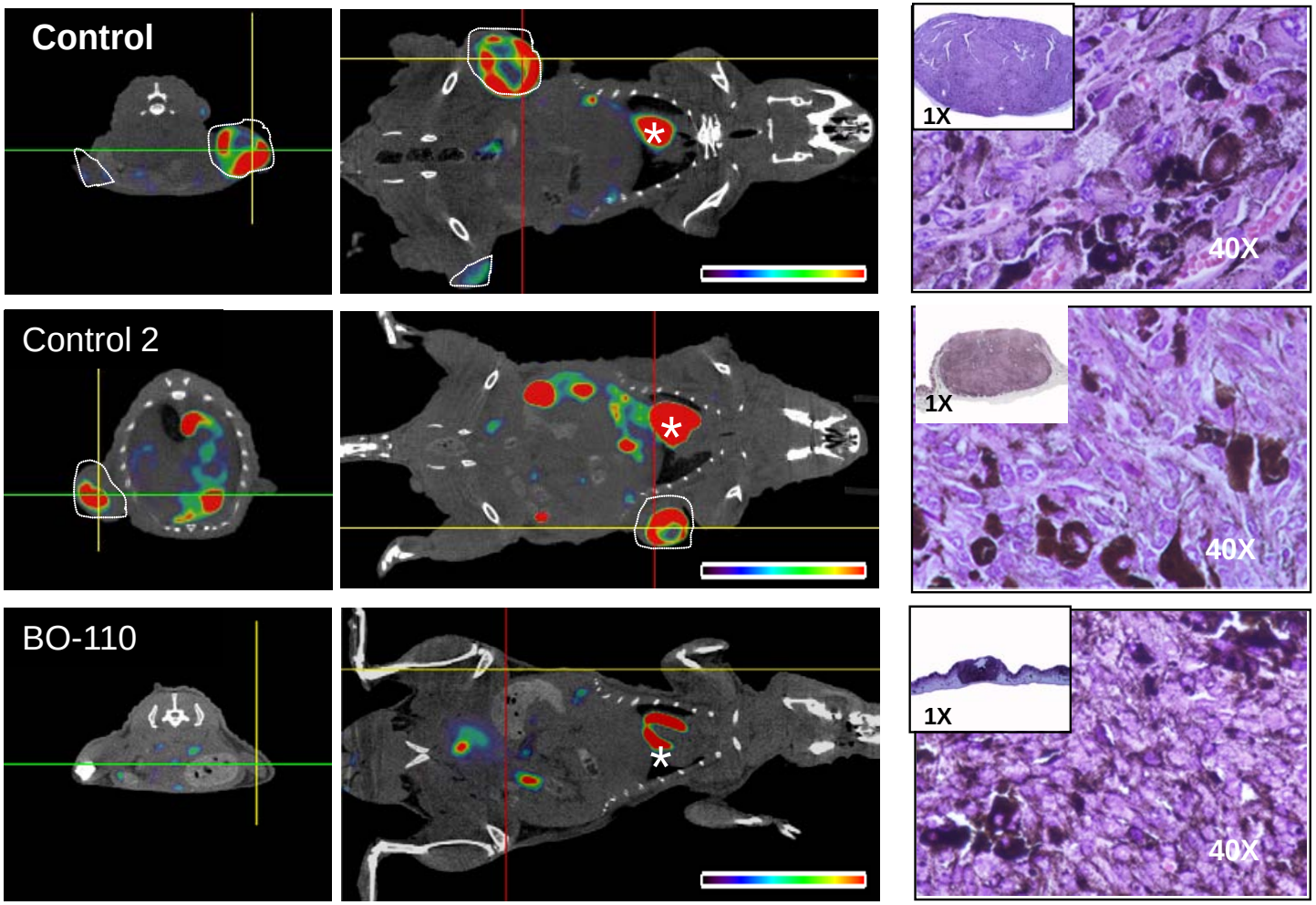
- Xenografts in Immunocompetent Mice
  - B16 melanoma ……subcutaneous tumors
  - B16 melanoma ……lung metastases
- Xenografts in Immunocompromised mice
  - B16 melanoma ……lung metastases
  - SK-mel-103 melanoma……lung metastases
  - U251 Glioblastoma ……subcutaneous tumors
  - 253J Bladder ……subcutaneous tumors
  - Others (under analysis)
- Genetically Modified Mice
  - Tyr:NRAS^{Q61K} x INK4a/ARF-/- …….endogenous tumors
- Toxicology
  - MED & MTD (pathologists)
  - ADME, PK & PD (rat) & MTD, telemetry (dog) on going

Anti-melanoma Activity of BO-110 in Highly Immunodeficient Mice

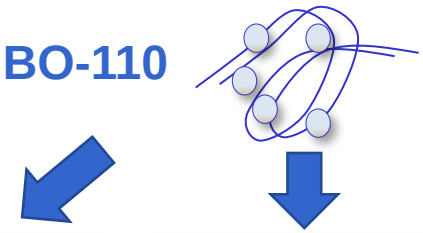


SCID-Beige: NK, T, B cell deficient mice
B16 melanoma / SK-Mel-103

Anti-melanoma Activity of BO-110 in Genetically Modified Mice Tyr:NRAS^{Q61K} x INK4a/ARF-/- model



BO-110: Summary of Mechanism and Unique features



Autophagy (MDA-5, LC3…)	Apoptosis (NOXA, Caspases…)	Innate Immunity (IFN, Cytokines…)

- **Therapeutic efficacy** in multiple human tumors
- **Selective** for tumor cells
- **No apparent side effects** in pre-clinical models

- Tormo D. *et al.* (Cancer Cell, 2009)
- Alonso-Curbelo D. *et al.* (Autophagy, 2009)
- Tormo D. *et al.* (Clinical & Translational Oncology, 2009)
- Poeck H. *et al.* (Nature Medicine, 2008)
- Besch R. *et al.* (Journal Clinical Investigation, 2009)

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Current Status of the project

CLINICAL DEVELOPMENT BO-110

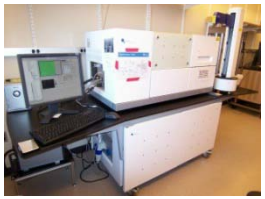
Melanoma

Pancreatic Cancer

Bladder Cancer

Hepatic Cancer

SCREENING PLATFORM



High Content Screen

Proprietary assay

Bioncotech Platform

PIPELINE

Reformulation BO-110

NME

Delivery strategy

BIO-MARKERS

Patient Selection

Patient response

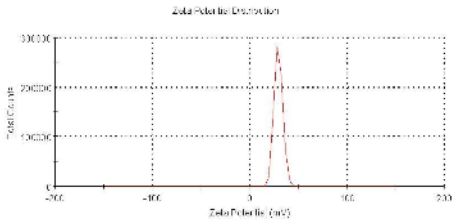
COMBINATIONS

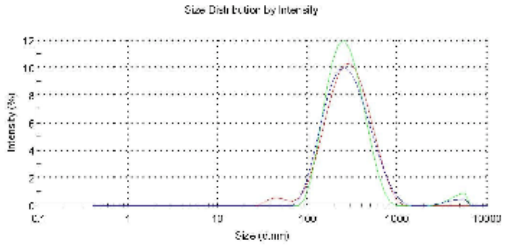
Combination with existing treatments in the market and other drugs currently under development

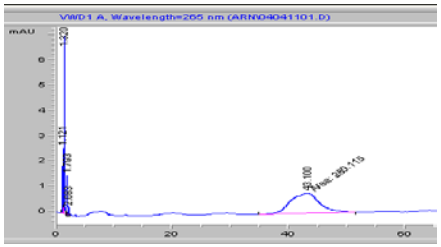
Programa Cooperación Farma-Biotech
Current Status of the project: Clinical Development

CMC: GMP Production & Analitics

Formulation: lyophilized vial for iv injection
Analytics & validation: HPLC; particle size, Z potential…
Manufacturing: On going in France and Switzerland
Expected GLP product: July 2011







Toxicology

Non GLP preclinical analyses:

Accomplished: hemolysis, MTD mice…

ongoing MTD, telemetry and PK/PD in dogs and rats

Expected GLP preclinical analyses: 3Q 2011
Expected IND: 2Q 2012

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IPR Protection

Patent

Priority: 4 July 2009 (PCT 03837, 4 July 2010)
Applicant: Centro Nacional Investigaciones Oncologicas
International Searching Office: European Patent Office
License: Exclusive for Bioncotech (July 2010)

Major Claims

1. Screening method
2. Medical use for cancer of dsRNA + polications
3. BO-110

FTO (estimated)

-International and National ITP search by the OEPM and Patent Lawyer analysis
-State of the technique (patents) by Einteligent/EOI program
-Final FTO after EPO notification.

FUTURE STRATEGY

-Patents from public institutions (Einteligent/EOI program)
-New patents for delivery, manufacturing and product.

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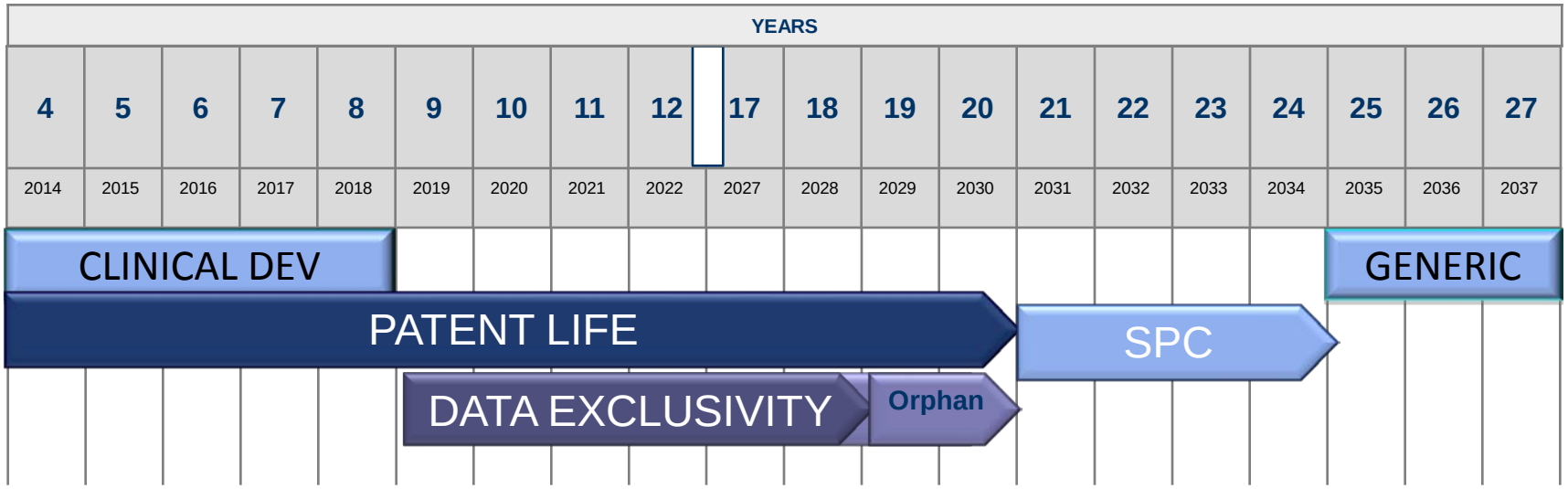
IPR Protection



Data Exclusivity: 10 Years

Orphan and Patent: 12 Years

Total Exclusivity Term: 16 Years

- ✓Strong protection – 10-12 Years after launch
- ✓Extension possibilities – 4-6 additional years
- ✓**No FTO issue**

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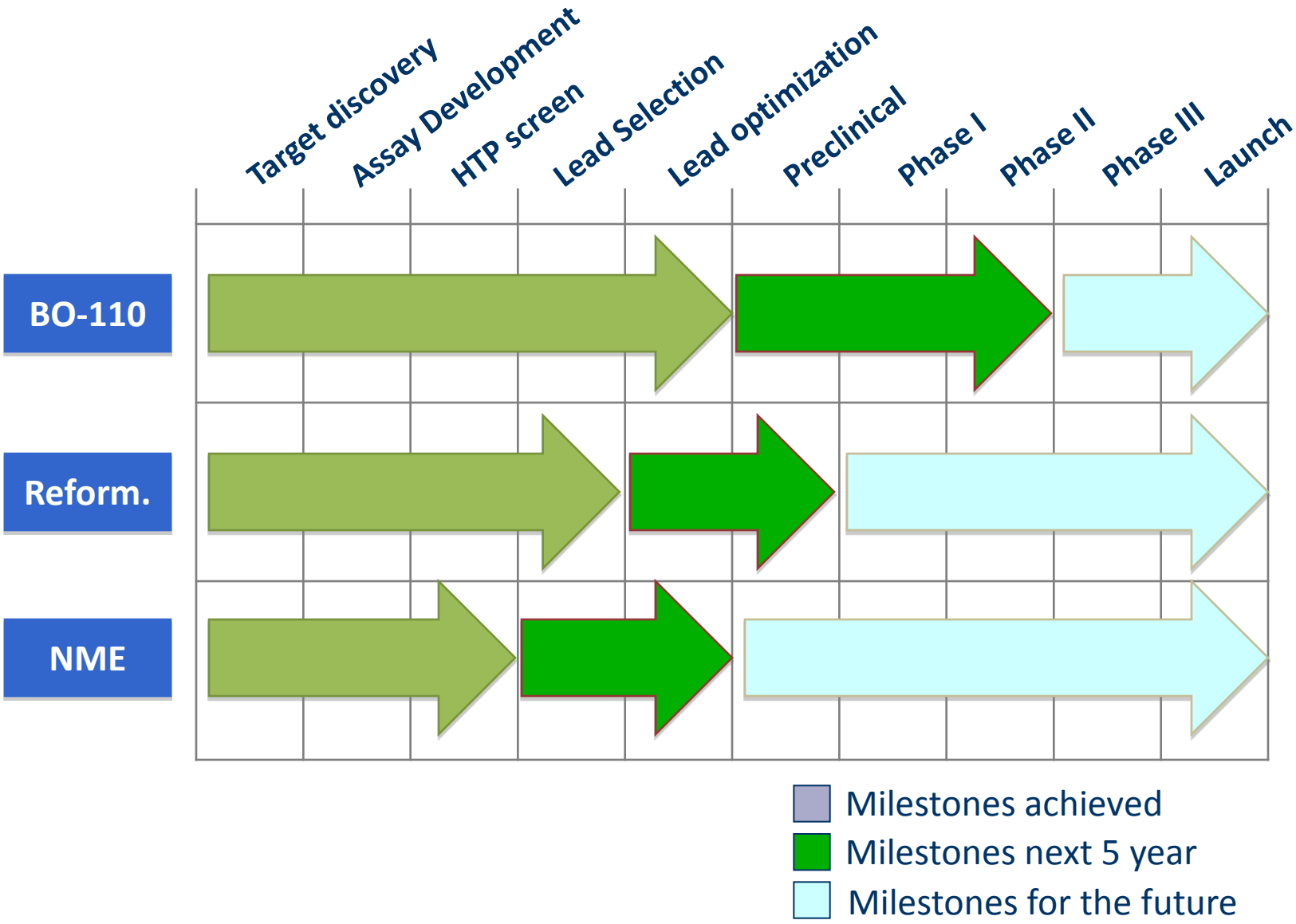
3. Availability for cooperation

Co-development of BO-110
(for one or more indications)

License in more advanced stage (Phase I/II)

www.bioncotech.com

Drug Development



In conclusion…

Strong Fundamentals

Attractive Market
Unmet Medical Need
Promising Efficacy and Safety
Strong IP Position
Great Human Interest

Creation of Value

Summary & Model

Coordinated Activation of Autophagy and Apoptosis