ANS-40 Dermosome Technology®, nanomedicines for the treatment of Actinic Keratosis

ADVANCELL

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ADVANCELL, S.A.

ADVANCELL is an emerging biopharmaceuticals company focused on the development of promising drug products with significant commercial potential

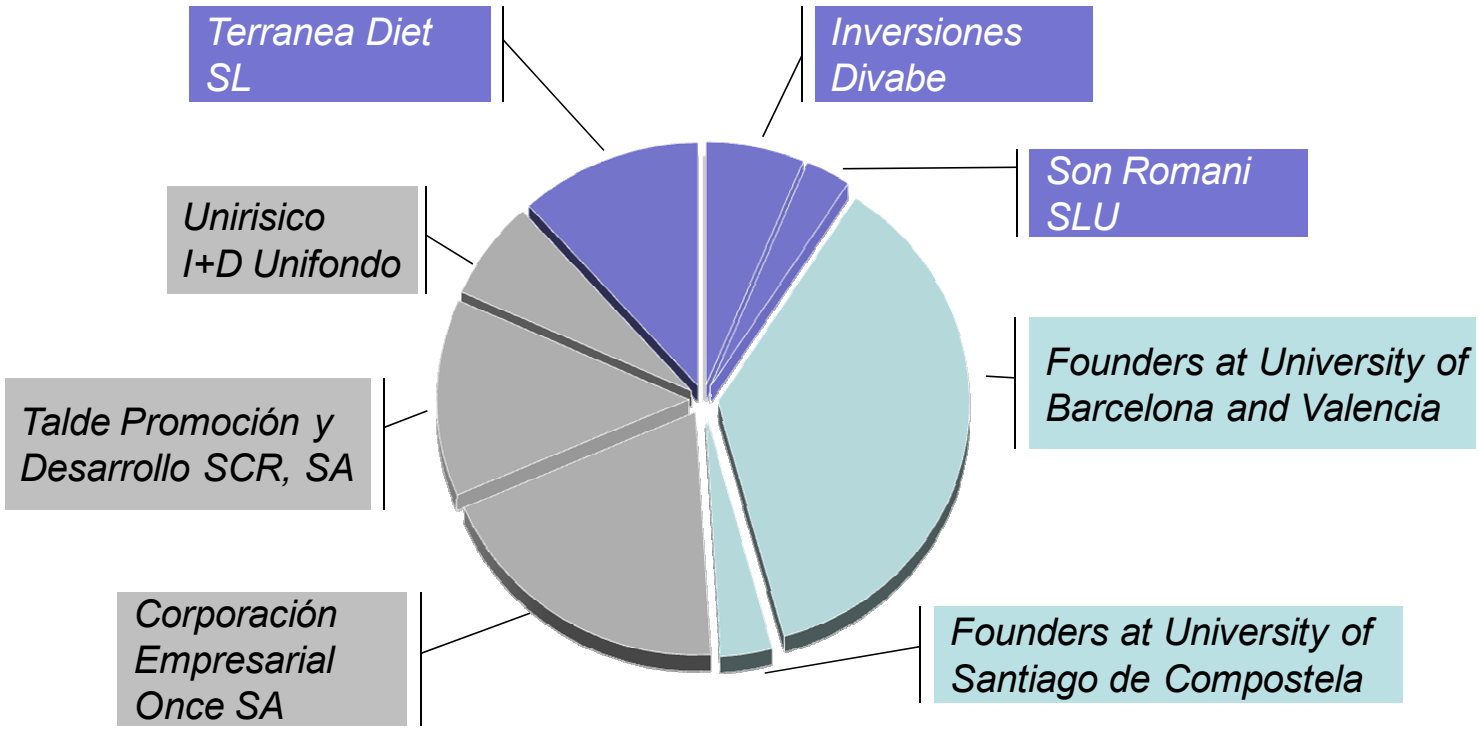
The Company generates proprietary drug candidates by:

- Identifying novel applications of known drugs (repositioning)
- Leveraging its nanosystems delivery technology (reformulation)

ADVANCELL, S.A.

- Privately held, ADVANCELL is led by a competent Management and Board with significant financial and pharmaceutical experience and strong academic roots
- Employs 16 staff, 80% with advanced academic degrees
- Draws on the expertise of internationally renowned clinicians and scientists
- Partially funds R&D from internal cash flow and partnered projects

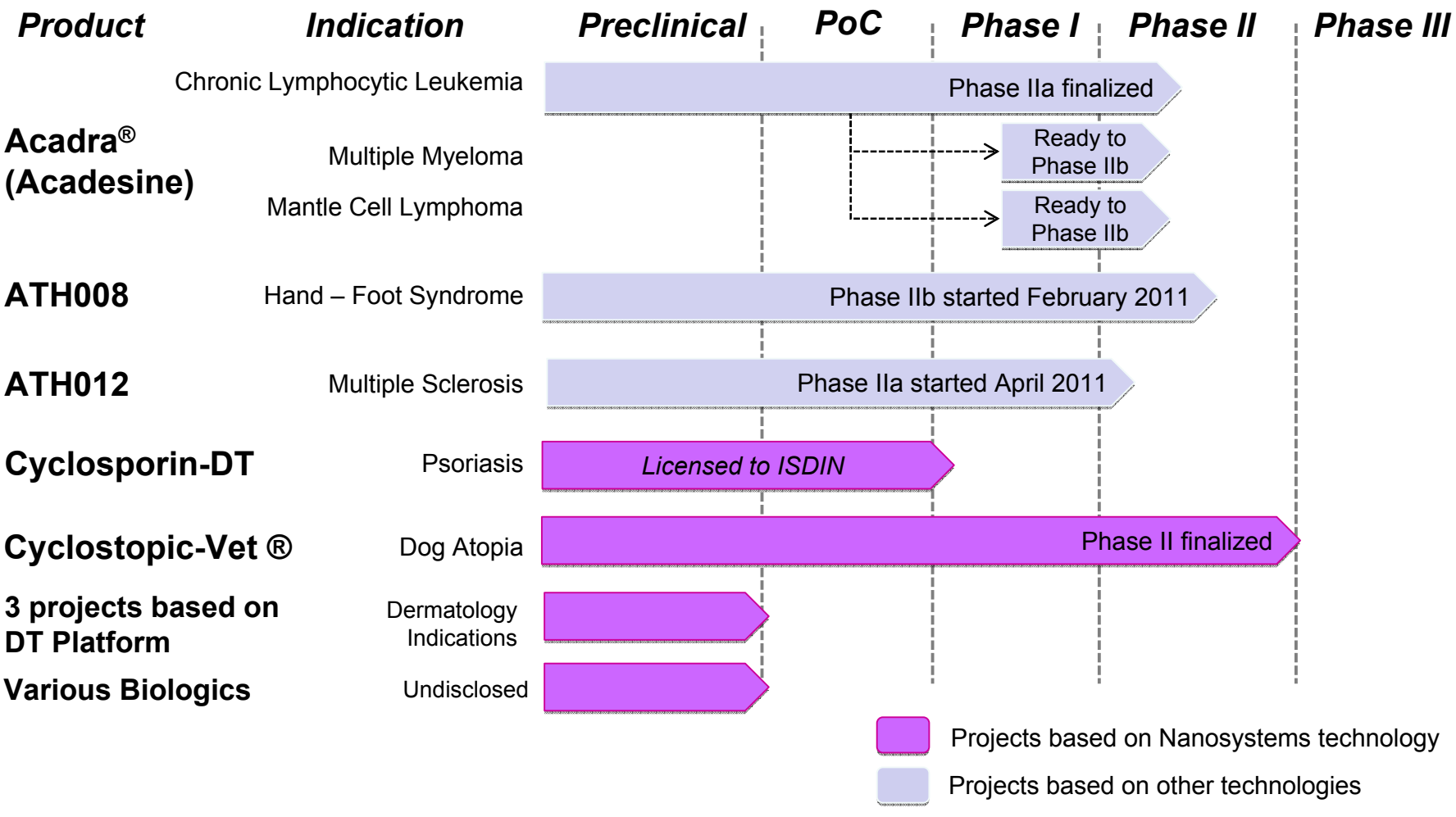
ADVANCELL - Shareholders



ADVANCELL - History

- Founded in 2001 as an spin-off from the University of Barcelona and Valencia offering ADME-Tox services and reagents
- In 2004, in-licensed a portfolio of patents in nanomedicine (USC) and a patent in oncology (UB)
- In 2006, first licensing agreement with ISDIN covering nanomedicine reformulation products for the treatment of skin diseases
- In 2008, clinical proof of concept for first nanomedicine product and entry of project Acadra® into phase IIa for CLL
- In 2010, successfully divested the Company's ADME-Tox service business and completed strategic transition focusing on the development of drug candidates for significant unmet medical needs

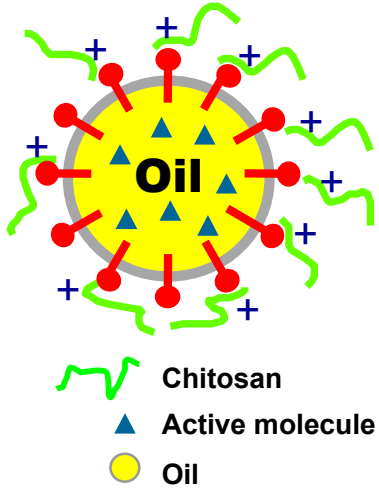
ADVANCELL – Pipeline 2011



Dermosome Technology®

It is a fluid emulsion consisting of "nano"-oily droplets in which the drug is dissolved and with a polysaccharide coating (IPRs 2006; Filled/Granted EU; 2009; Filled)

Droplet Size	350 ± 150 nm
Surface charge	+10 to +50 mV (long stability system)
Drug type	Lipophilic molecules (Ideally for higher MW Drugs)



This technology is useful for:

- **Enhancing the drug skin penetration (MW > 800 Da); (Re-profiling Strategies and new administration routes)**
- **Increasing the drug solubility**
- **Improving the chemical stability**

Dermosome Technology® - Properties

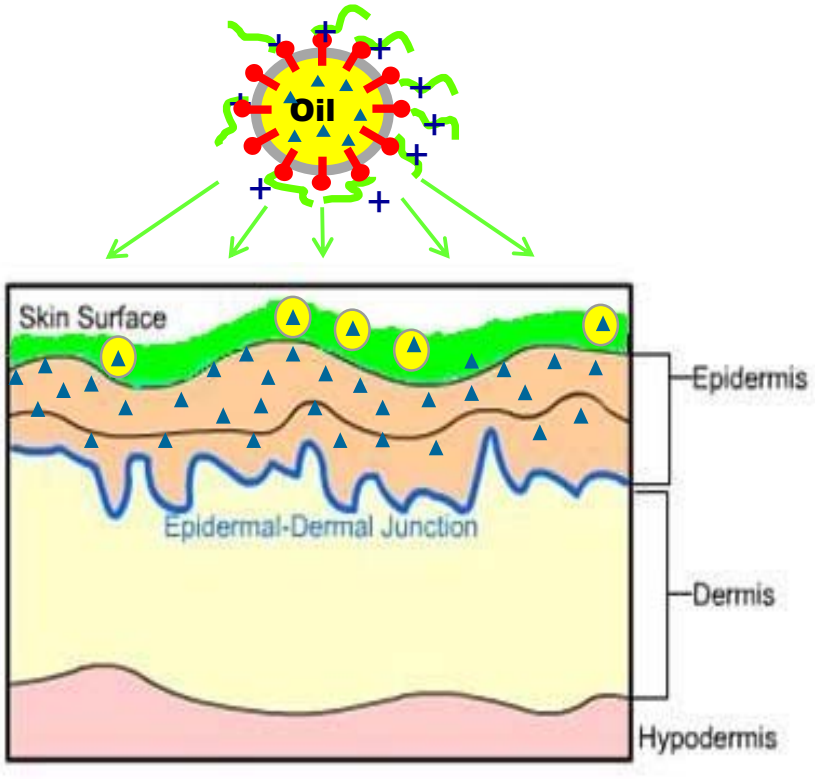
Dermatological Properties;

- ✓ **Well Known compounds in these applications (safety)**
- ✓ **Not irritant and well-tolerated (studies in rodents and rabbits)**
- ✓ **Moisturizing**
- ✓ **Wound healing (vehicle)**
- ✓ **Great cosmetic appearance (lotion)**

Manufacturing Technology Properties;

- ✓ **Simple preparation with standard equipment (solvent free)**
- ✓ **Scalable (50 Kg already achieved)**
- ✓ **Stable (2 years at ICH conditions)**

Dermosome Technology® - Mechanism



After application:

1.There is an adhesive-film formation (more absorption time)

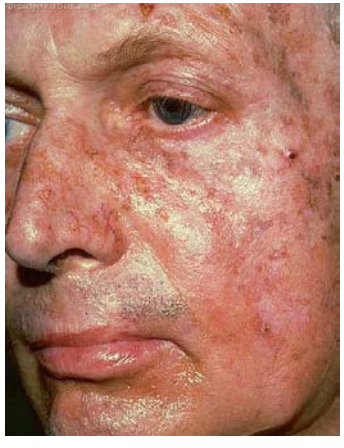
2.The active drug is released slowly from the nano-droplets (high specific surface)

3.Drug penetration and accumulation into the skin.

4.Also, hair follicles affinity

Project (ANs40): Therapeutic focus - Actinic Keratosis

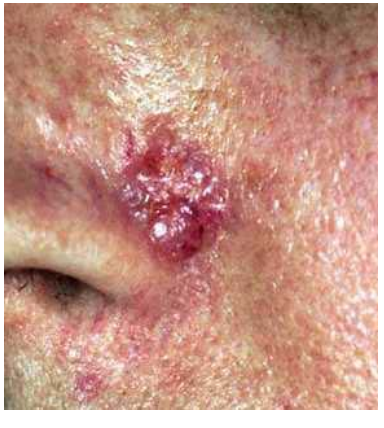
➢ Actinic keratosis (AK)



- Common sun-induced skin lesion
  - Erythematous lesion covered wiht scale
  - Precancerous lesion/carcinona *in situ*
- High prevalence, chronic condition
  - 50% caucasic population >40 years affected

➢ Non-melanoma skin cancer (NMSC)

- The most prevalent cancer in humans (5-22%)
- Risk factors: age, skin type and exposure to UV radiation
- The most common forms are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)



Project (ANs40): Therapeutic focus - Actinic Keratosis

✓ The most common malignancy occurring in white population; incidence increases 4-8% every year

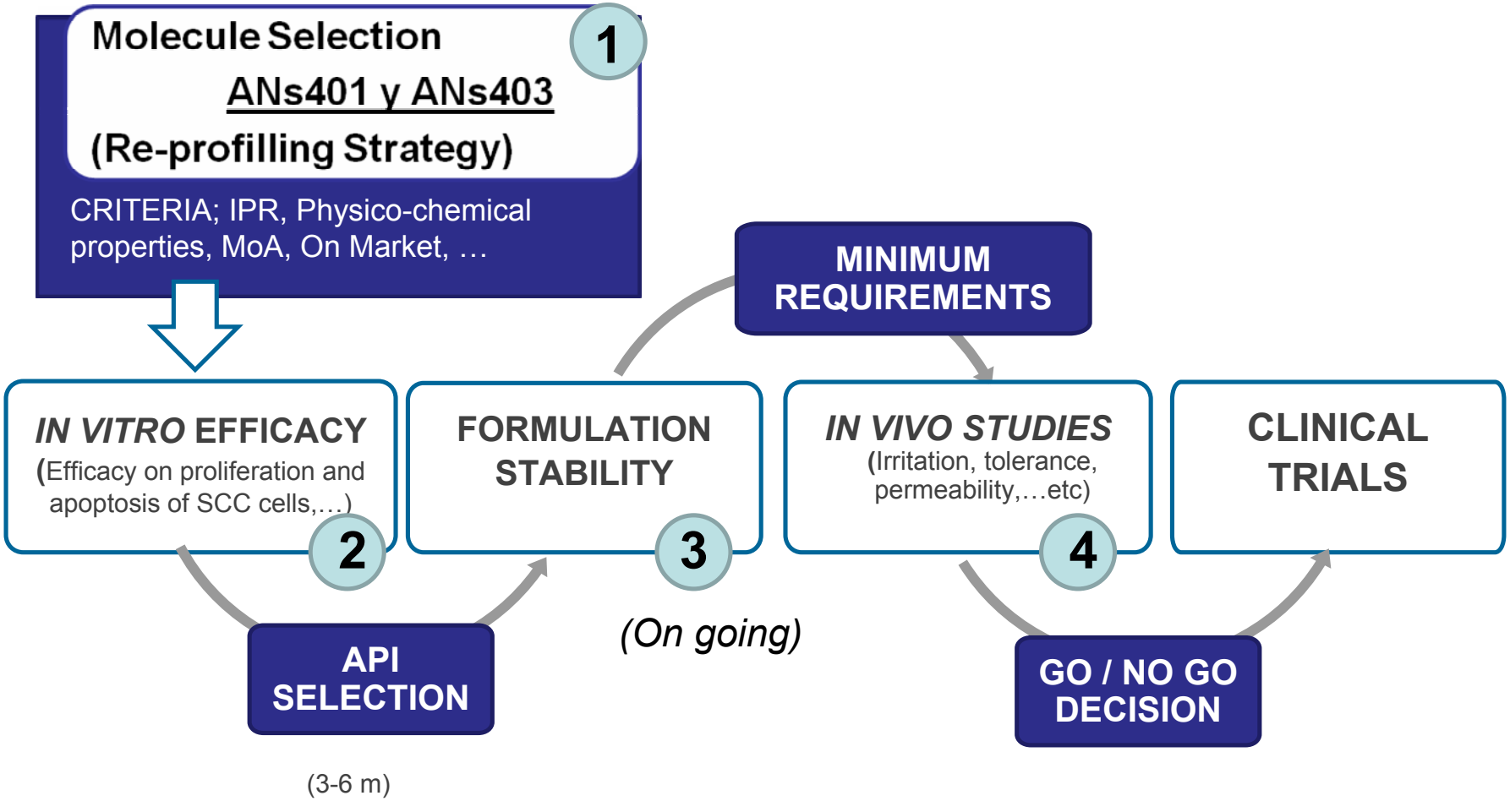
NMSC	Incidence/Prevalence	Market ($US millions)
Basal cell carcinoma (80%)	Incidence 0,3 – 0,8%	1200
Squamous cell carcinoma (20%)	Incidence 0,07- 0,2%	
Actinic keratosis	Prevalence 11-26% Incidence 0,43%	1400

Treatment: surgery, cryosurgery, chemotherapy, radiotherapy, photodynamic therapy…

Topical pharmacotherapy:

- Imiquimod and 5-fluorouracyl: important side effects, prolonged treatment
- Diclofenac

Project (ANs40) – Dermosome Technology® (DT) for treatment of Actinic Keratosis



Phase 2; In Vitro Efficacy

ANs401

Anticancer agent widely applied. It induces inhibition of cell mitosis.

✓**Complex apoptosis regulation which needs to be proven in SCC cells!!!**

ANs403

It induces cytolysis and inhibition of DNA synthesis in tumour cells.

✓**Anticancer effect needs to be demonstrated!!!**

IN VITRO EFFICACY: STUDIES IN CUTANEOUS CELL LINES

Determination of time, dose dependence and monitorization of the effects on apoptosis induction, cytotoxicity and cell proliferation

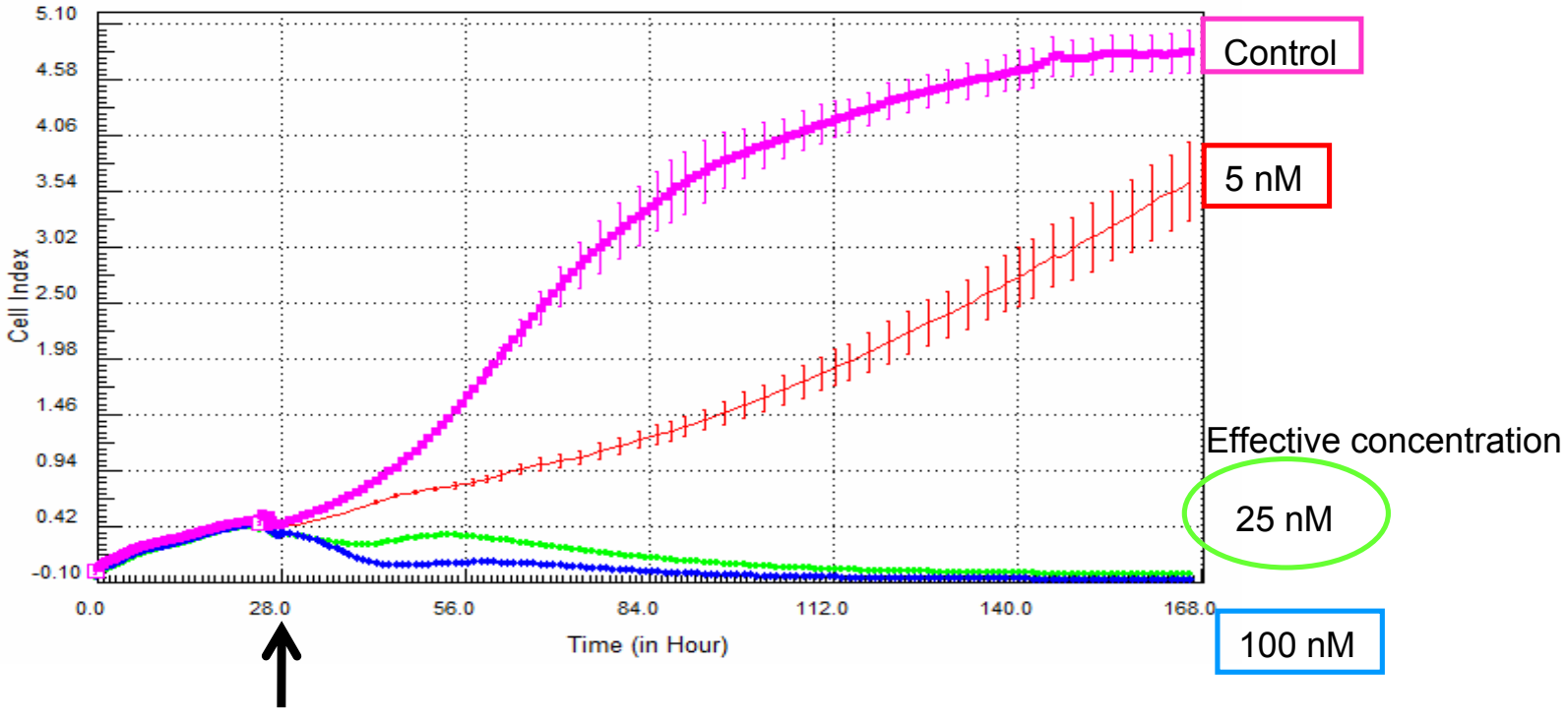
Cell growth and morphology: visible effects of both molecules on cell growth and cell morphology (strongly reduced cell numbers, early effects, all SCC lines responsive…)

Cell growth and attachment in real-time analysis: strong antiproliferative effects with both drugs, very quick responses

Apoptosis and citotoxicity: Report in process

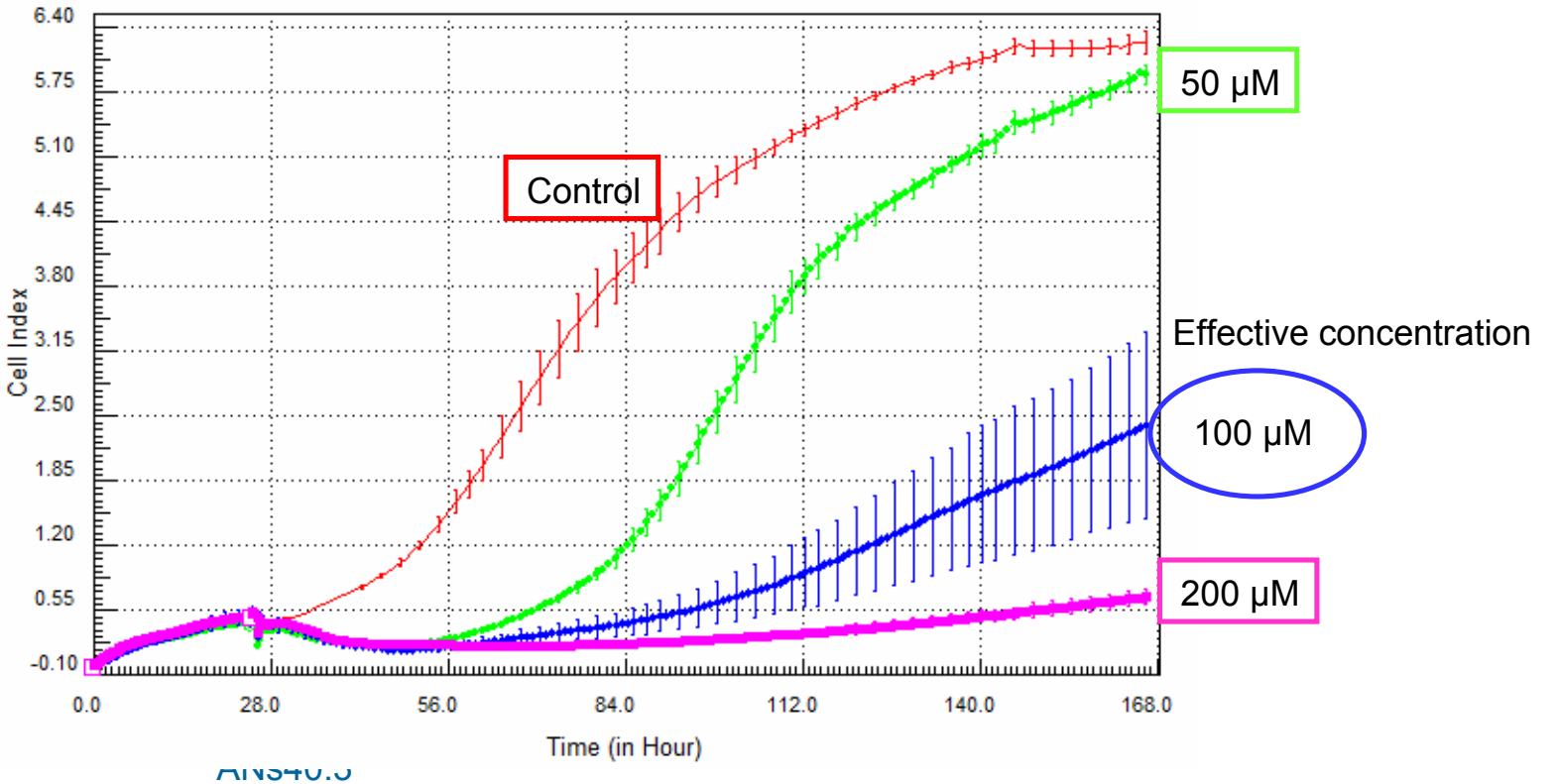
Phase 2; In Vitro Efficacy

Efficacy of ANs401 in cutaneous SCL-II cells



Phase 2; In Vitro Efficacy

Efficacy of ANs403 in cutaneous SCL-II cells



ANs403
administration

Project (ANs40): pitfalls, risks to consider and availability for cooperation

Risk	Risk Management
Long term Stability	Optimization alternatives in process (Back up)
Skin Irritation, penetration and absorption (new administration route)	Evaluate several doses (minimun dose effective)

ADVANCELL is available to co-develop this project with a dermatology partner

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