



# **Topotarget A/S**

**Swedish-American Life Science Summit 2011**

**Stockholm, 26 August 2011**

**CEO, Francois Martelet**

# Safe harbour statement

This presentation may contain forward-looking statements, including statements about our expectations of the progression of our preclinical and clinical pipeline including the timing for commencement and completion of clinical trials and with respect to cash burn guidance. Such statements are based on management's current expectations and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements.

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# Topotarget at a glance (1)




**An international Scandinavian-based biotech company dedicated to develop and market improved cancer therapies**

- Headquartered in Copenhagen, Denmark (Medicon Valley) with ~46 employees
- Focused on development and commercialization of new innovative drugs for cancer treatment
- Belinostat: Lead drug candidate and compelling Histone DeACetylase inhibitor (HDACi)
- Totect<sup>®</sup> (for anthracycline extravasation): Marketed by Topotarget USA, Inc. in the US

<b>Listing</b>	NASDAQ OMX Copenhagen
<b>Symbol</b>	TOPO.CO
<b>Market capitalization</b> (as of 25 August 2011)	€ 30M
<b>No. of shares</b> (as of 30 June 2011)	132,652,050

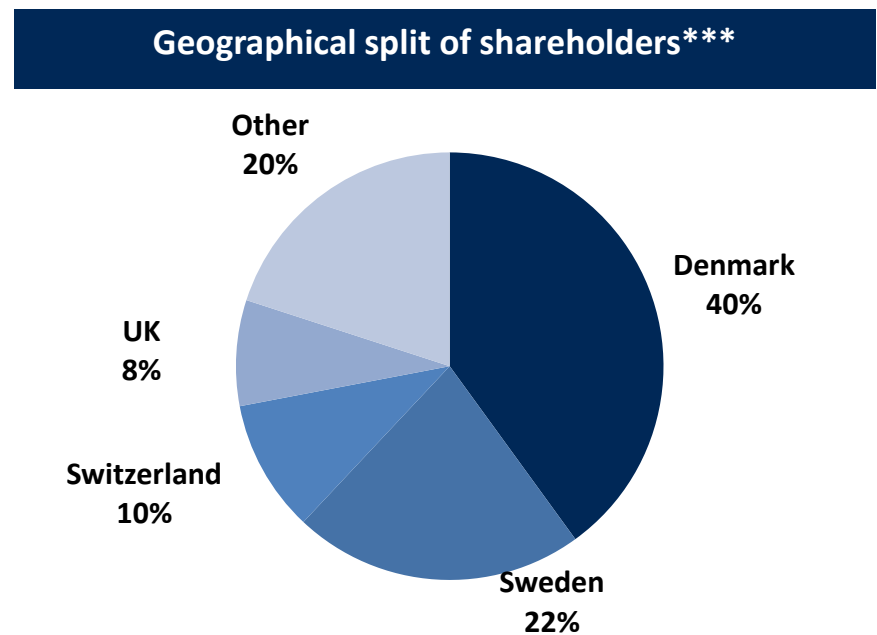
# Topotarget at a glance (2)

- Topotarget has, based on current plans, sufficient cash resources until at least 2012, without taking into account potential milestones

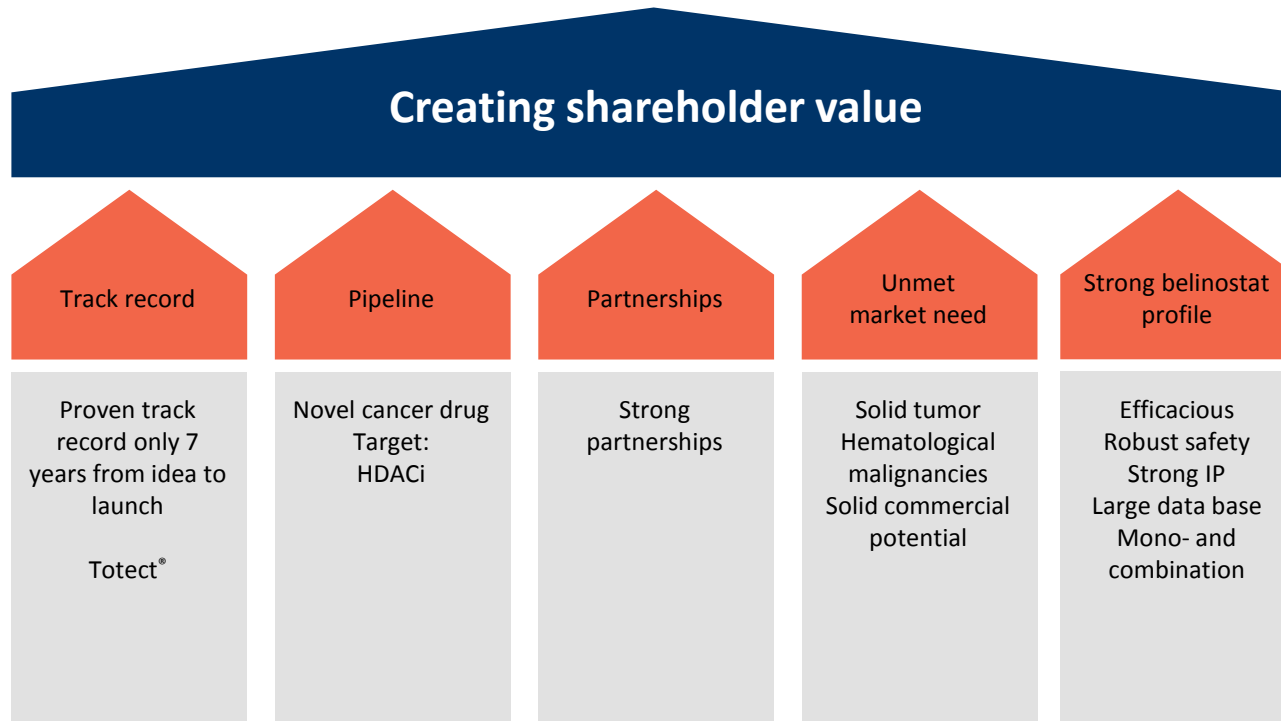
Shareholder	Ownership
The 10 largest shareholders combined **	+ 30%
HealthCap funds	 + 10%
Avanza Pension	 + 5%
3AP Fonden	 + 3%

\*\* As of August 2011. Including HealthCap fund, and excluding Avanza Pension

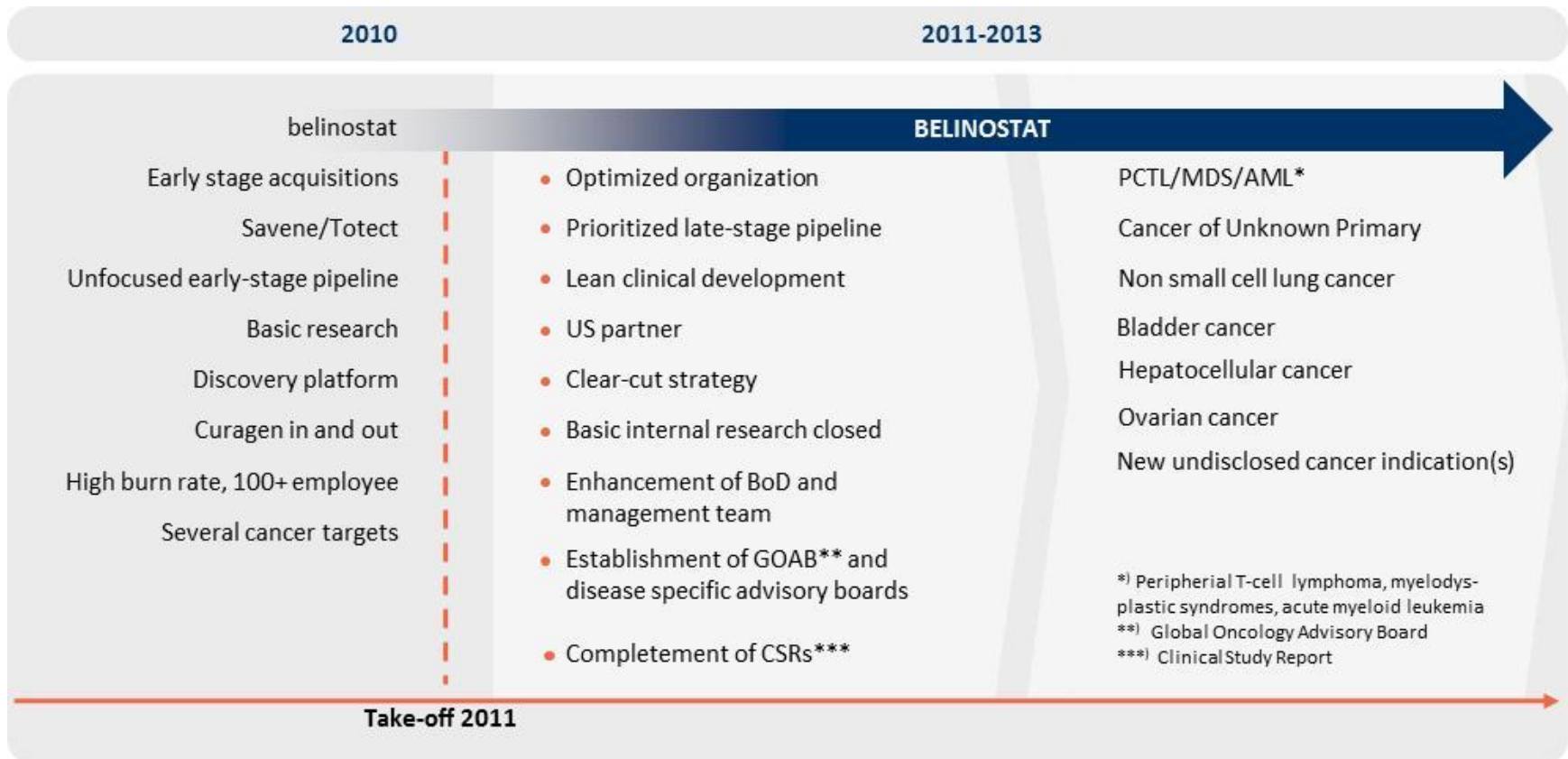
\*\*\* Estimated



# Topotarget – making a difference to shareholders and cancer patients



# Focus on belinostat – core of new strategy



# Topotarget progress on-track

## **PTCL**

- Data Monitoring Committee gave positive recommendation to pivotal PTCL study in March 2011
- Enrollment are ongoing and on track

## **CUP**

- Collecting and cleaning data
- Release in H2-2011

## **CLN-9**

- (Oral belinostat) completes enrolling

## **Scientific progress**

- Belinostat abstracts published at ASCO, ESMO, ASH, among others
- Completion of GOAB (Global Oncology Advisory Board)

## **Enhancement of management**

- Proposal for the election of two additional members of the Board of Directors (EGM 29 August 2011); Dr. Gisela Schwab and Dr. Karsten Witt

# Belinostat key clinical trials 2011-2012 (Topotarget and Spectrum)

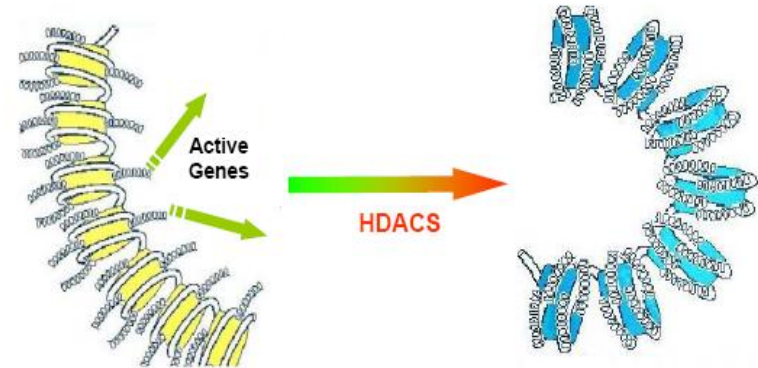
Study	Sponsor	Indication	Phase I	Phase II	Pivotal	Target	Status	Milestone	Time
BELIEF	SPPI	PTCL				100-120	Recruiting	NDA Rolling Submission	2012
CLN-17	TT	CUP				89	Complete	Top-line results	H2 2011
CLN-9	TT	Solid tumor				92	Complete	Scientific publ.	H2 2011
CLN-9	TT	Lymphoma				28	Complete	Top-line results	H1 2012
CLN-14	TT	Solid + STS				55	Phase I	LPFV stage I in phase II Results stage I	H2 2011
			Phase II	H2 2011					
CLN-20	SPPI/TT	Drug-Drug				24	Recruiting	Top-line results	H2 2011
SPI-1014 Bel	SPPI/TT	NSCLC				35	Recruiting	FPFV **)	H1 2011

\*) Last Patient First Visit \*\*) First Patient First Visit

# Histone DeAcetylase inhibitors (HDACi)

## Main characteristics of belinostat:

- "Turns on" suppressor genes
  - Inhibiting HDACs activate silenced genes
  - Some of these are apoptotic (cell death) genes
  - Activation causes selective cancer cell death
- "Turns off" oncogenes
  - Results in inhibitions of cancer cell growth



## Other mechanisms of action:

- Inhibition of the growth and development of new blood vessels in effect starving cancer cells
- Induction of immune system to target cancer cells
- Interacts with for example tubulin thus synergizing with various chemotherapies and potentially overcoming drug resistance which is the main reason for failure of cancer treatment

Belinostat works in both solid tumors and hematological malignancies

# Solid rationale for use of belinostat

## Cancer is divided into two major groups:

- Hematological malignancies (10%)
- Solid tumors (90%)

## It is known that a number of drugs are quite effective as single agents in hematological malignancies

- Topotarget and NCI explored several hematological malignancies using belinostat as single agent, for example: ALL, AML, MM, MDS, PTCL, CTCL
- Most of these studies were phase I or I/II

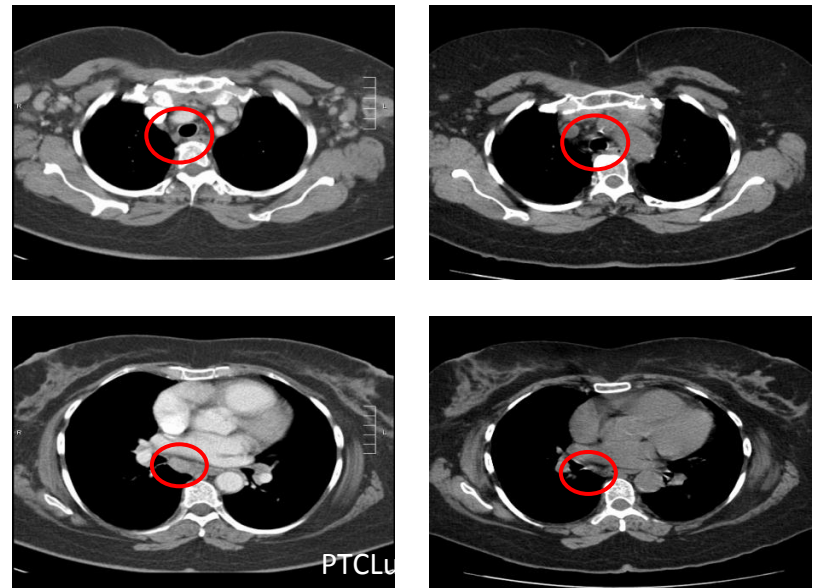
## It is well-established that in solid tumors, most drugs work as combination treatment only

# Promising monotherapy data from CLN-6 lead to the initiation of the BELIEF

## Study PXD101-CLN-6

- Phase II trial with patients who had refractory CTCL (28) or PTCL (25)
- Efficacy in 19 evaluable PTCL patients
  - CR: 2, PR: 4, SD: 4
  - Response rate:  
6/19 = 32% [CI: 16-45%]
  - Duration of
    - a) Response: +268
    - b) Stable disease: +133 days

## Case report PTCL (monotherapy)



# Pivotal BELIEF

## - important regulatory status

### FDA interaction

- Special Protocol Assessment (**SPA**) for pivotal trial specifies final statistical target of 20% response rate
- **Orphan Drug Designation**
- **Fast Track Designation**
- **NDA submission is targeted for 2012**

### Recommendations from DMC

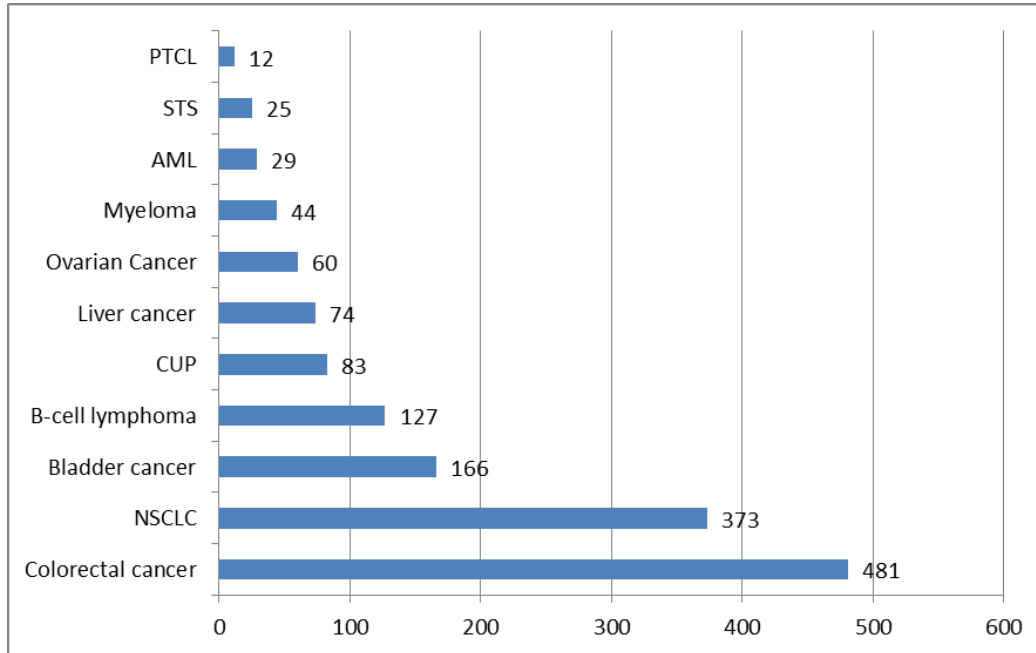
- No significant safety concerns
- DMC recommends that the study continues according to the protocol until 100 evaluable patients are enrolled
- Interim safety assessment and futility analysis were performed after the first 45 patients had entered the study and had received at least 1 dose of belinostat

# CLN-19 BELIEF pivotal trial for PTCL

- A multicenter, open-label trial of BELinostat In patients with relapsed or rEfractory Peripheral T-Cell Lymphoma
- Target accrual 120 (to get 100 evaluable) patients
- Dosing
  - I.V, 1000mg/m<sup>2</sup>, days 1-5 every three weeks
- Interim analysis (25 March 2011):
  - Futility based on < 5 responses in 41 evaluable patients
- Final data:
  - Positive outcome response rate at least 20%
- NDA submission is targeted for 2012
- Study is sponsored by Spectrum Pharmaceuticals, Inc.

# Belinostat – commercial potential

## New cancer patients per year in US, Japan and 5 major EU



Source: Datamonitor estimate (US + Japan + 5 major EU)

- Several competitive advantages with best-in-class profile:
  - Active in multiple drug resistant cancer cells
  - Mild or no bone marrow toxicity, enabling combination treatment with chemotherapy in full doses
  - The only HDACi administered as IV, CIV and oral
  - Opportunity to pre-select patients with a high probability for response allows the drug to be used earlier
- Estimated annual global peak market sale of belinostat in the current PTCL indication at least USD 100m
- Estimated annual global CUP market sales of the CUP indication ~ USD 0.5-0.6bn
- Price of Istodax® (romidepsin) approved November 2009 for CTCL/PTCL June 2011 is USD 30,000\* per patient per month

\*New York Times

# Belinostat – compelling profile

## **Efficacious**

- In solid and hematological malignancies
- Synergistic effect with established therapies

## **Flexible administration**

- Option of multiple administration and formulation modes (IV, CIV & oral)

## **Strong patent position**

- Composition of matter = 2021;  
IV formulation = 2026

## **Encouraging safety profile**

- Other HDACs have significant side effects with hematological toxicity in drug combinations
- Shown to be safe in the clinical use ( $\approx$ 900 patients), with an excellent safety and cardiac tox profile and minimal bone marrow toxicity

## **Ability to combine**

- In highest dose combined with main established chemotherapies and by that maximizing the commercial potential

# Key messages

- Belinostat unique HDACi with both oral and IV formulation available
- > 30 clinical studies completed or ongoing
- > 900 patients being exposed to belinostat
- Good safety profile
- Ongoing registration trial in PTCL. NDA filing 2012
- Randomized phase II in CUP enrollment completed
- Substantial and untapped potential in expansion into new oncology indications
- Improved news flow in 2011/2012

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# Thank you!

## Q&A