



**Topotarget A/S**  
**Orphan Drugs Summit**  
**Copenhagen 15 September 2011**  
**CEO Francois Martelet, MD**

# 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 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 13 September 2011)	€ 35m
<b>No. of shares</b> (as of 30 June 2011)	132,652,050

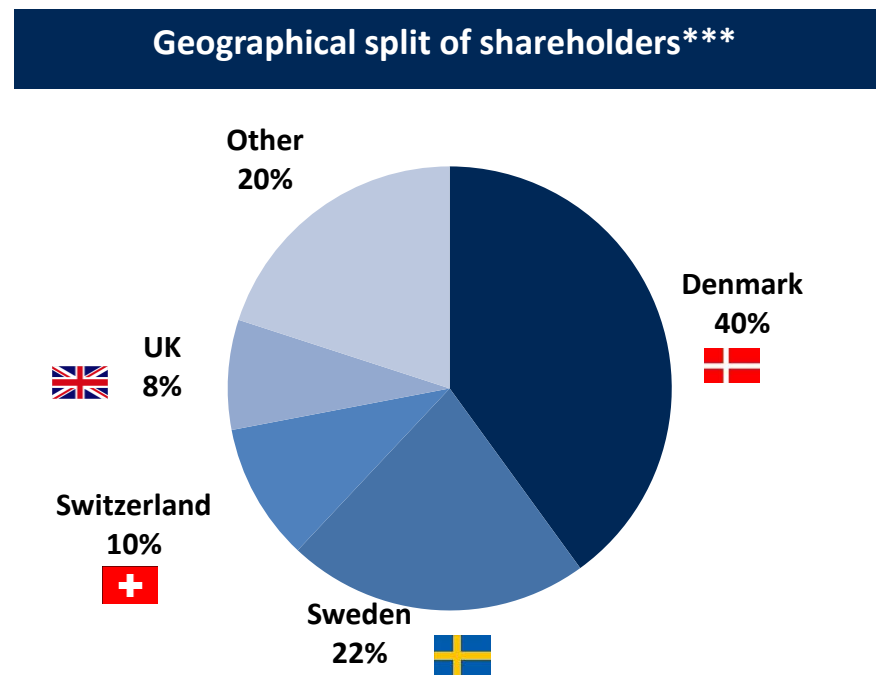
# Topotarget at a glance (2)

- 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 cancer patients and shareholders

## Creating shareholder value

### Track record

Proven track record only 7 years from idea to launch

Totect®

### Pipeline

Novel cancer drug  
Target:  
HDACi

### Partnerships

Strong partnerships

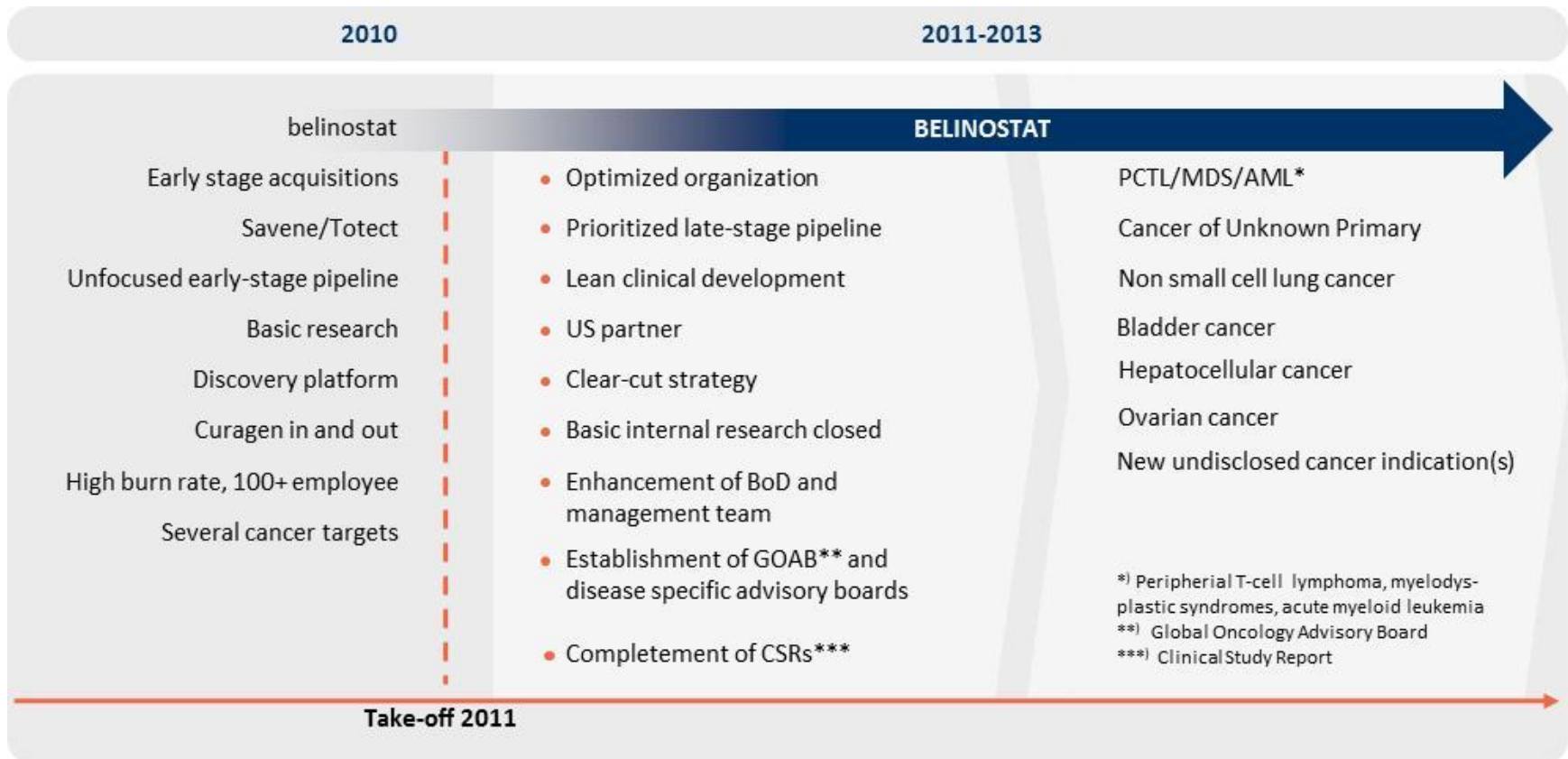
### Unmet market need

Solid tumor  
Hematological malignancies  
Solid commercial potential

### Strong belinostat profile

Efficacious  
Robust safety  
Strong IP  
Large data base  
Mono- and combination therapy

# Focus on belinostat – core of new strategy



# Belinostat partner agreement with Spectrum Pharmaceuticals, Inc.

- Agreement, 2 February 2010
- USD 30m cash upfront
- Potential value USD 320m in milestones
- + Double-digit royalties
- Spectrum funds PTCL BELIEF trial; Topotarget funds ongoing randomized phase II CUP study
- Resources for co-development in promising indications, cost sharing with Spectrum contributing 70% and Topotarget 30% of future development costs
- Joint development and commercialization committees
- Spectrum territory: North America and India as well as right of negotiation to China



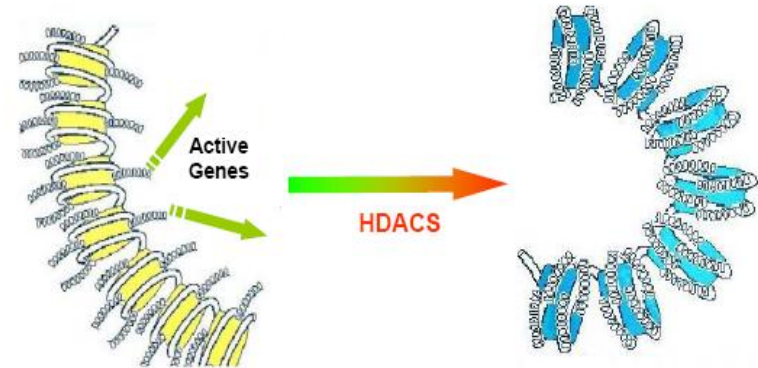
# The Topotarget corporate story (IPO 2005)

Year	Event	Product
1999	Topotarget founded	Savene/Totect
2002	Acquisition of Prolifix	Belinostat
2004	Curagen collaboration	Belinostat
2005	Acquisition of G2M	Zemab,
2006	Acquisition of BioImage asset	mTOR
2007	Acquisition of Apoxis	APO010, APO200, APO866
2008	Repurchase of US rights from Curagen	Belinostat
2010	Spectrum collaboration	Belinostat
2010	Divestment to SpePharm	Savene

# 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

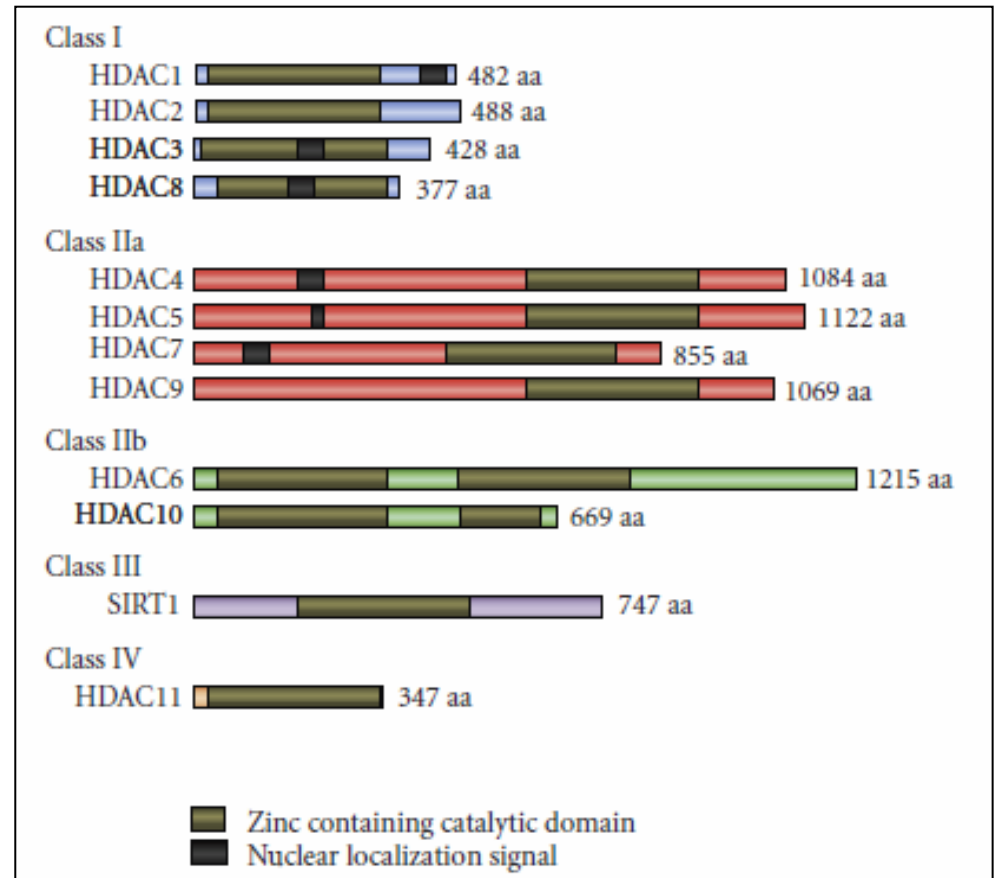
Belinostat works in both solid tumors and hematological malignancies

# HDAC classification tip-offs on potency

## Belinostat is a class I/II HDACi

- In order to effectively treat the tumor several HDAC members need to be modulated
- Therefore the multi-potent HDACi belinostat may be more effective than highly selective HDAC inhibitors

## HDAC classes



# Topotarget progress on-track

## PTCL

- Data Monitoring Committee gave positive recommendation to pivotal PTCL study in March 2011
- Enrollment are on track and to be concluded by H2 2011

## 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

- Two additional members of the Board of Directors elected at EGM 29 August 2011; Dr. Gisela Schwab and Dr. Karsten Witt

# Orphan drug - key tool for Topotarget

- **Incentives** to retain orphan drug status:
  - Market exclusivity,
  - Free protocol assistance
  - Potential fee reductions
  - EU or NIH funded research,
- Orphan drugs can be **advantageous** for smaller biotech companies and give valuable development and marketing advantages
- Orphan drug is common within cancer
- **Topotarget** have **successfully gained** orphan drug status i.e. for belinostat in PTCL (US) and for anthracycline extravasation treatment drug (US) Totect<sup>®</sup>

# Orphan drug – EU and US (I)

EU	US
<ul style="list-style-type: none"><li>• 10 years market exclusivity</li></ul>	<ul style="list-style-type: none"><li>• 7 years market exclusivity</li></ul>
<ul style="list-style-type: none"><li>• Clinical superiority clause</li></ul>	<ul style="list-style-type: none"><li>• Clinical superiority clause</li></ul>
<ul style="list-style-type: none"><li>• Research money from national authorities</li></ul>	<ul style="list-style-type: none"><li>• Research money by NIH</li></ul>
<ul style="list-style-type: none"><li>• Financial incentives on a EU and national basis</li></ul>	<ul style="list-style-type: none"><li>• Tax reduction</li></ul>
<ul style="list-style-type: none"><li>• Use Centralised procedure obligatory</li></ul>	

# Orphan drug – EU and US (II)

EU	US
<ul style="list-style-type: none"><li>• Max~246,00 patients in EU affected or financially non-viable</li></ul>	<ul style="list-style-type: none"><li>• Max. 200,000 patients in the US affected or financially non-viable</li></ul>
<ul style="list-style-type: none"><li>• Fee waiver via request</li></ul>	<ul style="list-style-type: none"><li>• Always fee reduction</li></ul>
<ul style="list-style-type: none"><li>• Development and Regulatory assistance</li></ul>	<ul style="list-style-type: none"><li>• Development and Regulatory assistance</li></ul>
<ul style="list-style-type: none"><li>• Possible access to accelerated review</li></ul>	<ul style="list-style-type: none"><li>• Possible access to fast track</li></ul>
<ul style="list-style-type: none"><li>• Pediatric development obligatory for new MAA</li></ul>	<ul style="list-style-type: none"><li>• Pediatric development exempted</li></ul>

# Belinostat – compelling profile

## Supercharging chemotherapy

### 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

# 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
- Key clinical trial within hematological malignancies is the pivotal BELIEF study in PTCL

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

- Belinostat, Carboplatin and Paclitaxel are used as the back bone of combinations therapies in our clinical studies within solid tumors

**Strong rationale for using belinostat is endorsed by the strong academic interest and the many investigator trials (more than 15)**

# Potential belinostat new indications

Hematological malignancies (i.v.) – first entrance to market

Hematological malignancies	Data support	Market potential	Competition	Belinostat clinical trials
PTCL	++	Small	High	CLN-6, pivotal study (BELIEF) is ongoing
MDS/AML	+	Medium	Low/medium	CLN-15 NCI (Odenike, # 7285)

# Potential belinostat new indications

Solid tumor (i.v.) – attractive market potential

Solid tumor	Data support	Market potential	Competition	Belinostat clinical trials
<b>CUP</b>	<b>+</b>	<b>Medium</b>	<b>Low</b>	<b>CLN-17, randomized phase II is ongoing</b>
<b>NSCLC</b>	<b>(+)</b>	<b>Large</b>	<b>High</b>	<b>SPPI-1014-bel, NCI (Bates, # 8238)</b>
Bladder	(+)	Small	Low	CLN-8
Ovarian	(+)	Medium	Moderate	CLN-8, GOG-0126T
Colorectal	(+)	Medium	Moderate	CLN-4
<b>Sarcoma</b>	<b>(+)</b>	<b>Small</b>	<b>Low</b>	<b>CLN-14</b>
Thymic carcinoma	(+)	Small	Low	NCI (Giacone, # 8602 and # 8174)

# 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	H2 2011
			Phase II	Results stage I	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

# PTCL – NDA filing 2012

- promising data from CLN-6 headstarted pivotal BELIEF trial

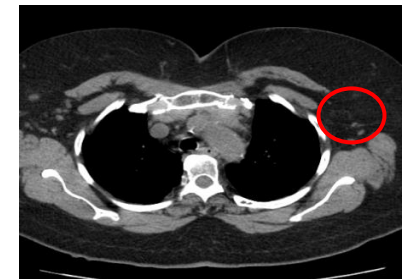
## Study PXD101-CLN-6

- Phase IIa 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 days
    - b) Stable disease: +133 days

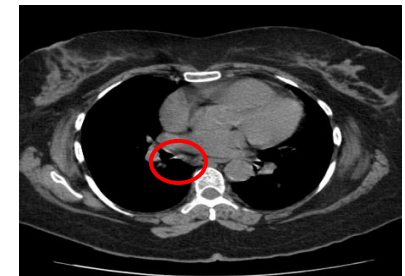
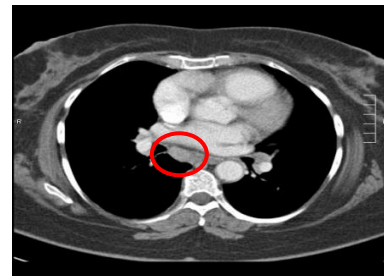
## Case report PTCL (monotherapy)



Pretreatment



On treatment



# PTCL – a niche area with unmet need

## Key facts for PTCL

- Niche market. Belinostat WW peak sales US\$ 100m
- Unmet medical need
- 12,000 new cases per annum (US, Japan and EU top-5)
- PTCL is aggressive and treatment is imperative to quality of life and survival

## PTCL definition

- Peripheral T-cell Lymphoma (PTCL) is a sub-type of non-Hodgkins lymphoma
- Aggressive, high-grade cancer
- It generally has a poor prognosis
- 15% of non-Hodgkins lymphoma patients have a PTCL subtype
- Average age of patients with PTCL is 65 years

# PTCL – belinostat market entrance

A multicenter, open-label trial of **BEL**inostat In patients with relapsed or **rEF**ractory Peripheral T-Cell Lymphoma

- BELIEF trial is our pivotal trial in PTCL
- 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):
  - Safety and 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.

# Pivotal BELIEF

## - regulatory status in focus

### FDA interaction

- **Special Protocol Assessment (SPA)** for pivotal trial BELIEF is in place with a required response rate of 20%
- **Orphan Drug Designation**
- **Fast Track Designation**
- **NDA submission** is planned for for 2012

### Recommendations from DMC

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

# Key messages

- Belinostat unique HDACi with both oral and IV formulation available
- > 30 clinical studies completed or ongoing, large academic attention
- > 900 patients being exposed to belinostat
- Good safety profile
- Shown good benefit in patients
- 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
- Enhanced news flow in 2011/2012

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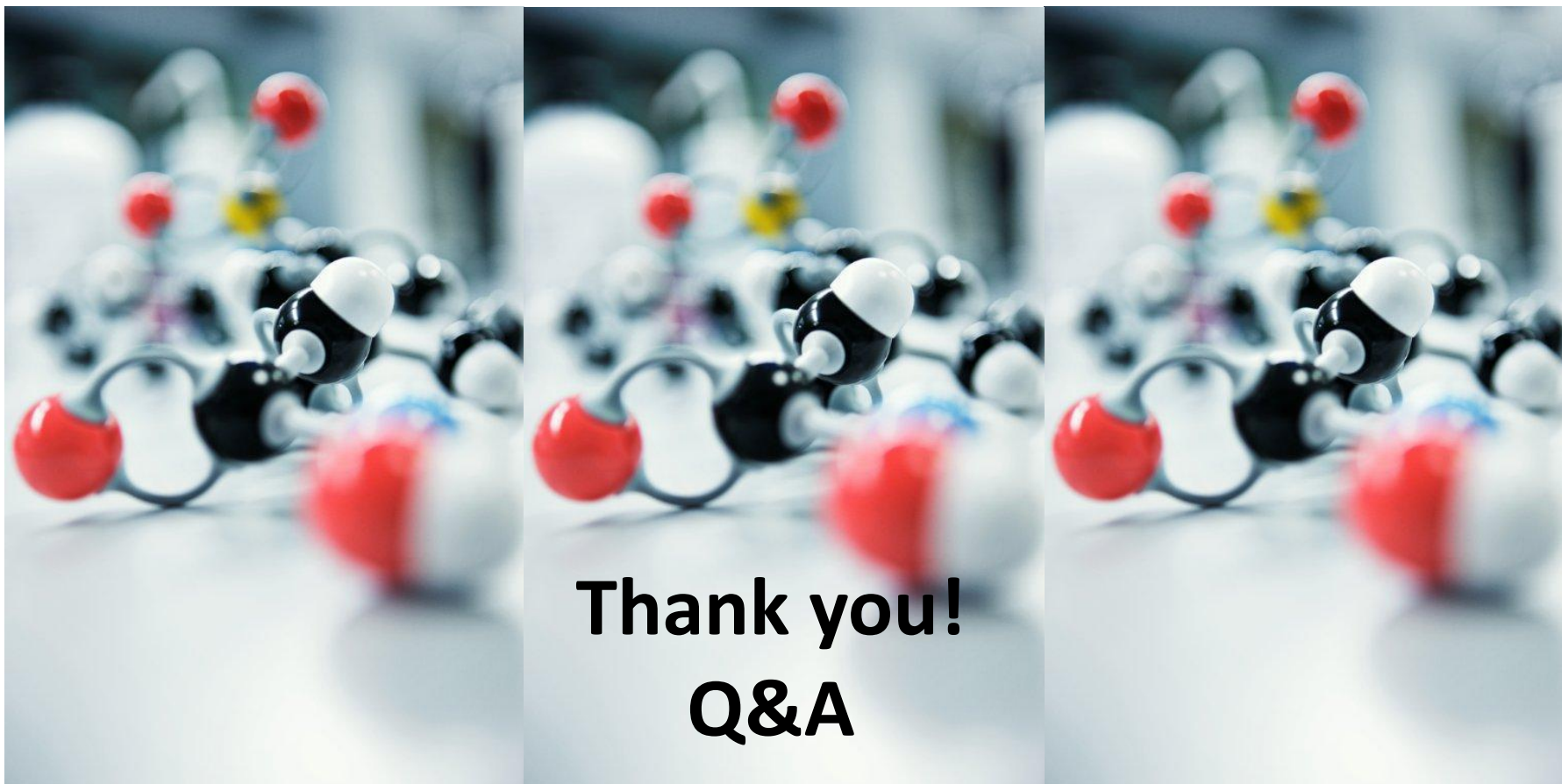
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**Thank you!**  
**Q&A**