



**NORDIC  
NANOVECTOR**

## **Q1 2016 Results Presentation – 19 May 2016**

Luigi Costa, CEO



# Forward-looking statements

This presentation may contain certain forward-looking statements and forecasts based on uncertainty, since they relate to events and depend on circumstances that will occur in the future and which, by their nature, will have an impact on Nordic Nanovector's business, financial condition and results of operations. The terms "anticipates", "assumes", "believes", "can", "could", "estimates", "expects", "forecasts", "intends", "may", "might", "plans", "should", "projects", "will", "would" or, in each case, their negative, or other variations or comparable terminology are used to identify forward-looking statements. There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in a forward-looking statement or affect the extent to which a particular projection is realised. Factors that could cause these differences include, but are not limited to, implementation of Nordic Nanovector's strategy and its ability to further grow, risks associated with the development and/or approval of Nordic Nanovector's products candidates, ongoing clinical trials and expected trial results, the ability to commercialise Betalutin<sup>®</sup>, technology changes and new products in Nordic Nanovector's potential market and industry, the ability to develop new products and enhance existing products, the impact of competition, changes in general economy and industry conditions and legislative, regulatory and political factors.

No assurance can be given that such expectations will prove to have been correct. Nordic Nanovector disclaims any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

# Strong progress in all priorities and execution on track

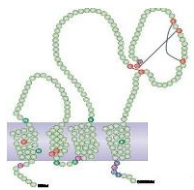
<b>Updated results with Betalutin®</b>	<ul style="list-style-type: none"><li>• Confirm promising efficacy</li><li>• Further increase in Duration of Response</li><li>• Highly favourable safety profile</li></ul>
<b>Progress on Betalutin®'s clinical development plan</b>	<ul style="list-style-type: none"><li>• Recruitment of sites for both Phase 1 and Phase 2 completed</li><li>• Patient enrolment on track</li><li>• IND open for DLBCL study (new indication)</li></ul>
<b>ARC pipeline development</b>	<ul style="list-style-type: none"><li>• First GMP batch of chimeric HH1 antibody manufactured</li></ul>
<b>Partnership agreement</b>	<ul style="list-style-type: none"><li>• Collaboration with Paul Scherrer Institute</li></ul>

# NHL patients clearly need better treatment options



- A cancer of the white blood cells (lymphocytes)/immune system
- 10th most common cancer: estimated 850,000 prevalent patients with B-cell NHL
- 66% of diagnosed patients aged 55-74 years
- High mortality rate, despite available treatments
- A market opportunity estimated to be worth over USD 12 billion by 2018

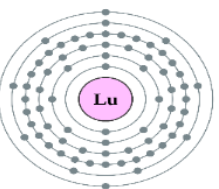
# Betalutin<sup>®</sup> is specifically designed to treat NHL



**CD37:**  
a validated target for  
B-cell NHL



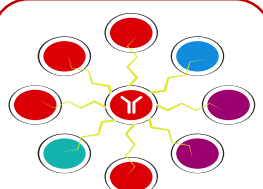
- CD37 is an **important therapeutic target** for NHL patients relapsed after CD20-based therapy
- **Internalization** results in a **prolonged irradiation** of the cancer cell nucleus



**Lutetium-177:**  
ideal therapeutic and  
safety properties



- Beta-emitting particles with half-life matching the antibody's circulation time **to ensure that tumour mass is optimally irradiated**
- **Mean range** of radiation **treats 'bulky' tumours** while limiting damage to healthy tissue



**Multi-cell kill**  
approach



- Prolonged irradiation of tumour cells **within ~50-cell radius** enables “**multi-cell kill**” effect, even of malignant cells **that do not express CD37** or have limited blood supply

**ARCs can deliver better treatment outcomes than immunotherapies (monoclonal antibodies or ADCs), which rely on a single cell kill approach**

# Betalutin®'s unique value proposition is based on important differentiating factors

## High and durable response

- **Two-fold higher Complete Response** than marketed competitors, as a single agent
- **Duration of Response exceeding 12 months** in patients who have failed many prior treatments

## Predictable and manageable toxicity

- **Manageable and reversible** haematological side effects, minimal non-haematological toxicity

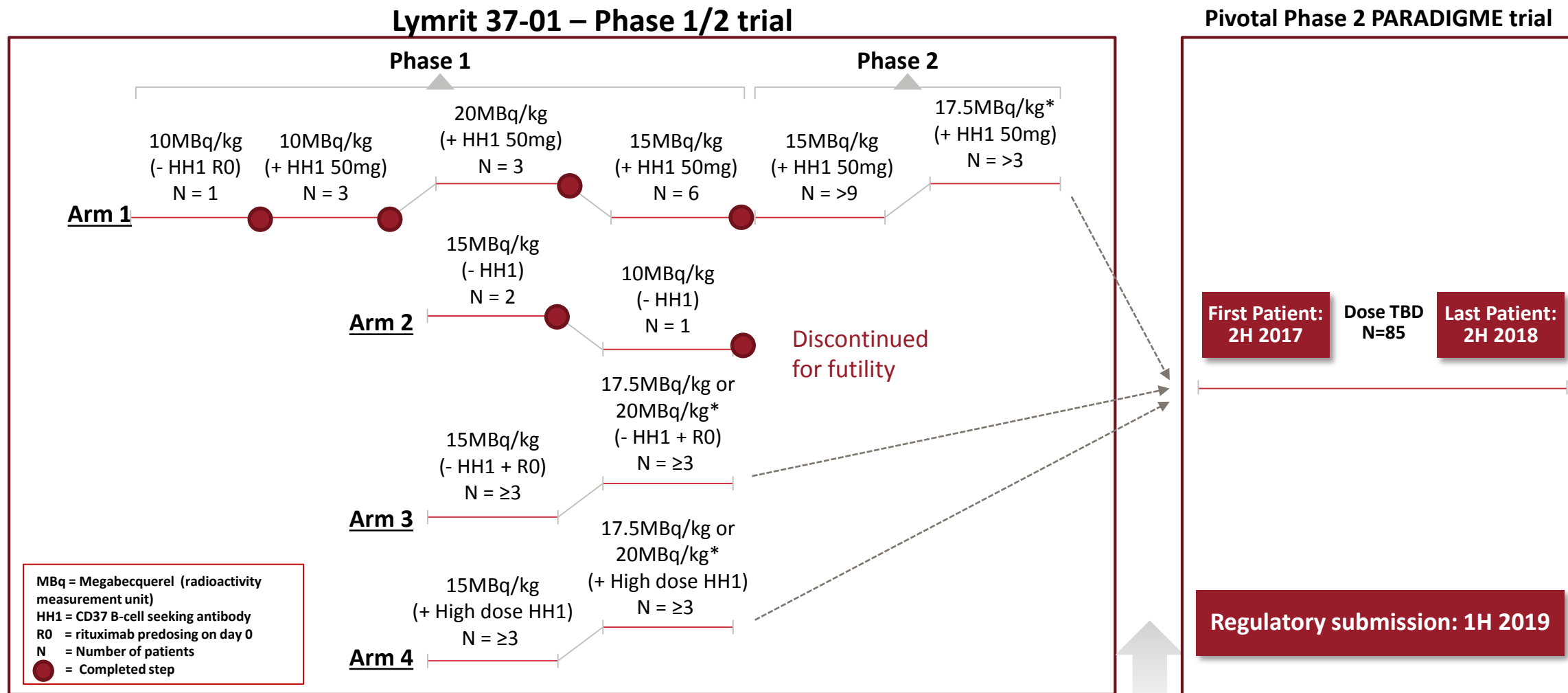
## Convenience for patients and physicians

- **One-time therapy:** 100% patient compliance and improved convenience vs. oral TKIs
- Improved **patient's quality of life**
- Efficient **healthcare resource utilization**

## Combination potential and new target

- **Potential synergy** from **combination with anti-CD20 mAb**
- **New target (CD37)** ideal for patients who relapse after rituximab-based regimens

# Clinical development plan in Follicular Lymphoma (FL) designed to maximize efficacy

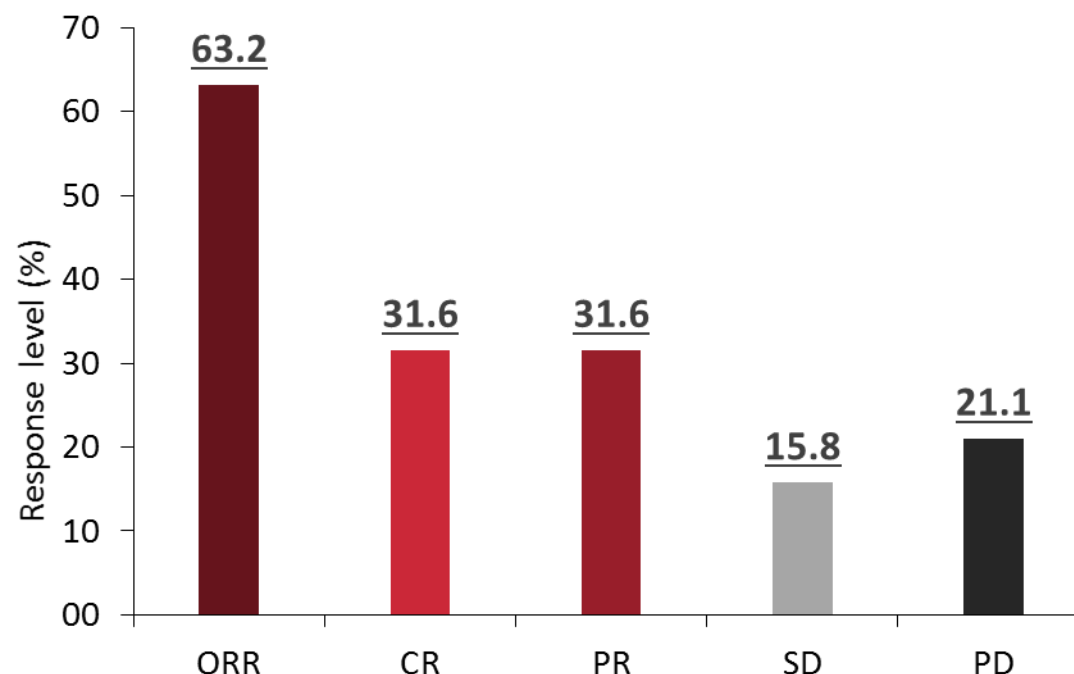


\* Dose decision based on safety data and Safety Review Board's recommendation

**PARADIGME dose decision:**  
1Q 2017



# Efficacy data presented at AACR confirms Betalutin<sup>®</sup>'s strong potential



- Data from 19 of 24 evaluable NHL patients reported (April 2016)
- Consistent Overall Response Rate (ORR) vs prior presentation in larger patient sample
- Complete Response (CR) consistently above benchmark

ORR = Overall response rate, CR = Complete response, PR = Partial response, SD = Stable disease, PD = Progressive disease

Tumour response assessed according to Cheson criteria 2007

One patient with a transformed lesion has been excluded from the efficacy analysis of the 15MBq/kg group but included the incidence of DLTs

AACR 2016, Poster version of the Abstract LB-252, Prof. A. Kolstad *et al.*



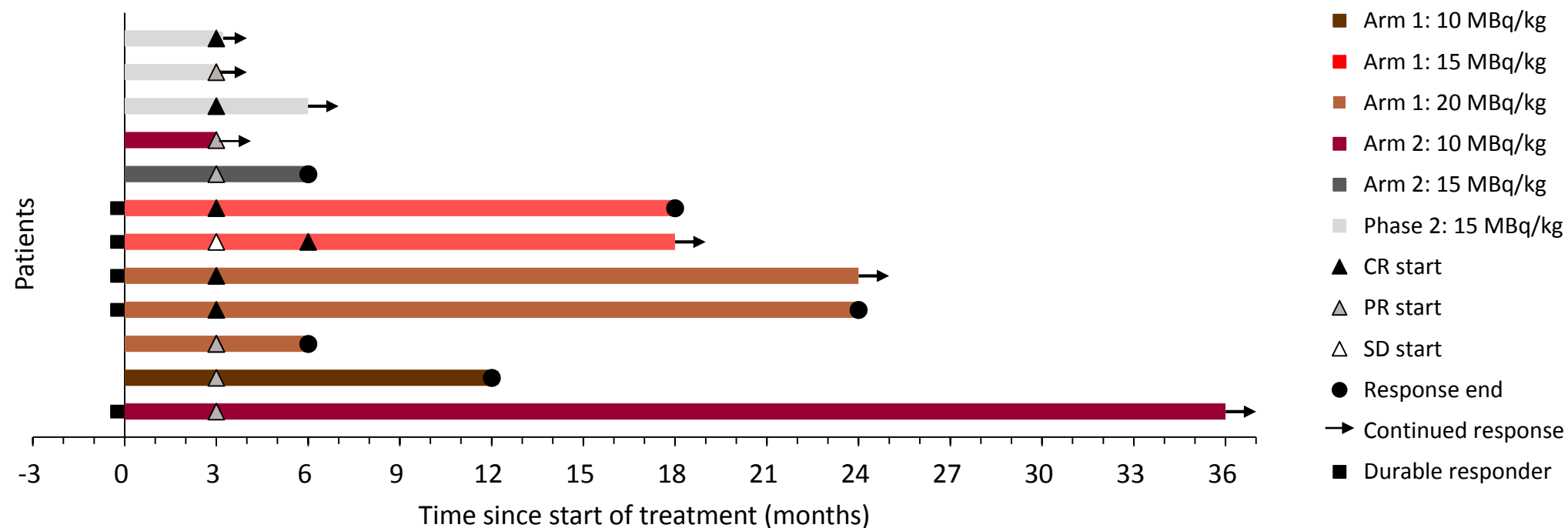
# Best efficacy shown between 15-20 MBq/kg with pre-dosing of HH1

	Arm 1						Arm 2		
	Phase 1				Phase 2	Phase 1 & 2	Phase 1		Phase 1 & 2
	10MBq/kg + R0	10MBq/kg + 50mgHH1	20MBq/kg + 50mgHH1	15MBq/kg + 50mgHH1	15MBq/kg + 50mgHH1 (Phase 2)	All 15MBq/kg + 50mgHH1	15MBq/kg - HH1	10MBq/kg - HH1	OVERALL
N	1	3	3	5*	4	9*	2	1	19
ORR	1	1	3	2	3	5	1	1	12
% ORR	100%	33%	100%	40%	75%	55%	50%	100%	63%
CR	0	0	2	2	2	4	0	0	6
% CR	0	0	67%	40%	50%	44%	0	0	32%

\* One patient with a transformed lesion has been excluded from the efficacy analysis of the 15MBq/kg group but included the incidence of DLTs

- Pre-dosing optimisation is expected to allow more effective binding of Betalutin® to CD37+ tumour cells
- Key hypothesis is that pre-dosing reduces non-tumour binding, hence minimising haematological side effects
- Optimised pre-dosing can potentially improve Betalutin®'s risk/benefit profile and allow use of higher and more efficacious doses

# Competitive Duration of Response emerging from single treatment



- DoR exceeds 12 months in most responders in the 15 MBq/kg group followed up for at least 12 months

# Highly favourable, predictable and manageable safety profile

Adverse events	Phase 1, Arm 1						Phase 1, Arm 2				Phase 2		Total	
Dose levels	10 MBq/kg N=3		15 MBq/kg N=6		20 MBq/kg N=3		10 MBq/kg N=2*		15 MBq/kg N=2		15 MBq/kg N=5		N=21	
CTCAE grade**	3	4	3	4	3	4	3	4	3	4	3	4	3	4
Platelet count decrease	0	0	2	1	0	3	1	0	0	2	0	0	3	6
Neutrophil count decrease	1	0	1	1	1	2	1	0	1	1	0	0	5	4
Dose Limiting Toxicity	0		2		3		0		2		0		7	

\* First patient received 250 mg/m<sup>2</sup> rituximab on day -7 and day 0 prior to Betalutin® and is included in this group.

\*\* CTCAE grade version 4. CTCAE = Common Terminology Criteria for Adverse Events

Serious adverse events (SAE) reported by more than one patient are summarised in a table in the poster. In addition, an SAE of epistaxis, fracture of sternum, decreased neutrophil count, pharyngitis, pneumonia, pulmonary embolism and sepsis were reported by one patient each. The event of pulmonary embolism was deemed unrelated as the subject had a prior medical history of pulmonary embolism. The remaining events were deemed to be possibly or probably related to the administration of Betalutin®.

# Leveraging ARC platform to develop a broad pipeline in haematology

Indication	Product candidate	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
FL, 3 <sup>rd</sup> line	Betalutin <sup>®</sup>					
FL, 2 <sup>nd</sup> line	Betalutin <sup>®</sup> + CD20					
Other NHL	Betalutin <sup>®</sup> + CD20					
DLBCL, ineligible for ASCT	Betalutin <sup>®</sup>					
DLBCL, conditioning	Betalutin <sup>®</sup>					
FL, 1 <sup>st</sup> line	<sup>177</sup> Lu-NNV003 ARC					
Leukemia (CLL, AML)	NNV003 ARCs					
Multiple myeloma	Affilutin					

ARC: antibody -radionuclide conjugate; ASCT: autologous stem cell transplant; chHH1: chimeric HH1 antibody; DLBCL: diffuse large B-cell lymphoma; FL: follicular lymphoma; NHL: non-Hodgkin lymphoma

# DLBCL is the most prevalent NHL subtype with the greatest unmet medical need

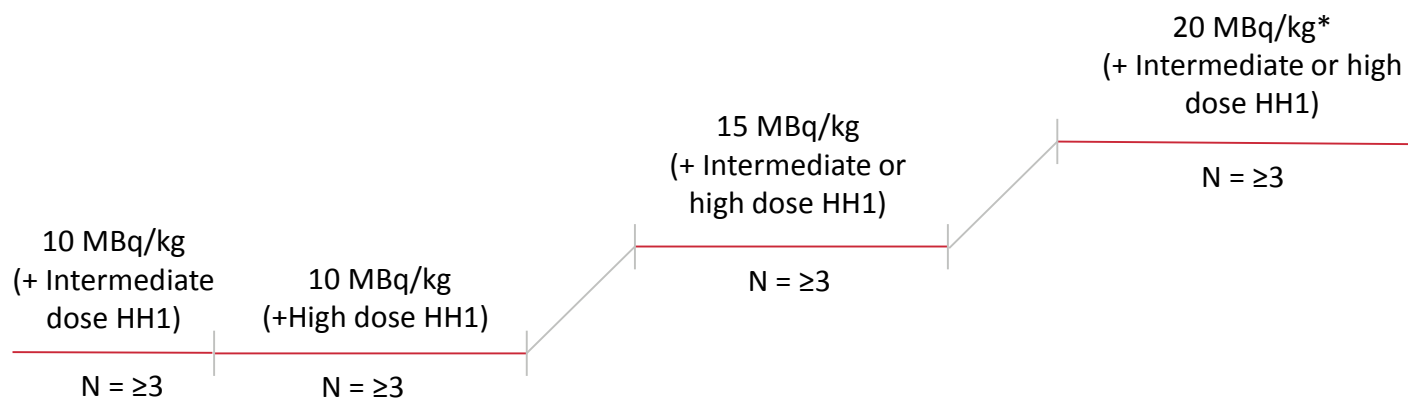
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- Over 40% of all B-cell NHL
- Approx. 21,000 pts. relapse to 2<sup>nd</sup> line
- For 70% of them - ineligible for stem cell transplant (SCT) – available therapies are marginally effective
- Significant unmet medical need
- Value of DLBCL market (US, EU-5, JP) growing from USD 1.8 billion to USD 4.7 billion over the next few years

# Advancing clinical development plan in SCT-ineligible DLBCL

## Lymrit 37-05 – Phase 1

CLEARANCE OF IND APPLICATION



N = 3-24  
Day -14: rituximab  
Day 0: Intermediate dose HH1  
Day 0: High dose HH1  
Day 0: Betalutin\*

Protocol design pending SAB and regulatory validation

## Pivotal Phase 2 trial

Several combinatorial approaches to be explored

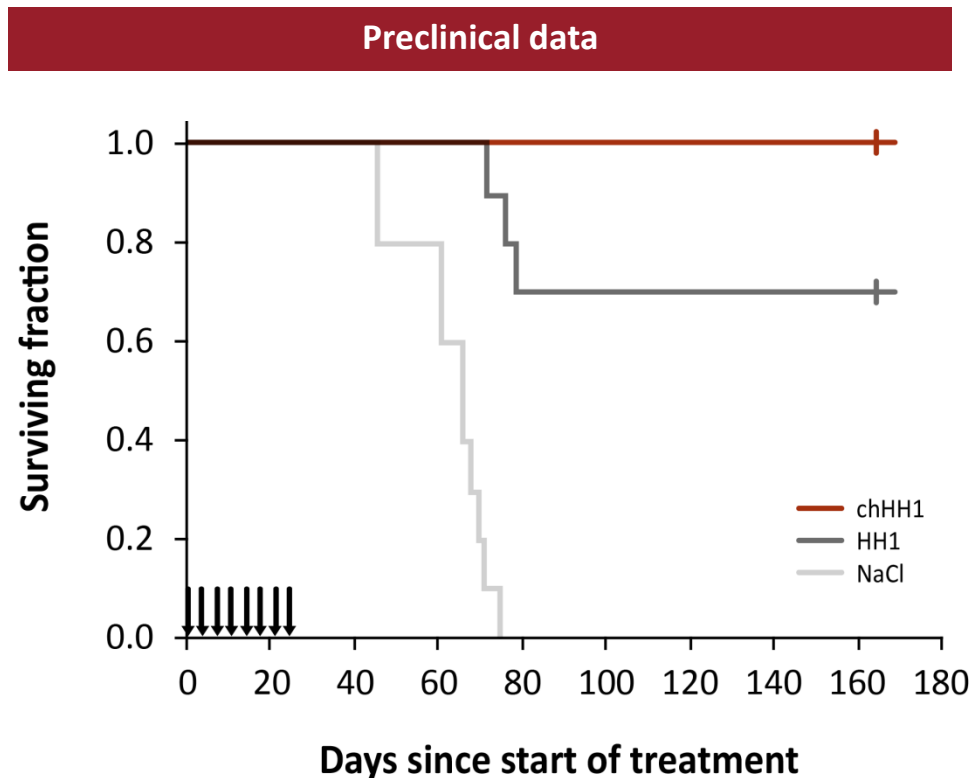
First patient:  
2H 2018

Dose TBD

Last patient:  
2H 2019

Phase 2 dose decision:  
1H 2018

# Lu-177 chimeric HH1 targeting 1<sup>st</sup> line treatment of B-cell malignancies



- First GMP batch of completed at contract manufacturer in USA
- Similar internalisation and selectivity to human lymphoid tissues as HH1 antibody
- Higher Antibody Dependent Cellular Cytotoxicity (ADCC)
- Less immunogenic, enabling safer repeated use
- Lu-177 chHH1 being investigated in preclinical studies for potential in 1<sup>st</sup> line FL



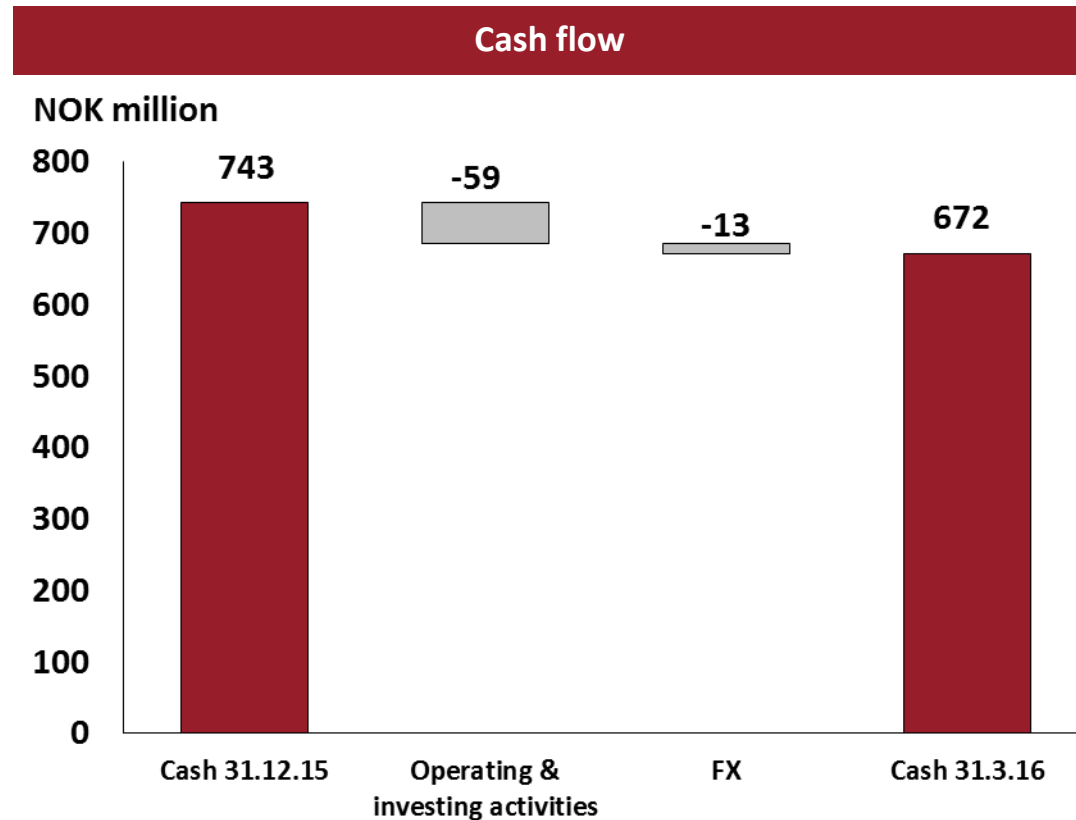
# Collaboration with Paul Scherrer Institut designed to develop new ARCs

- First partnership to combine Nordic Nanovector's ARC expertise with external payload expertise
- Goal to develop new ARCs optimised for treating single cell leukaemias, e.g. CLL\* & AML\*
- CLL and AML are serious orphan diseases and significant unmet medical need
  - 5-year survival rate: AML – 26%; CLL – 82%
  - Affects >50,000 patients per year worldwide
  - Growing market estimated at over USD 4 billion per year.
- Supported by grant funding from the Research Council of Norway



\* CLL: chronic lymphocytic leukaemia, AML: acute myeloid leukaemia

# Solid cash position, expected to be sufficient to reach first regulatory submission for Betalutin in 3L FL in 1H 2019

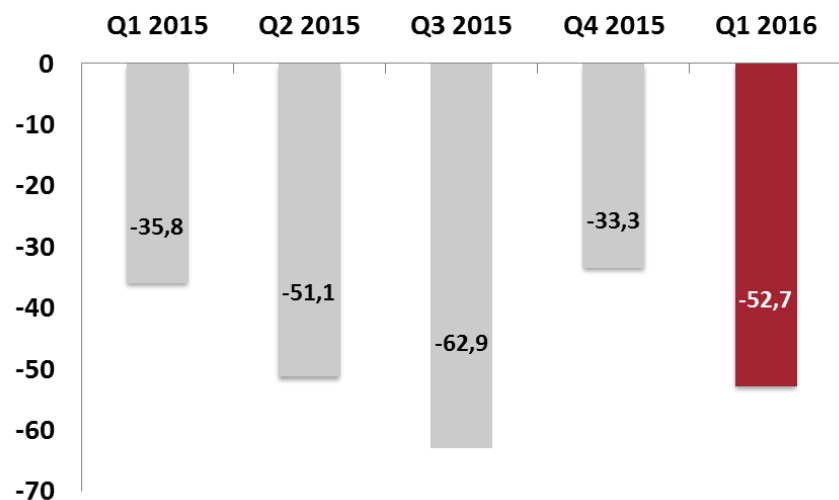


- Cash flow main drivers:
  - Increased development activity
  - Foreign exchange fluctuation

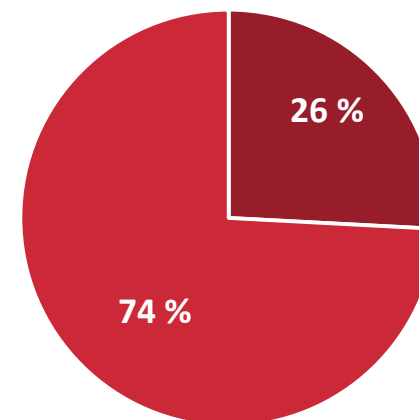
# Operating loss reflecting increase in development activities

Operating loss

NOK million



Operating expenses distribution



■ Administration ■ Development\*

\*Development costs: preclinical, clinical, regulatory and CMC activities

- Higher clinical study activities for Betalutin®
- R&D activities related to new product candidates in the discovery and preclinical phase

# Key milestones through 2017

• Initiate DLBCL clinical programme	✓
• Initiate Arm 3 in Phase 1/2 FL study	✓
• Initiate Arm 4 in Phase 1/2 FL study	✓
• First patient treated in Arm 3 in Phase 1/2 FL study	✓
• First patient treated in Arm 4 in Phase 1/2 FL study	✓
• First patient treated in DLBCL study	2H 2016
• Dose-escalation in Arm 1, 3, 4 of Phase 1/2 FL study	2H 2016
• Dose-regimen selection for PARADIGME based on data from Arm 1, 3 and 4	1Q 2017
• First patient treated in PARADIGME study	2H 2017

# Summary & outlook

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- Strong operational progress on all priorities
- Updated results from the ongoing Phase 1/2 study with Betalutin® continue to support strong profile
- Clinical development plan in FL advancing as planned
- Advancing with DLBCL clinical development plan following opening of IND
- R&D plans to develop ARC pipeline moving forward with PSI collaboration
- Continued management focus on efficient execution of development plans to meet anticipated clinical milestones
- Current cash resources expected to reach first regulatory submission for Betalutin® in 3L FL in 1H 2019

**Capital Markets Day 2016**  
**Tuesday, 31 May**  
**Registration from 8 am**  
**Hotel Continental, Oslo**



**Thank you for your attention!**

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# Glossary of terms

**1L, 2L, 3L:** first, second and third line of treatment

**ARC:** Antibody-Radionuclide-Conjugate

**(A)SCT:** (Autologous) stem cell transplant

**ASH:** American Society of Hematology Annual Meeting

**B-cell:** A type of lymphocyte (white blood cell) in the humoral immunity of the body's adaptive immune system. Can be distinguished from other lymphocytes by the presence of a protein on the B-cell's outer surface known as a B cell receptor (BCR). This specialised receptor protein allows a B-cell to bind to a specific antigen.

**CD20:** B-lymphocyte antigen CD20 is an activated-glycosylated phosphoprotein expressed in the surface of all B-cells beginning at the pro-B phase and progressively increasing in concentration until maturity

**CD37:** B-lymphocyte antigen CD-37 is a protein, a member of the transmembrane 4 superfamily, also known as the tetraspanin superfamily of cell surface antigens

**CR:** Complete response

**DLBCL:** Diffuse Large B-Cell Lymphoma

**FL:** Follicular Lymphoma

**FDA:** Food and Drug Administration

**HH1:** Betalutin® consists of the radionuclide lutetium-177 which is joined to the B-cell seeking antibody HH1. The HH1 antibody in Betalutin® binds to the CD37 antigen B-cells (NHL cells).

**IFRS:** International Financial Reporting Standard

**IND:** Investigational New Drug

**IPO:** Initial Public Offering

**KOL:** Key opinion leader

**LCM:** Lifecycle management

**Lu-177:** Radionuclide lutetium-177

**MBq:** Megabecquerel (radioactivity measurement unit)

**M.D:** Medical doctor

# Glossary of terms

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**nASCT:** Not eligible for autologous stem cell transplant

**NHL:** Non-Hodgkin Lymphoma

**OSE:** Oslo Stock Exchange

**ORR:** Overall response rate (the CR and PR, jointly)

**PARADIGME:** Name of Nordic Nanovector's pivotal Phase 2 study

**PFS:** Progression free survival

**PR:** Partial response

**QoL:** Quality of life

**R:** Rituximab

**RIT:** Radioimmunotherapy

**SAB:** Scientific Advisory Board

**SD:** Stable disease

**T-cell:** A type of lymphocyte (white blood cell) that plays a central role in cell-mediated immunity. Can be distinguished from other lymphocytes by the presence of a T-cell receptor (TCR) on the cell surface. They are called T-cells because they mature in the thymus.