
onco
invent

Results of the 2nd Quarter 2019

Jan A. Alfheim
CEO

Agenda

1. Welcome to 2nd quarter 2019 presentation
2. Status Radspherin development
3. Plans for the clinical development of Radspherin
4. Financials
5. Q&A

Status Radspherin® development

Radspherin®

alpha-emitting microparticles for local applications

SPECIALLY DESIGNED $CaCO_3$ microparticles

- Carriers for the alpha-emitting isotope
- Degradable and non-toxic
- Good regional retention, low systemic exposure

A NEW alpha-emitting radioisotope Ra-224

- High energetic radiation for efficient tumor cell kill
- Local deposition of radiation
- Therapeutic relevant temporal and spatial window
- Low probability of unintended radiation damage

Product concept

The current indication under development is for treatment of peritoneal carcinomatosis (PC) originating from epithelial ovarian cancer (including fallopian tube cancer), colorectal cancer or other malignancies where PC (including primary PC) is present. It is intended to be used after surgical resection with removal of all macroscopic visible tumours.

Summary of Q2 (& Q3 to date) experimentation:

Radspherin® optimization

- ✓ Four new formulations of Radspherin® have been developed and tested
- ✓ All give an increased survival at the same level as previous discovery formulations
- ✓ All give a clear improved survival compared to the first intended clinical formulation of Radspherin®
- ✓ All give a good control of the size of the microparticles

One formulation has been selected, the development of a GMP production process is ongoing

Background for the Radspherin® optimization

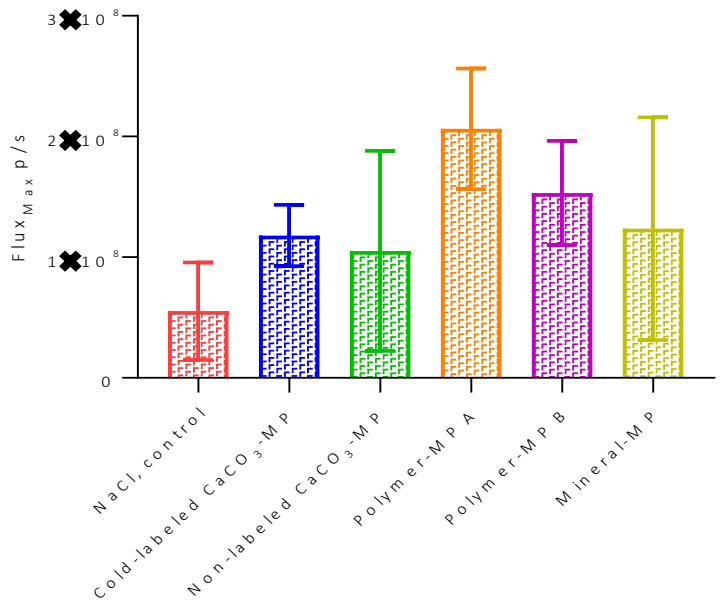
- The first intended clinical formulation of Radspherin® developed during the autumn 2018 showed good product stability and good biodistribution in animal models
- A confirmation therapy study with this formulation showed inferior survival data in a mouse tumor model in the beginning of 2019 compared to all previous Radspherin® test products
- Due to this, clinical start-up was put on hold, and a program for further optimization of the Radspherin® formulation was initiated

Effect of particles on tumor growth in Radspherin® preclinical models

- All types of non-radioactive microparticles tested initiated an increased tumor cell growth in the immunocompetent animal tumor models.
  - This is most likely due to a foreign body reaction (FBR) in combination with the cancer cells in the tumor model

- Test results indicate that Radium-224 is a well suited effector to arrest tumor growth regardless of FBR or not in these models

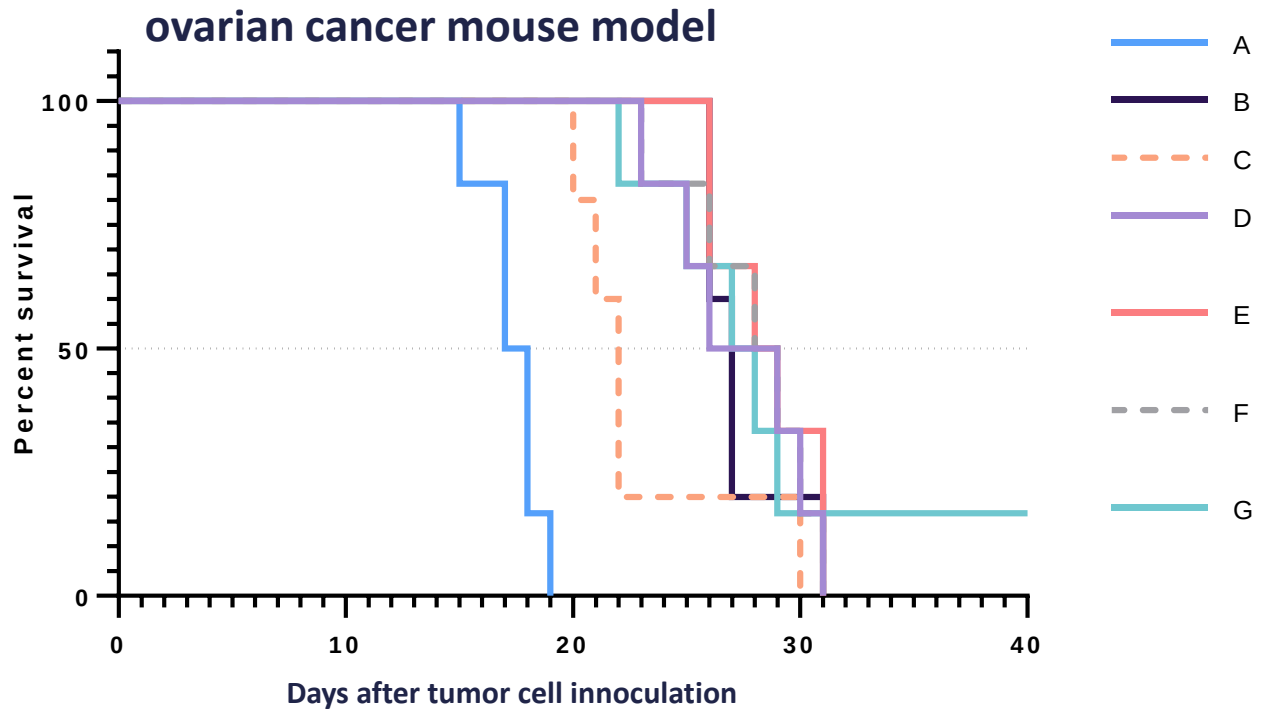
Tumor hyperproliferation initiated by IP injection of all types of microparticles tested



- Injection of different types of microparticles on day 1 after cell inoculation
  - Calcium carbonates
  - Polymers (degradable and non-degradable)
  - Other minerals than calcium carbonate
- The median size of the different microparticles tested range from 3-21 µm
- Tumor cells measured with bioluminescence on day 14 after inoculation

The observed hyperproliferation in this preclinical model lead to the determination that the intended clinical formulation of Radspherin was inferior to earlier formulations of the product

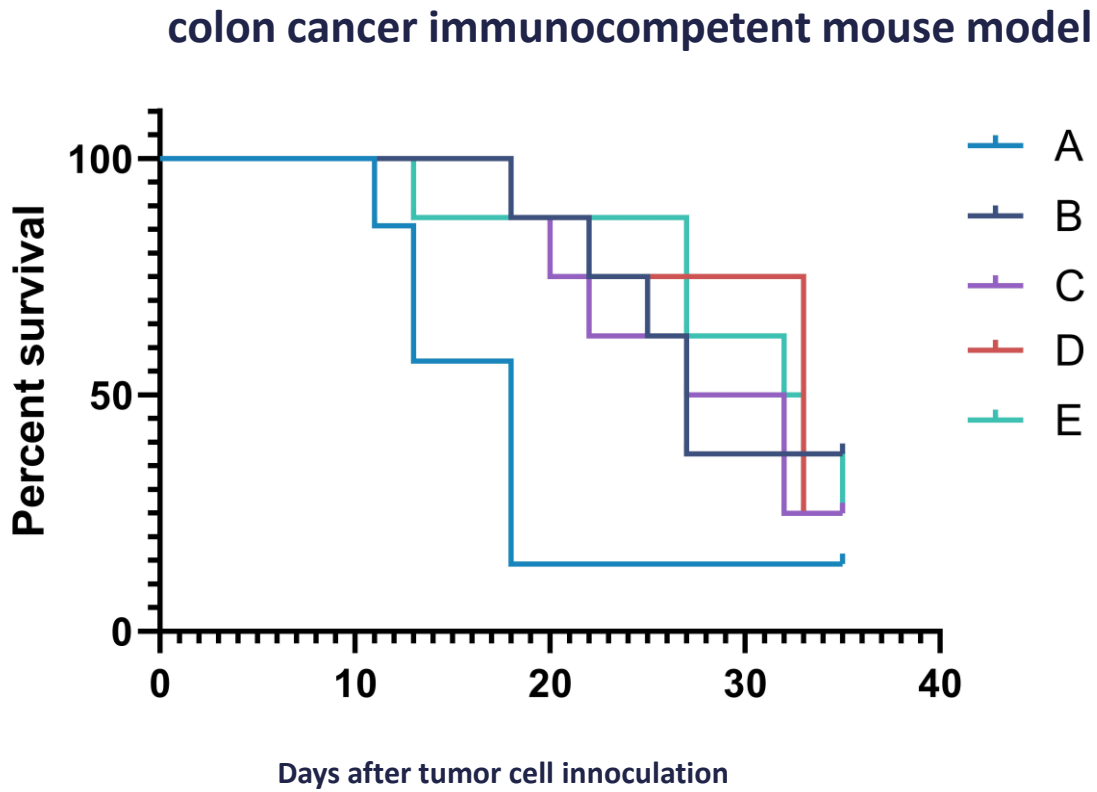
Survival in two different tumor models – ovarian cancer model



group	Immunodeficient mouse model with human ovarian cancer	Median Survival	Therapeutic Index
A	NaCl, control group	17,5	1,00
B	Radspherin, previous discovery formulation	27,0	1,54
C	Radspherin, previous clinical formulation	22,0	1,26
D	Radspherin, new formulation 1	27,0	1,54
E	Radspherin, new formulation 2	28,5	1,63
F	Radspherin, new formulation 3	28,5	1,63
G	Radspherin new formulation 4	27,5	1,57

The results indicate that the new Radspherin formulations are superior to the previous intended clinical formulation in terms of providing increased survival

Survival in two different tumor models – colorectal cancer model



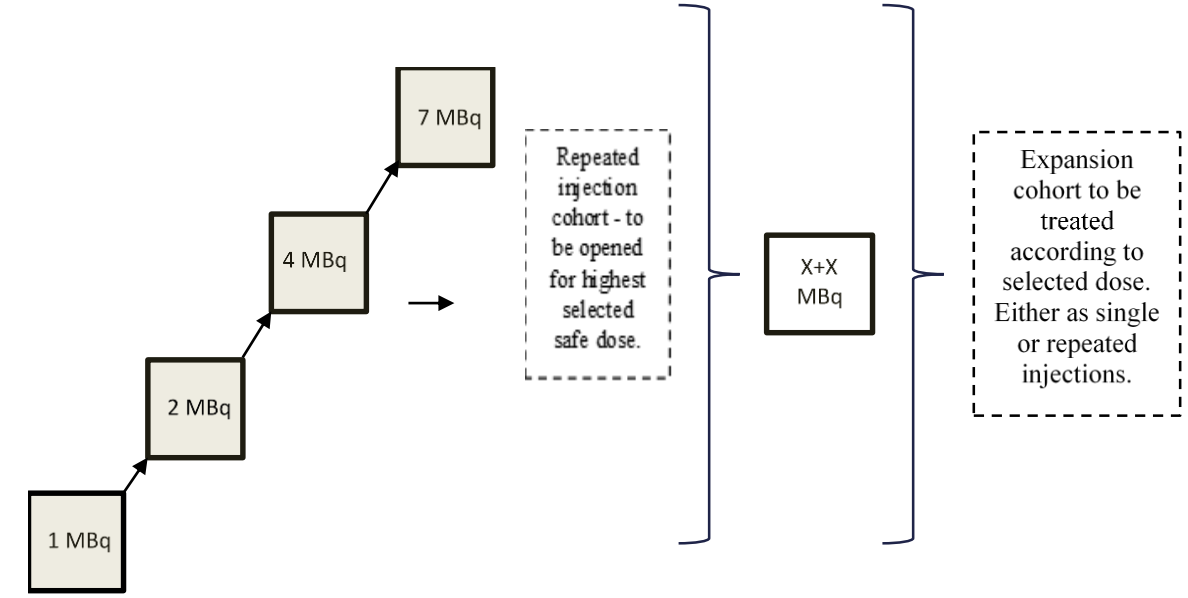
group	Immunocompetent mouse model with murine colon cancer	Median Survival	Therapeutic Index
A	NaCl, control group	18,0	1,00
B	Radspherin, previous discovery formulation	27,0	1,50
C	Radspherin, new formulation 1	29,5	1,64
D	Radspherin, new formulation 2	33,0	1,83
E	Radspherin new formulation 4	32,5	1,81

Moving to the next stage of development

- Issues related to the intended clinical formulation have been resolved
- There is now even more robust proof of principle data for the Radspherin product concept
- The company has a tighter control over important product characteristics
- The company will now concentrate efforts to generate the necessary documents to send in a new clinical trial application in Q4

Clinical development of Radspherin

First-In-Man dose escalation study – revised design with improved time and cost efficiencies



** DLT- Dose Limiting Toxicity*

Base case scenario:
- 1 MBq: No DLT- 3 patients
- 2 MBq: No DLT- 3 patients
- 4 MBq: 1 DLT- 3+3 patients
- 7 MBq: 1 DLT- 3+3 patients

Total escalation phase: 18 patients

Total # subjects base case: 18+3+6= 27 patients
Best case: 12+3+6=21 patients
«Worst» case: 4x3x2+3+6= 33 patients

The clinical trial design has been revised to eliminate unnecessary cohorts of patients

Additional clinical sites

The company has decided to open two clinical sites in addition to the sites in Leuven Belgium and the Radium Hospital in Oslo in order to ensure rapid patient recruitment to the trials

- Current sites in Norway and Belgium are prepared to initiate study as soon as regulatory acceptance has been received
- Possible additional sites in Sweden and Germany have been identified and discussions are ongoing
- Regulatory assessment and filing are ongoing

Presentations in Q2

Ra-224 presentations

- Research Scientist Elisa Napoli held a talk entitled “Ra-224 standardization progress at NIST” at the **22nd International Conference on Radionuclide Metrology** in Salamanca Spain in May.

- Ms. Napoli also presented a poster entitled; “A primary activity standard for the alpha-emitting radionuclide Ra-224” at the **Society of Nuclear Medicine and Molecular Imaging** annual conference in Anaheim California in June.

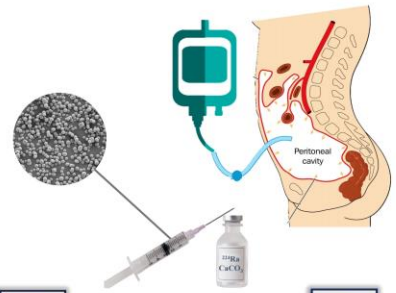
A primary activity standard for the alpha-emitting radionuclide Ra-224

Elisa Napoli[§*ǂ], Jeffrey T. Cessna[*], Ryan P. Fitzgerald[*], Leticia Pibida[*], Ronald Collé[*], Lizbeth Laureano-Pérez[*], Brian E. Zimmerman[*] and Denis E. Bergeron[*]

[§] Oncoinvent AS, Oslo, Norway; [†] University of Oslo, Oslo Norway;
[ǂ] institute of Clinical Medicine, University of Oslo;
[*] Department of Radiation Biology, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo, Norway.
[*] National Institute of Standards and Technology, Gaithersburg MD, USA.

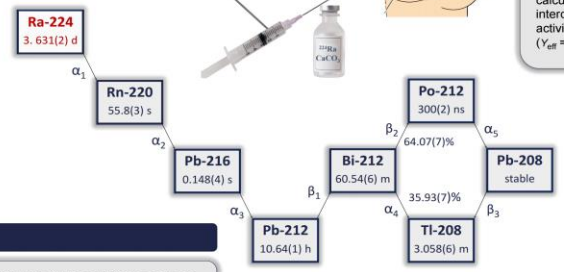
ABSTRACT

Alpha-emitting radiotherapies can offer cancer patients highly effective treatments with minimal side effects. For cavitary micro-metastatic diseases, a new therapy consisting of a suspension of injectable microparticles labeled with ^{224}Ra is showing promise in pre-clinical studies. With a 3.631(2) d half-life and a decay scheme that includes the emission of four energetic alpha particles, ^{224}Ra can deliver a high dose of therapeutic radiation to the metastasis, resulting in double-strand DNA breaks with minimal toxicity to surrounding healthy tissues. Prior to commencing clinical trials, it is essential to develop a radioactivity standard for ^{224}Ra to assure consistent dosage administration.



Daughter nuclide	Beta-Gamma transitions					
	A	P_{br}	B	P_{br}	C	weight
^{212}Pb	$\beta_{0,3}\gamma_{3,1}\gamma_{1,0}$	0.0499	$\beta_{0,2}\gamma_{2,0}$	0.817	$\beta_{0,0}$	0.1331
^{208}Tl	$\beta_{0,2}\gamma_{2,1}\gamma_{1,0}$	0.492	$\beta_{0,3}\gamma_{3,1}\gamma_{1,0}$	0.221	$\beta_{0,4}\gamma_{4,2}\gamma_{2,1}$	0.287

Tab.1 Simplified decay scheme for the beta-emitting daughters of ^{224}Ra used in MICELLE2 efficiency calculations. Branch probabilities (P_{br}) are renormalized such that "missing" decays are assigned to energetically similar cascades.



METHODS

The primary activity standardization was performed at NIST, with two liquid scintillation-counting based methods: live-timed $4\pi\alpha\beta$(LS)-γ(NaI) anticoincidence counting (LTAC) and triple-to-double coincidence ratio (TDCR) counting. Monte Carlo simulations were used to model instrument responses, assuring appropriate corrections and establishing theoretical links between methods.

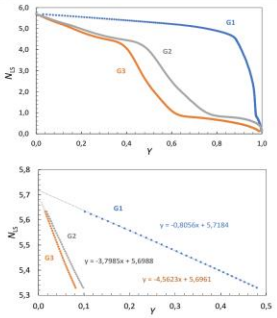


Fig. 1 LS channel count rates as a function of inefficiency, Y. The blue, orange, and gray data correspond to data acquired with G1, G2, and G3, respectively. Efficiency variation is achieved by increasing the lower-level discriminator threshold for the LS channel. (Top) LS channel count rate as a function of inefficiency, Y. (Bottom) Extrapolations over linear regions give convergent intercepts at $Y=0$.

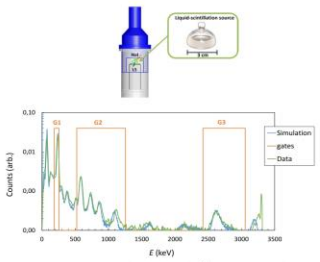


Fig.2 NaI(Tl) spectrum obtained with a ^{224}Ra source at secular equilibrium. The green trace is experimental data acquired in the γ-ray channel of the LTAC. The blue trace is from a Monte Carlo simulation. The anticoincidence gate settings are shown in orange.

RESULTS

Activity determinations using the TDCR method, were achieved by varying the efficiency with gray filters, achieving a triple-to-double coincidence ratio (K) range of (0.986 to 0.992) and corresponding to doubles counting efficiency (ε_D) range of (5.05 to 5.66) counts per ^{224}Ra decay, according to the MICELLE2 model. As expected for such a high-efficiency radionuclide, no trending with efficiency is seen in the calculated activities.
In LTAC experiments, all coincidence gates were set to monitor the LS counting efficiency for the different types of decay in the scheme All gates sampled yield also the LTAC data, with inefficiency extrapolations giving nearly convergent intercepts (Fig.1). Applying correction factors calculated from the Monte Carlo simulations, the accordance between intercepts obtained with different gates improved. For the final LTAC activity, an effective inefficiency:
($Y_{eff} = 0.29 * Y_1 + 0.67 * Y_2 + 0.04 * Y_3$) was used.

	EXP2		EXP3		EXP4	
	A / A_{TDCR}	u	A / A_{TDCR}	u	A / A_{TDCR}	u
TDCR	1	0.0019	1	0.0044	1	0.0024
LTAC	1.0023	0.0030	0.9998	0.0033	-	-
AutoIC	0.9983	0.0001	0.9981	0.0003	1.0002	0.0002
HPGe	0.9614	0.0222	0.9460	0.0141	-	-

Tab.2 Comparison of methods and experiments. Within each experiment (E2, E3, and E4), results are normalized to TDCR. For AutoIC, the given uncertainty (u) is the counting uncertainty only; all others are relative combined standard uncertainties ($k = 1$). The VIC results (orange band) are normalized by the K_{VIC} determined in E2 to provide and experiment-to-experiment comparison.

CAPINTEC IONIZATION CHAMBER		CRC-15R	CRC-55tR	CRC-35R	CRC-25PET	CRC-55tPET
5 mL ampoule		739(4)	736(4)	747(9)	739(5)	731(4)
20 mL $^{224}RaCl_2$ in 20 mL vial		737(4)	735(4)	-	741(5)	-
2 mL $^{224}RaCl_2$ in 20 mL vial		744(4)	740(4)	-	747(5)	-
12 mL $^{224}RaCl_2$ in 20 mL syringe		753(5)	752(4)	762(9)	755(5)	747(4)
12 mL suspension of ^{224}Ra labeled $CaCO_3$ mp in 20 mL syringe		745(4)	745(4)	754(9)	747(6)	741(5)

Tab.3 Preliminary data dial settings determined by the calibration curve method to give the correct activity for 5 mL of a 1 mol/L HCl solution of ^{224}Ra in equilibrium with its daughters in a NIST standard 5 mL flame sealed ampoule and several other geometries. Uncertainties on the dial settings are given in parentheses and are expanded ($k = 2$) uncertainties.

CONCLUSIONS

The activities determined by multiple methods and across multiple experiments were consistent within uncertainties. The primary activity standard carries a combined standard uncertainty of 0.30 %.

napoli@oncoinvent.com

The Research Council of Norway
UiO : University of Oslo
SNMMI SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING
JUNE 22–25 Anaheim, CA

Financials

Financial figures per 30.06.2019

KEY FIGURES	2nd QUARTER		YTD		FULL YEAR
AMOUNTS IN NOK	2019	2018	2019	2018	2018
TOTAL REVENUES AND OTHER INCOME	**339 000**	**2 369 061**	**1 569 730**	**2 836 774**	**10 458 850**
Payroll and related expenses	4 127 643	2 637 726	10 696 955	6 185 026	15 617 140
Other operating expenses	6 957 983	5 419 130	13 640 856	11 936 922	29 579 761
TOTAL OPERATING EXPENSES	**11 085 626**	**8 056 856**	**24 337 811**	**18 121 948**	**45 196 901**
Finance cost and other income	11 030	5 969	- 21 626	9 759	1 686 127
NET OPERATING PROFIT(LOSS) FOR THE PERIOD	**- 10 735 596**	**- 5 681 826**	**- 22 789 707**	**- 15 275 415**	**- 33 051 924**
Net Proceeds from equity issue	125 000	25 000	125 000	25 000	25 000
Cash and cash equivalents, end of period	135 080 934	170 889 980	135 080 934	170 889 980	153 553 317
Total number of shares, beginning of period	13 187 181	13 184 681	13 187 181	13 184 681	13 184 681
Total number of shares, end of period	13 190 411	13 187 181	13 190 411	13 187 181	13 187 181

- Delay in start of clinical trial is expected to have minor financial implications
- Operating expenses MNOK 5.5 below planned


onco
invent