Advanced Accelerator Applications
A Novartis Company

Novel nuclear medicine to advance patient care

Addressing Societal Challenges Through Advancing the Medical, Industrial and Research Applications of Nuclear and Radiation Technology

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Advanced Accelerator Applications: Leveraging innovation to address societal challenges of modern molecular nuclear medicine for 16 years

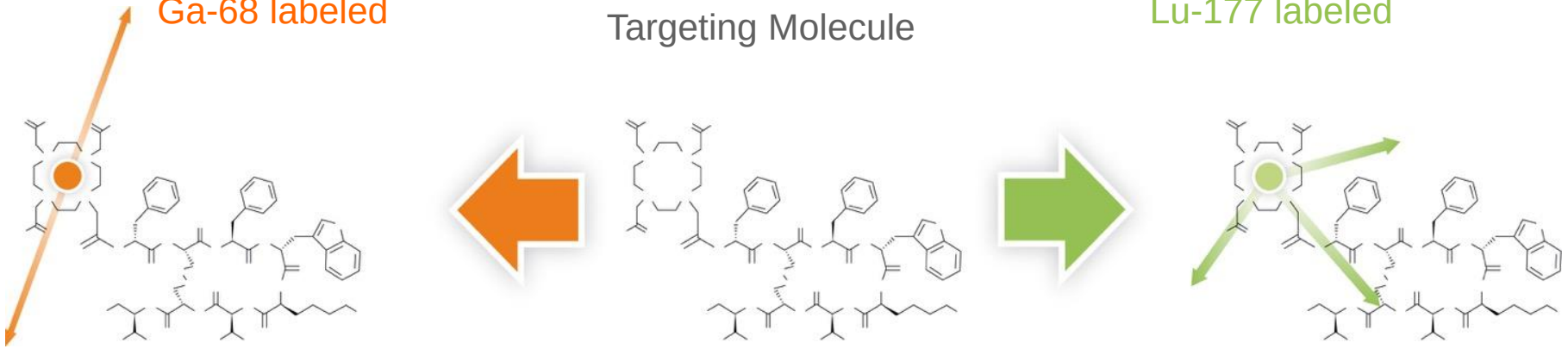
- A radiopharmaceutical company founded by Stefano Buono in France in 2002
  - Registered 8 diagnostic drugs and one therapeutic drug
  - Registered first ever radiopharmaceutical **theragnostic pairing** for oncology based on radiolabeling of a single targeting molecule with different radioisotopes for diagnosis (**Ga-68**) and therapy (**Lu-177**)
  - Established or acquired state-of-the-art **manufacturing** in **20 locations** across **8 countries** in Europe, the US, and Israel
  - Grew to over **630 employees** in **13 countries** (Belgium, Canada, France, Germany, Italy, Israel, The Netherlands, Poland, Portugal, Switzerland, Spain, UK & USA).
  - Completed **13 acquisitions** and analyzed over **200 Business Development opportunities** in the field of Nuclear Medicine
  - Reached €150m in sales prior to the launch of its first therapeutic
  - **Listed on NASDAQ** in November 2015; price appreciation of over 300% prior to acquisition by **Novartis** in 2018 for a total value of **€3.9b**

The theragnostic opportunity: a unique asset of molecular nuclear medicine

Ga-68 labeled

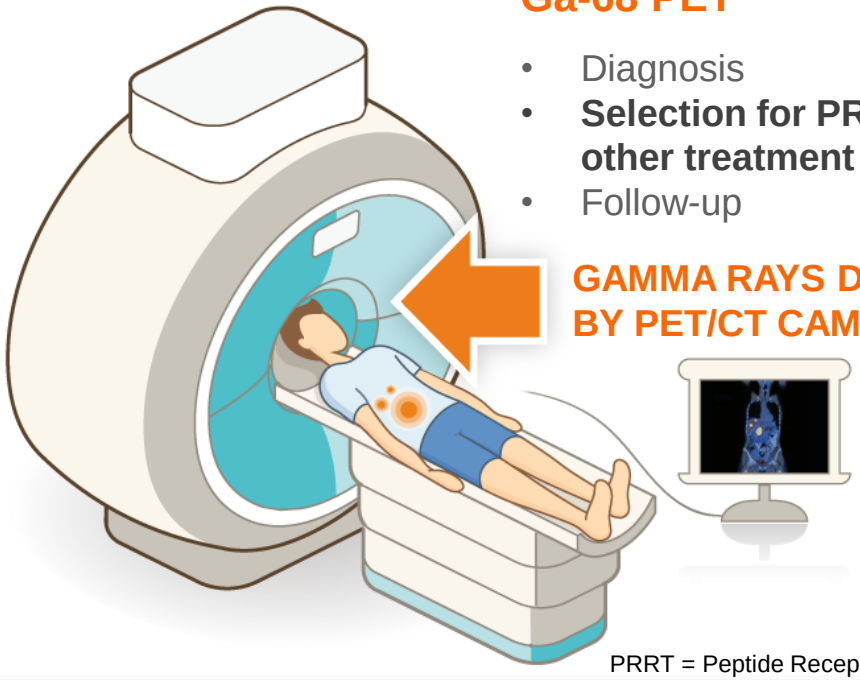
Same
Targeting Molecule

Lu-177 labeled



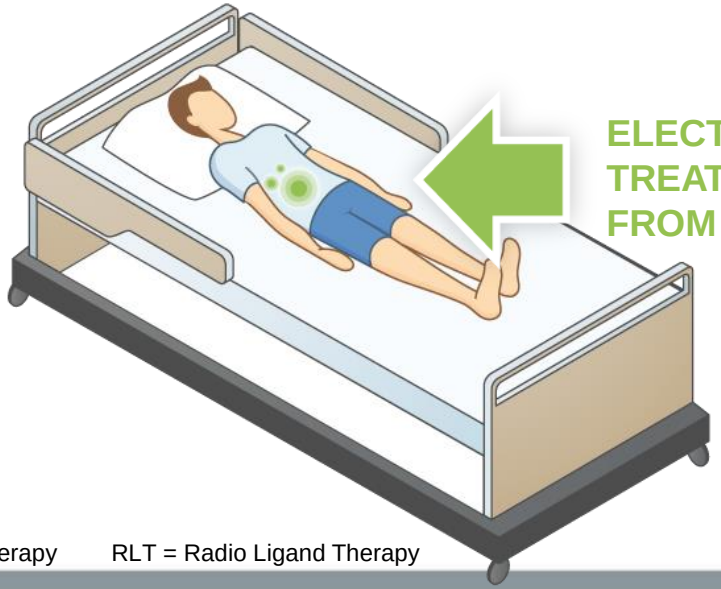
Ga-68 PET

- Diagnosis
- **Selection for PRRT / RLT or other treatment**
- Follow-up



GAMMA RAYS DETECTED BY PET/CT CAMERA

Lu-177 PRRT / RLT



ELECTRONS TREAT TUMORS FROM WITHIN

PRRT = Peptide Receptor Radionuclide Therapy RLT = Radio Ligand Therapy

Impact of Theragnostics

Patients

- More effective care through personalized interventions
- Reduce or eliminate unnecessary treatment

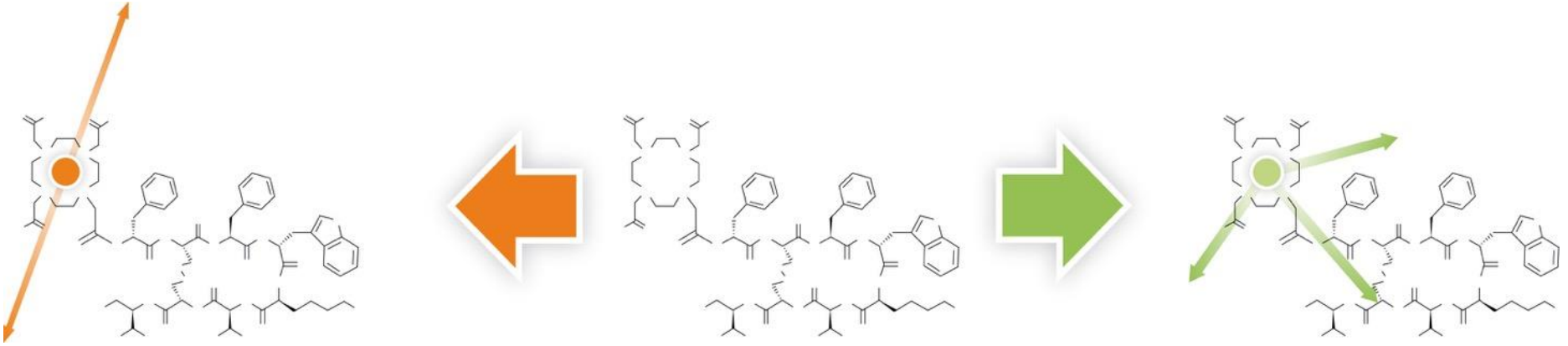
Physicians

- Better diagnose and stage disease
- Select optimal therapies
- Monitor treatment response and disease progression

Payors

- Reduce costs from unnecessary treatments
- Improve patient management & outcomes

A practical example in the field of Neuro Endocrine Tumors (NET)



Ga-68 labeled
First-in-class **Diagnostic**
4 hour shelf-life

dotatate

Lu-177 labeled
First-in-class **Therapy**
3 day shelf-life

NETSPOT®

- 71% of patients had impact on disease management in clinical study
- One avoided surgery pays for 3 years of drug in one US hospital

LUTATHERA®

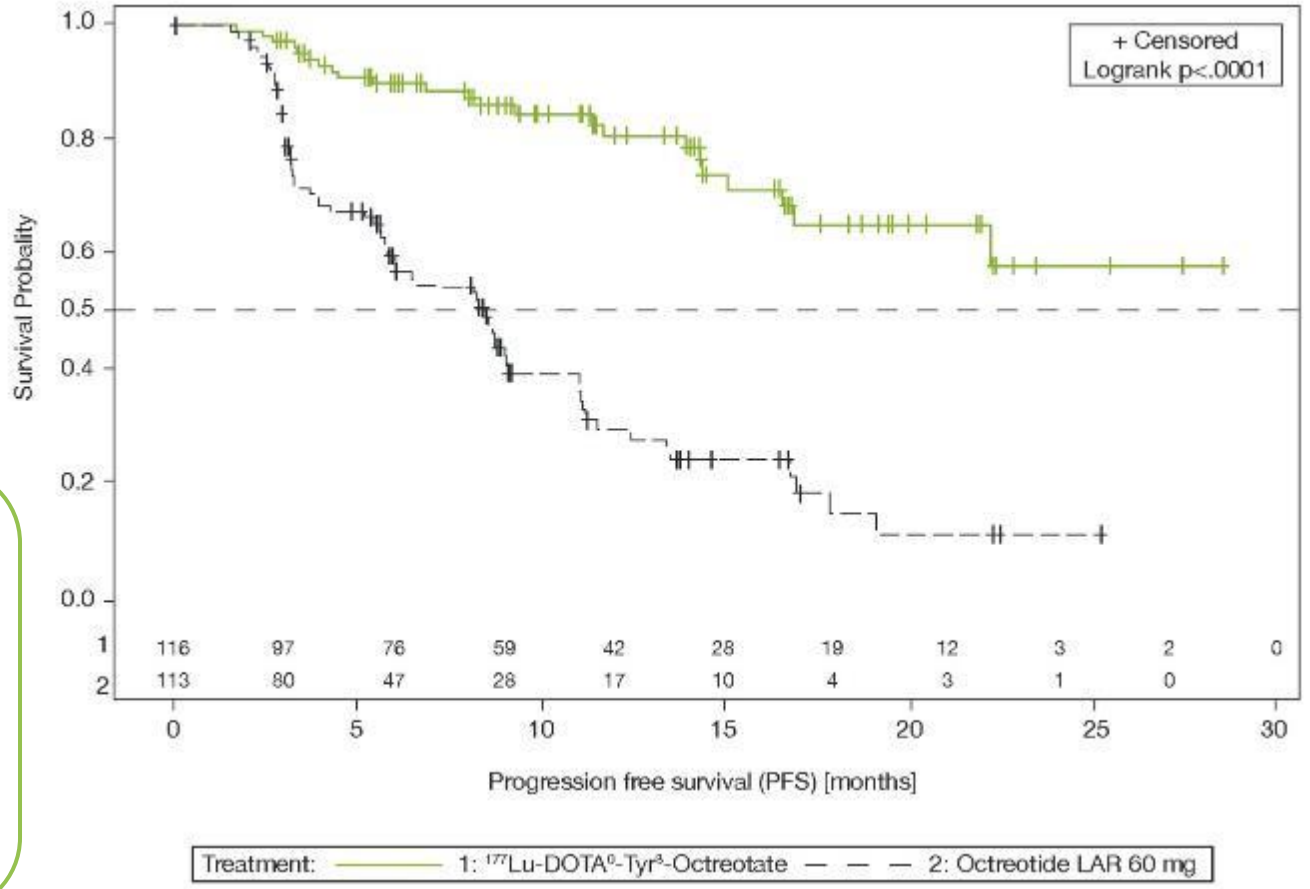
- 79% reduction in the risk of disease progression/death based on clinical study
- Improved quality of life and favorable safety profile

NETTER-1 Final Analysis: Progression-Free Survival Published in *The New England Journal of Medicine*

N = 229 (ITT)
Number of events: 91
LUTATHERA® arm : 23
Oct 60 mg LAR: 68

Hazard ratio: **0.21**
[0.13 – 0.33]
p < 0.001

79% reduction in the risk o
disease progression/death



All progressions centrally confirmed and independently reviewed for eligibility (SAP)

Strosberg J, et al. N Engl J Med. 2017;376:125-35

* USAN lutetium Lu 177 dotatate / INN: lutetium (^{177}Lu) oxodotreotide

Theragnostics represent the next evolution in medicine after Immuno-Oncology

- The academic world is experiencing similar outstanding results with other drug candidates (e.g. targeting PSMA on prostate cancer) and many companies are investing in the field.
- Three major challenges for industry to overcome:
  1. Outpatient administration of therapeutics
  2. Reimbursement of diagnostic drugs
  3. Regulation of institutional “home-brew” drug formulations after commercial registration.
- Industry needs the support of regulators!

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Thanks for your attention