

Orano Med

Fight cancer using ^{212}Pb

Galien Prize – Startup category

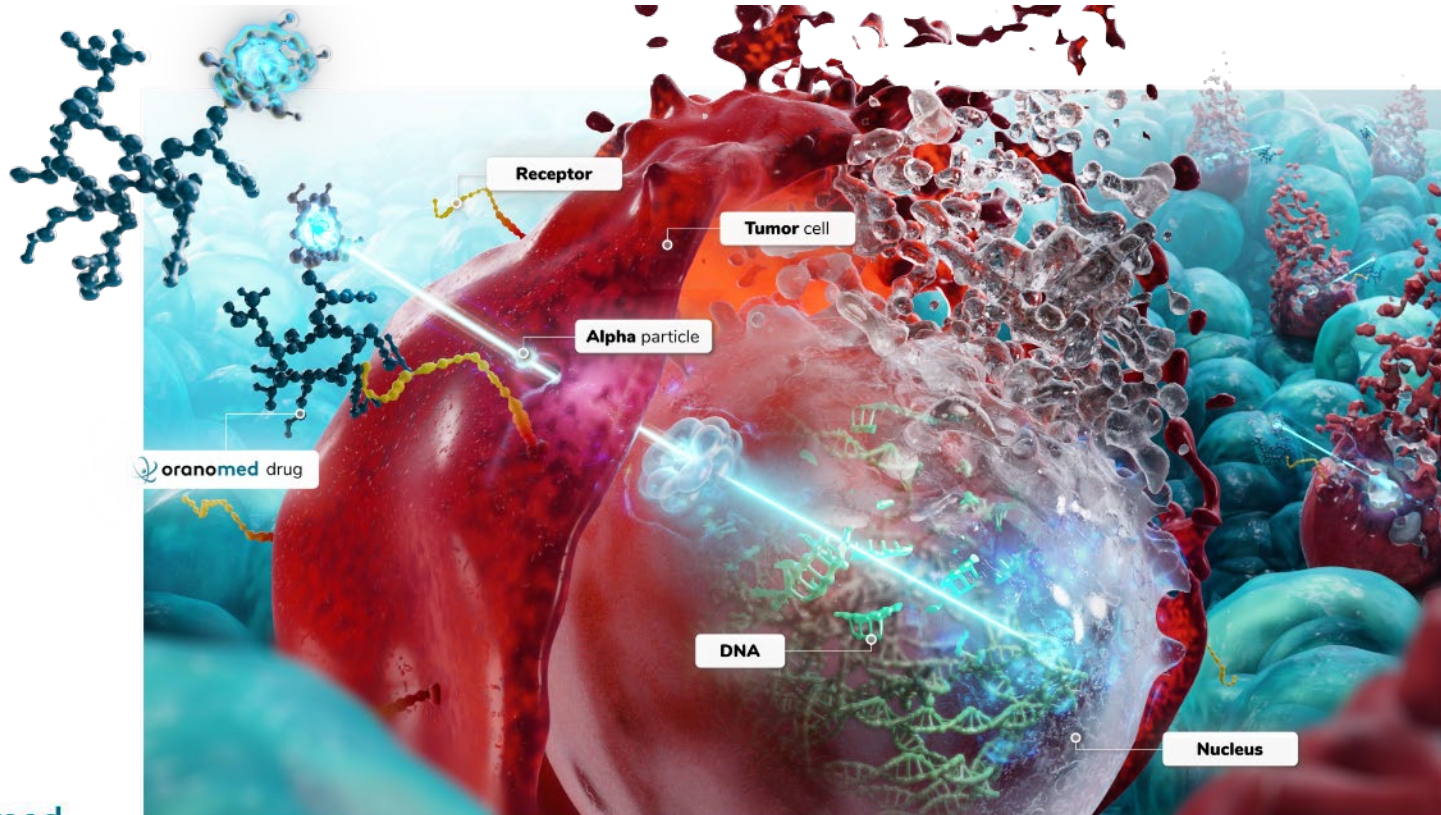




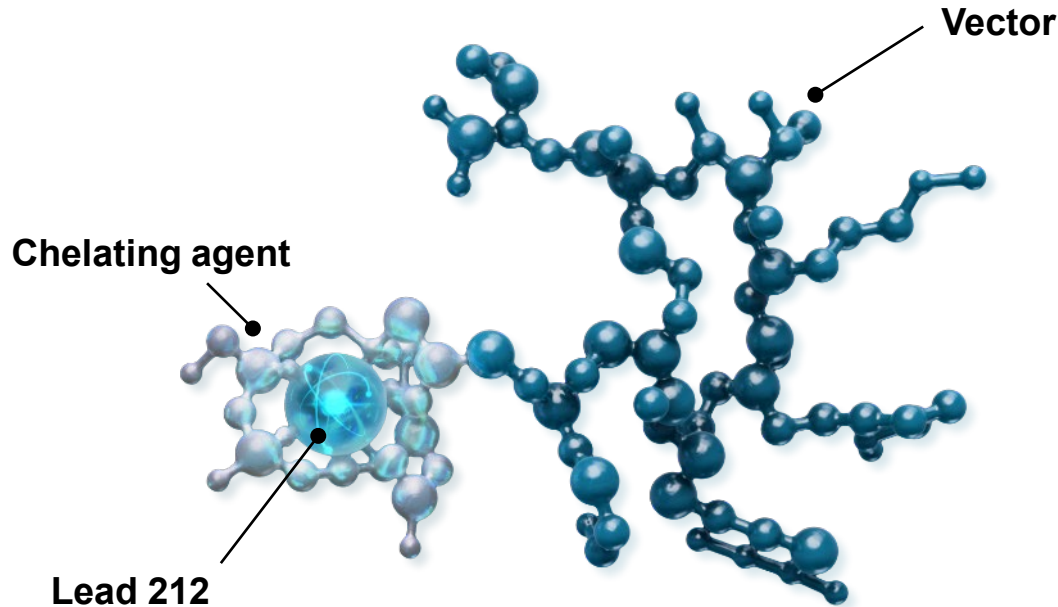
01

**Orano Med:
Fight cancer using ^{212}Pb**

Radioligand therapy using ^{212}Pb : target and destroy cancer cells



^{212}Pb : a radioactive atom with a range of applications in oncology

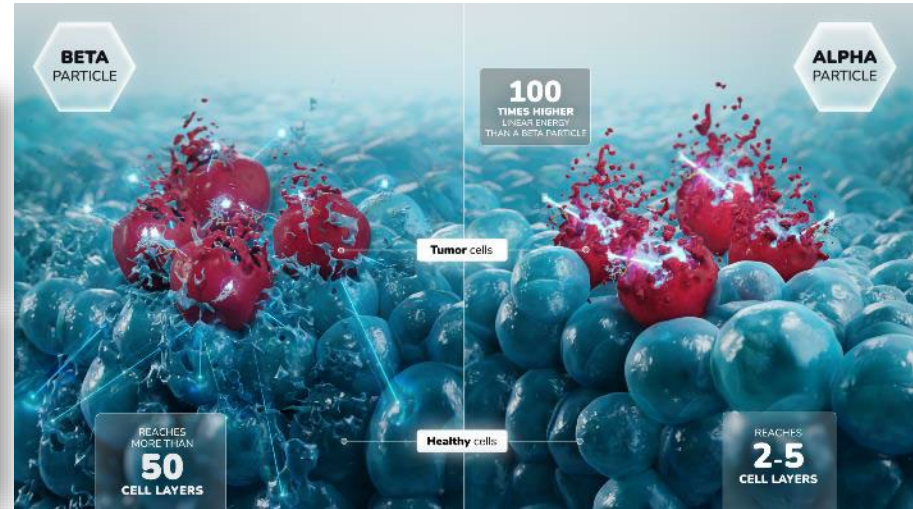


Potential for combining ^{212}Pb with a large number of biological vectors for a range of applications in oncology

Alpha emitters: strong potential in the fight against cancer

The radioligand therapies currently on the market are **beta therapies**, using **lutetium-177 (^{177}Lu)**, commercialized by Novartis (Lutathera, Pluvicto)

Alpha therapies	Beta therapies
Linear energy transfer:	
100 keV/ μm	<1 keV/ μm
20-times higher probability of inducing DNA double-strand breaks: much higher cytotoxicity	
Limited range of action:	
Limited to 2-5 cell layers	More than 50 cell layers
Reduction in the irradiation of healthy tissues	
Needed to destroy a cancer cell:	
1 to 5 alpha emissions	100 to 1,000 beta emissions
<i>Thousands of chemotherapy molecules</i>	



 Alpha therapies are more effective than the drugs currently on the market.

^{212}Pb : an element with numerous advantages compared to other alpha emitters

Ideal radioactive and chemical properties for application in radioligand therapies

1

Only one single alpha decay, **limiting toxicity** to healthy organs



Relatively short half-life (11 hours):

- **Easier waste management**
- **Outpatient** administration possible



Existence of an effective chelating agent for lead, allowing **effective targeting** of cancer cells



Theranostic approach :
Use of ^{203}Pb , a gamma emitter, to do **companion imaging** of therapies





02

**Make ^{212}Pb Targeted Alpha
Therapy a success**

Orano Med's strategy has 2 complementary goals

1

Develop a robust pipeline of ^{212}Pb -based therapies, in partnership or internally, to meet **medical needs not covered in oncology**

Objective to launch clinical trials of new drugs every year



2

Provide a reliable supply chain for these innovative drugs

Development of an **industrial platform that is unparalleled worldwide** demonstrating our capacity to guarantee **a reliable global commercial supply** of ^{212}Pb -based treatments (production and distribution facilities).

Orano Med today: a scale-up that is rapidly gathering pace



**80 employees
in France and the United States**



**2 ongoing
clinical trials**



**2 preclinical laboratories
dedicated to the development of
alpha therapies**



**12 patented
inventions**



**+30% per year:
Growth in the
radioligand therapy market**



**1 industrial platform
for the production of ²¹²Pb**

















03

Make ^{212}Pb Targeted
Alpha Therapy a success

a

Develop a robust pipeline of
 ^{212}Pb -based therapies

A pipeline of therapies targeting different types of cancers

Programme	Indication	Discovery	PoC	Pre-IND	Phase 1	Phase 2/3	Partenaire
2 ongoing clinical trials	AlphaMedix™ NETs (somatostatin receptors)	<div><div></div></div>					
	²¹² Pb-GRPR Solid tumors (breast and prostate cancer)	<div><div></div></div>					
²¹² Pb PRRT	Solid tumors (several targets)	<div><div></div></div>					 
²¹² Pb PRIT	Solid tumors	<div><div></div></div>					 
Alpha 37	Leukemia / Lymphoma overexpressing CD37	<div><div></div></div>					 
²¹² Pb TAT / Crescendo Biologics	Undisclosed target	<div><div></div></div>					 
²¹² Pb TAT / M ² OLIE	Undisclosed target	<div><div></div></div>					 
²¹² Pb PRRT	Several targets	<div><div></div></div>					 
²¹² Pb TAT	Several targets	<div><div></div></div>					Non divulgué
²¹² Pb TAT	Several targets	<div><div></div></div>					Non divulgué

AlphaMedix: a drug with promising results



Indication: **neuroendocrine tumors** expressing somatostatin receptors
The **medical community has high expectations** for the treatment of these cancers for which there are currently few drugs available.

Development in partnership with RadioMedix,
a US biotech company specialized in innovative targeted radiopharmaceuticals



Phase 1 clinical trial:
2018 - 2021

**Results: reduction of over 30%
in the size of tumors in 75%
of patients (ORR of 75%)**

Much better than the results for Lutathera,
the beta therapy currently on the market

"Refractory cohort":
ORR of 50% in patients **previously treated
with Lutathera** in whom the cancer
continued to progress



Phase 2:
2021 - 2024

**In progress in 4 clinical
sites in the USA**



Phase 3:
Launch in 2023

**More than 30 clinical sites
in the USA and in Europe**



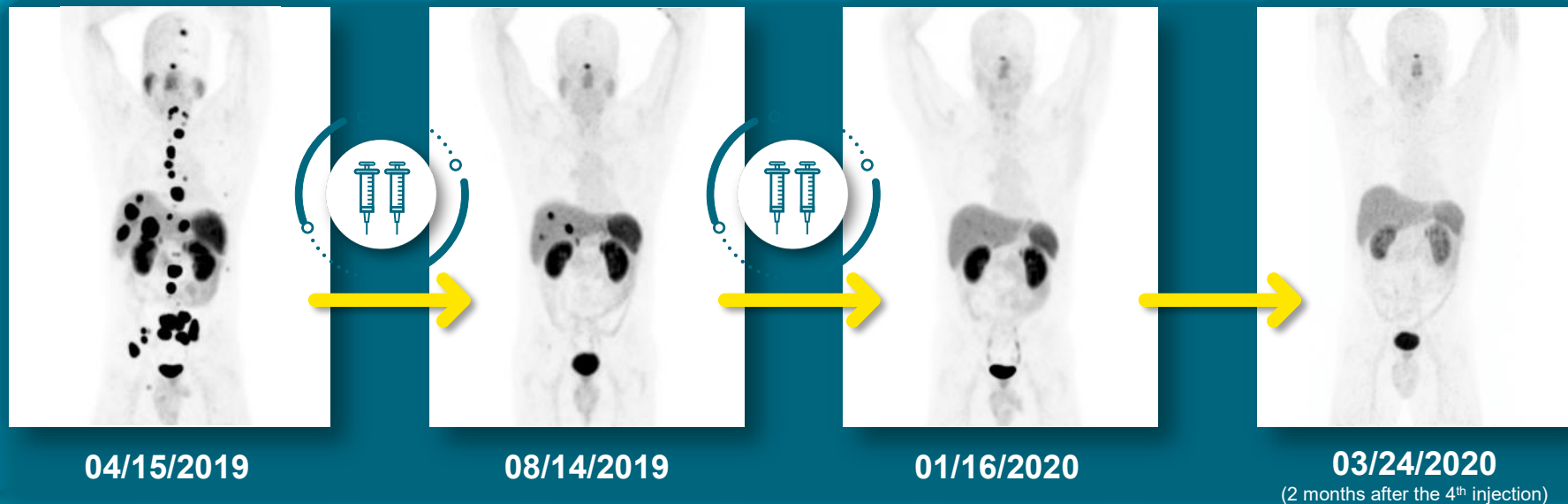
Commercialization
Planned for
2025-2026



Limited side effects

**The impact on renal function requires further monitoring,
as with all radioligand therapy treatments**

AlphaMedix: a drug with promising results



Patient with widespread metastatic neuroendocrine tumors which resolved after treatment with AlphaMedix



03

Make ^{212}Pb Targeted
Alpha Therapy a success

b

Provide a reliable supply chain
for ^{212}Pb -based therapies

A reliable process for the production of ^{212}Pb , including on a large scale



22,000 drums of ^{232}Th in interim storage at Cadarache

Purified raw material abundantly available from the Orano group's former mining activities.

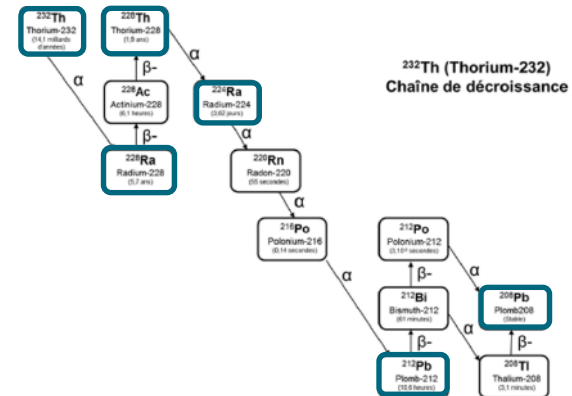


^{212}Pb is a product of the decay chain of ^{232}Th .

It is obtained chemically by several successive steps of extraction and purification.

It is then combined with the targeting molecule to form the drug and be administered to the patient by injection.

Lastly, it is transformed into ^{208}Pb , a stable element, and is eliminated by the patient.



^{212}Pb : an element with numerous advantages compared to other alpha emitters

Large-scale, reliable and independent production capacities



Reliable production
on a large scale

Other radioisotopes

Production mostly either by cyclotrons or in nuclear research reactors.

- Limited production capacities
- Difficulties covering global needs

^{212}Pb

Orano Med has developed an **entirely chemical** industrial process.

- Easy to scale up
- Less costly



An independent
production chain

Other radioisotopes

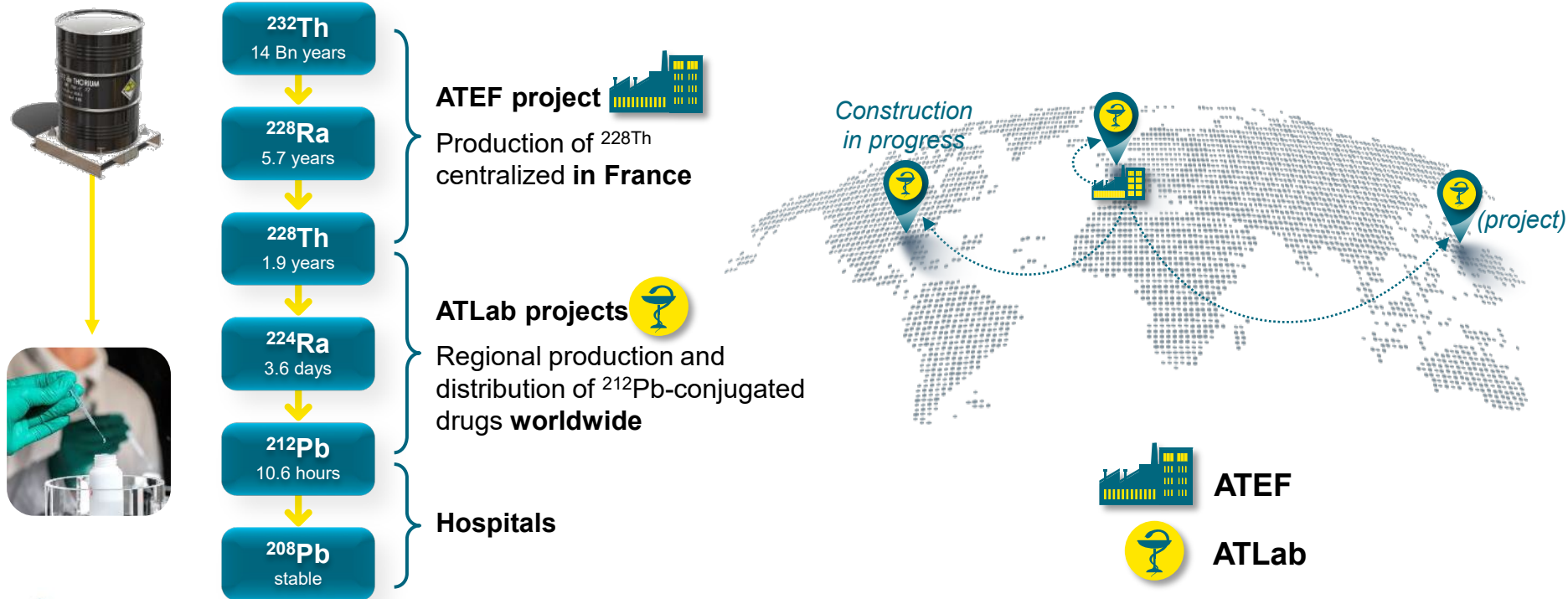
Production of numerous radiopharmaceuticals, including Lutetium 177, **heavily dependent** on precursors **produced abroad**.

^{212}Pb

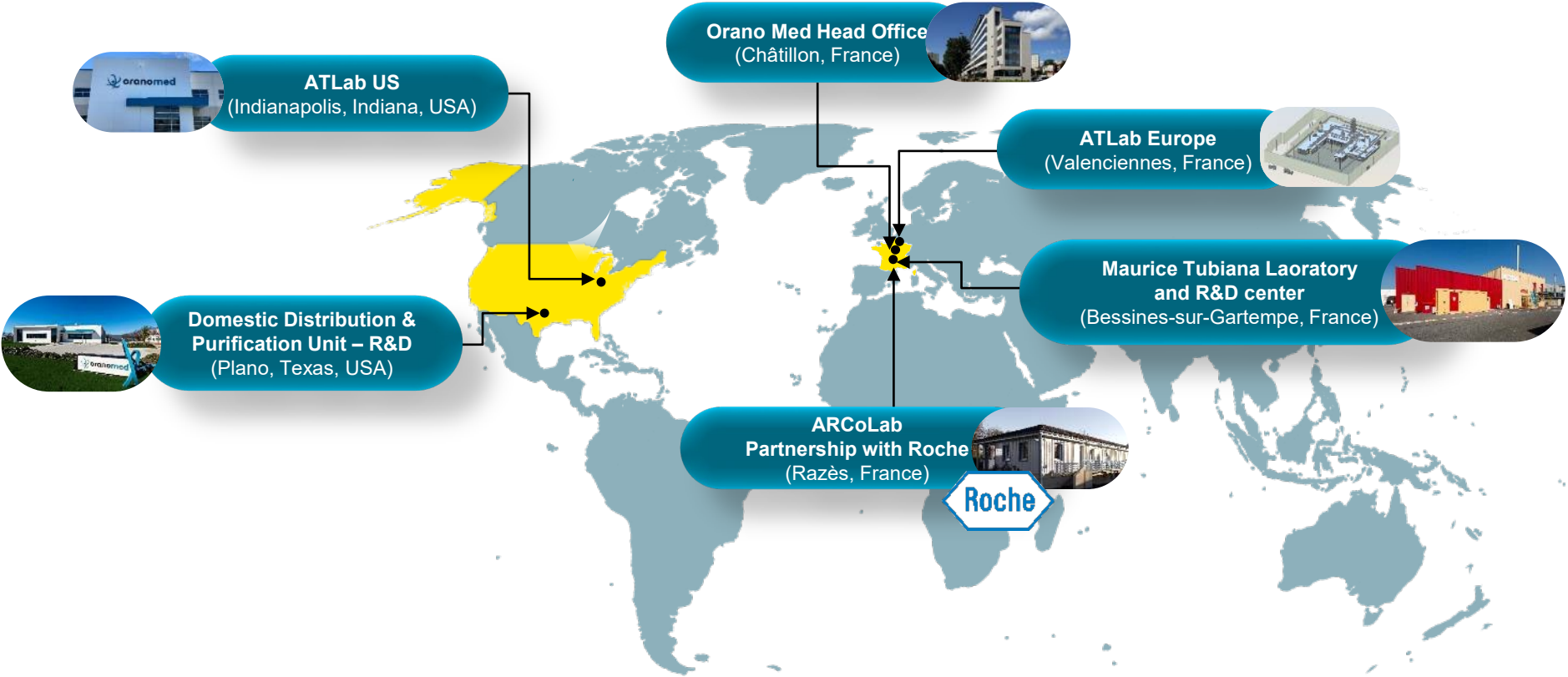
Orano Med has a substantial inventory of purified raw material (thorium 232)
Strategic autonomy for the production of drugs

Orano Med is deploying an industrial platform that is unique worldwide

In order to produce ^{212}Pb -conjugated drugs and distribute them, Orano Med is constructing industrial facilities throughout the world.



Our locations





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^{212}Pb for Targeted Alpha Therapy