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Where It's ^{211}At:

The Potential of Astatine-211 as a Therapeutic Radionuclide



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Contents

Introduction 3

Overview of Astatine-211 3

Properties 3

Astatine-211 as a Radiopharmaceutical Isotope 6

Production of Astatine-211 8

Suppliers of Astatine-211 9

Companies Investigating Astatine-211 13

Alpha Fusion 13

Atonco 13

NAYA 13

Telix 15

dGenThera 15

Trevarx 15

Asta Bio 15

Z-Alpha 15

Astatine-211 in the Clinic: Trials and Data 16

Clinical Trials 16

Clinical Data 18

Outlook 20

Introduction

As the field of targeted therapeutic radiopharmaceuticals evolves, the story no longer focuses solely on beta-emitting lutetium-177. In particular, alpha emitters have risen as intriguing radionuclides given their ability to emit more powerful radiation and induce double-stranded DNA breaks. Just a few years ago, actinium-225 was trendy, but lead-212 has since emerged as a competitive player in the alpha emitter race. More recently, we have also heard increased dialogue about astatine-211. Although centralized production and the need for covalent chemistry are frequently cited as hurdles in using this isotope for radiopharmaceuticals, the physical properties of the isotope (which are somewhat analogous to lead-212) have inspired investigation of astatine-211 from both clinical and manufacturing perspectives. Therefore, for this edition of our radiopharmaceuticals periodical, we aim to provide investors with an outline of astatine-211, including an overview of the isotope, of production methods/supply chain, of companies with programs that center on astatine-211, and of clinical trial evaluating the radionuclide's therapeutic potential.

For a broader overview of the radiopharmaceuticals industry as a whole, please refer to our recent update report: Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Fifth Edition. For additional background information, we point readers to our reports from earlier years:

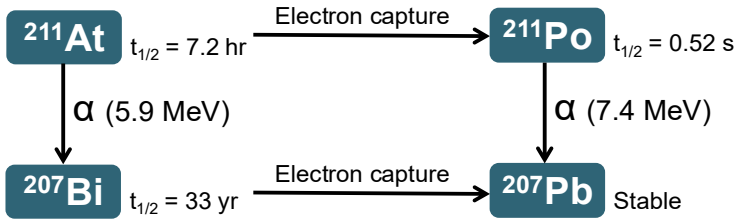
- 2022: historical background on the field and fundamental nuclear chemistry concepts (Bioluminescence—Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals)
- 2023: supply chain deep dive (Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Second Edition)
- 2024: industry update (Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Third Edition)
- Early 2026: role in Alzheimer's disease imaging and diagnosis (Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Fourth Edition)

Overview of Astatine-211

Properties

Astatine-211 is an alpha-emitting radioisotope with a half-life of about 7.2 hours. There are two pathways available to yield the stable lead-207 daughter isotope (exhibit 1). One pathway, which occurs with 58% probability, is electron capture to yield polonium-211, which then rapidly decays (in roughly half a second) through alpha emission to lead-207 with an energy of 7.5 MeV. The other pathway, which occurs about 42% of the time, involves alpha emission to bismuth-207 with an energy of 5.9 MeV, followed by electron capture to yield lead-207, though the half-life of this second emission is roughly 31.6 years. Similar to lead-212, astatine-211 emits x-rays in the range of 77 keV to 92 keV when decaying to polonium-211, allowing for direct planar or SPECT imaging. Another interesting aspect of astatine-211 decay is that there are an average of 6.2 Auger electrons emitted for each decay. In comparison, terbium-161 emits 11 Auger electrons per decay. A summary of the physical properties of astatine-211 compared to select medically relevant therapeutic radionuclides in development is provided in exhibit 2.

Exhibit 1
Radiopharmaceuticals
Astatine-211 Decay Chain



Source: William Blair Equity Research

Exhibit 2
Radiopharmaceuticals
Characteristics of Common Therapeutic Radioisotopes

	Lutetium-177	Actinium-225	Lead-212	Terbium-161	Astatine-211
Decay particle	β^-	α	α	β^-	***α***
Half-life	6.6 days	10.0 days	10.6 hr	7.0 days	***7.2 hr***
Radiolabeling method	Chelator	Chelator	Chelator	Chelator	***Covalent chemistry***
Direct imaging	Yes	Difficult to implement broadly[1]	Yes	Yes	***Yes***
Patient isolation required	Minimal	No	No	Minimal	***No***
Production equipment	Nuclear reactor	Cyclotron/accelerator or generator	Generator	Nuclear reactor	***Cyclotron***
Starting material	Rare	Rare to available, depending on route	Available	Rare	***Available***
Key potential contaminant(s)	Lu-177m	Ac-227	Th-228 Rn-220	Tb-160	***Bi-207***
Typical waste decay time[2]	~66 days	~100 days	≤5 days	~70 days	***<5 days***

[1]Can use SPECT on daughter isotopes francium-221 and bismuth-213.
[2]Waste time can be extended if certain impurities are present.
Source: William Blair Equity Research

Astatine is a difficult element to study given that no known stable isotopes exist. Although not perfect, iodine is often used as a proxy for astatine and has been instrumental in developing astatine chemistry. However, the astatine-carbon bond is much more labile than the iodine-carbon bond. Although the bond energy for astatine-carbon is not as well studied, the International Atomic Energy Agency (IAEA) published a report (albeit, from 1981) that lists a bond energy of about 39 kcal/mol for n-astatopropyl. In comparison, the iodine-carbon bond is associated with a bond energy of about 53 kcal/mol for isopropyl iodide (for reference, the bond energy of a carbon-carbon bond is 80 kcal/mol, when considering isobutane). Astatine is also polarized in the astatine-carbon bond and so is susceptible to nucleophilic attack. In the body, free astatine-211 mimics free iodine-131 and accumulates in the thyroid and stomach. Upon oxidation, accumulation in the lungs and spleen is also possible. Lower-molecular-weight compounds radiolabeled with astatine-211 typically display greater deastatination than larger biomolecules like antibodies.

Overall, we believe that the instability of the astatine-carbon bond complicates the use of astatine-211 in radiopharmaceuticals for cancer treatment. In our experience, difficulties in astatine chemistry are one of the most-cited explanations for the currently limited use of astatine-211 as a medically relevant radioisotope. However, we recognize that research is underway to develop chemistries for stronger astatine bonds. Below, we briefly summarize some of the key chemistries used for astatine. In many cases, reactions evolving astatine have been derived from analogous iodine reactions and incorporate astatine-aryl bonds, which are slightly stronger than aliphatic astatine carbon bonds. In the IAEA report mentioned above, astatobenzene was reported to have a bond energy of about 45 kcal/mol.

Nucleophilic astatination
Astatine-211 can be oxidized to a –1 oxidization state with agents such as sodium sulfite or dithiothreitol and reacted with one of several precursors. Although various aryl salts, aryl halides, aryl ylides, and aryl boronates can be used as precursors, the reaction conditions should be carefully considered. Some precursors require very harsh conditions, including heating to 90°C, which may not be compatible with biomolecules.

Electrophilic aromatic substitution
This technique involves reducing astatine-211 to a +1 oxidation state with agents such as N-chlorosuccinimide, chloramine-T, peroxides, or peroxydisulfate ion. An astatine-labeled aryl compound is then formed through astatodemetalation. Although a number of precursors can be used for this reaction, many are highly toxic. The use of silicon-, germanium-, or boron-based organo precursors appear to be particularly promising due to relatively limited toxicity.

Prosthetic groups
Although the strategies previously discussed above could be useful for developing radiopharmaceuticals that incorporate astatine-211, they are not necessarily compatible with in vivo applications or biomolecules, especially given relatively harsh reaction conditions. One alternative is the use of prosthetic groups, which can either be astatinated and then conjugated to the targeting moiety (two-step approach) or first conjugated to the targeting moiety and then astatinated (direct radiolabeling). Prosthetic groups are commonly used for peptides, antibody fragments, monoclonal antibodies, and other proteins, and allow for conjugation through lysine, tyrosine, or cysteine (including site-specific N-terminal cysteine) residues. Common prosthetic groups are based on precursors used for radioiodination.

While a promising strategy, reactions with prosthetic groups can require high concentrations of the precursor to obtain acceptable yields. This necessitates extra purification to remove unreacted precursors, a process that is not necessarily efficient and can limit translation to clinical applications. Although still being studied, there have been reports of new click-chemistry-based prosthetic groups that result in quantitative yields in 10 to 20 minutes without the need to separate the precursor after the reaction. Furthermore, these new reagents are compatible with aqueous reaction conditions, which is particularly important for radiopharmaceuticals that incorporate biomolecules.

Ketones
The Department of Energy (DOE) recently reported on the use of ketones to generate strong bonds that could enable a new class of astatine-211–based radiopharmaceuticals.

Specifically, a group incidentally identified that the carbon-astatine bond of an astatine labeled at the position alpha to a ketone is highly stable unless exposed to strong reducing or oxidizing agents. The astatine-ketone compound originated from shipments of astatine-211 in 3-octanone. The astatine-211 and octanone formed a bond that must be cleaved (using hydroxylamine, permanganate,

or hypochlorite) to extract the astatine-211 from solution. Although additional research would be needed, we believe that this example illustrates the potential of developing astatine bonds that are less susceptible to deastatination in vivo.

Astatine-211 as a Radiopharmaceutical Isotope

In exhibit 3, we summarize the potential advantages and disadvantages of astatine-211 discussed below.

Exhibit 3
Radiopharmaceuticals
Advantages and Disadvantages of Astatine-211 as a Therapeutic Radionuclide

Property	Advantages	Disadvantages
7.2-hr half life	• Fractionated dosing possible • Reduced effect on immune cells • Compatible with small molecules/peptides	• Complicates centralized manufacturing • Increased potential for radioactive emission off-tumor
Emits one alpha	• Streamlined decay reduces daughter radionuclides and potential safety liability	• Potential reduced potency per decay
Not chelated (requires covalent chemistry)	• If stabilized, can avoid recoil effect complications	• Potential for in vivo deastatination • More complex radiolabeling
Bismuth-209 starting material	• Readily available and affordable	• Low melting point requires cooling apparatus
Emits X-rays	• In vivo visualization	

Source: William Blair Equity Research

Potential advantages

Although astatine-211 is not heavily investigated in radiopharmaceutical therapy, it is rising as an intriguing alpha emitter and is beginning to gain traction among investors and investigators. Astatine-211 has been described as a "tamer" version of actinium-225 given that it only releases a single alpha particle. The isotope can also be visually tracked through X-ray emissions (similar to lead-212) during decay of the pollonium-211 daughter particle, enabling safety and dosimetry assessments. Although astatine-211 can be imaged directly, it is hypothesized that a radioiodinated analogue that includes iodine-123 or iodine-124 could also be a suitable diagnostic partner for theranostic applications.

Also analogous to lead-212, the short half-life (7.2 hours) opens the possibility for optimizing dosing schedule through fractionated dosing and for reducing adverse effects on infiltrating immune cells in the tumor microenvironment. Fractionated dosing involves administering smaller doses of radiation over time rather than one large dose at once. This can lead to more effective tumor cell killing while also reducing radiation damage to healthy tissue and can even lower bone marrow toxicity. Regarding the second point, immune cells often need several days to recruit to the tumor site in response to radiation. Given the short half-life, astatine-211 has already decayed by the time immune cells arrive and therefore does not suppress the immune response (i.e., does not release

harmful radiation on immune cells). Longer-lived isotopes, such as actinium-225, may still be decaying when immune cells arrive, resulting in a dampening of the immune response as the alpha particles destroy not only cancer cells but also immune cells.

Compared to actinium-225, the simplified decay chain of astatine-211 is viewed by many as advantageous from a clinical perspective as the fate of the daughter particles poses less of a concern. The shorter half-life of astatine-211 also makes the isotope more compatible with small molecules or ligand targeting moieties, rather than antibodies. However, as discussed above, smaller targeting moieties could be more susceptible to deastatination. Compatibility with larger biomolecules could be plausible if injected directly into the tumor site or through pre-targeting of the tumor. However, the latter approach could be challenging longer term from a regulatory perspective. There is also a view in the industry that having a covalently bound isotope (rather than chelated) could have advantages for certain treatment applications, including those that require crossing the blood-brain barrier.

Potential challenges

Many in the industry have expressed enthusiasm for astatine-211 from a biological perspective. Meanwhile, the primary hesitations have originated from instability of astatine chemistry. Free astatine-211 can accumulate in the thyroid, leading to toxicities, although there are strategies to mitigate this risk. For example, thyroid accumulation can be at least partly blocked by using perchlorate. In addition, newer chemistries have made meaningful progress in greatly reducing or even preventing deastatination (some examples are discussed in more detail earlier in the report). Meanwhile, some isotopes (such as actinium-225) require chelation, for which there are no strategies, to our knowledge, to prevent release of the isotope from the chelator upon emission of the alpha particles (a process also known as the recoil effect).

In addition, there are concerns regarding centralized manufacturing for such a short-lived radioisotope. Unlike lead-212, which can be produced on a generator, astatine-211 requires cyclotron technology. However, some speculate that imaging isotopes, such as fluroine-18, which are also produced on a cyclotron (though much smaller in scale), could help inform methods for manufacturing isotopes like astatine-211. Overall, although less established compared to many other medically relevant radionuclides, several isotope supply companies are pursuing the production of astatine-211, and a number of academic centers routinely produce the isotope (discussed in more detail below).

Similar to diagnostic radiopharmaceuticals, such as those labeled with fluorine-18 or carbon-11, automation is likely required to carry out the covalent chemistry necessary for astatine-211-based radiopharmaceuticals. In general, the covalent nature of astatine-211 chemistry (along with iodine-131 chemistry) is sometimes described as messy and much more complicated compared to the simple mixing of radionuclides and binders/chelators for isotopes that can be chelated, such as lead-212 and actinium-225. Skeptics have also noted that while the short half-life of astatine-211 could be beneficial from a clinical perspective, there is a theoretical concern that the short half-life may contribute to higher off-target effects as the radioisotope "bomb" may deploy before arriving at the tumor site and thus impact healthy tissue.

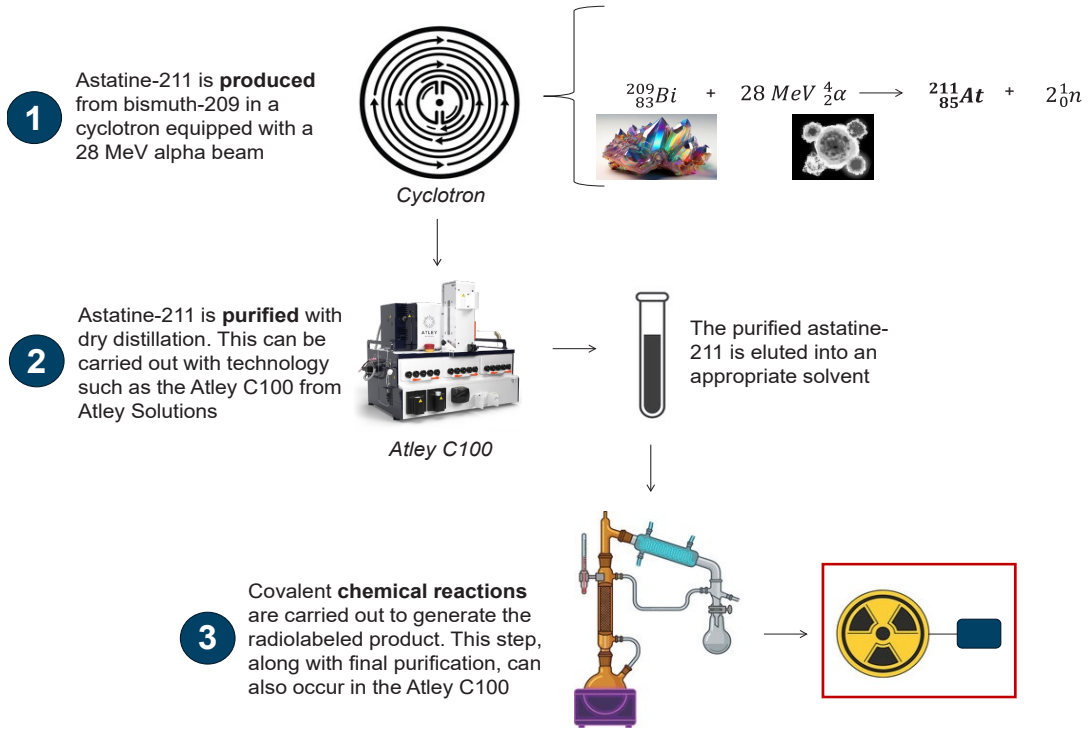
Overall, like many other radionuclides, astatine-211 is associated with both advantages and disadvantages. In our view, pending clinical and manufacturing results, we believe that astatine-211 is likely to hold a place in the radiopharmaceuticals industry. As historical precedent suggests, a one-size-fits-all paradigm is unlikely to materialize, and a variety of both alpha emitters and beta emitters are likely to be incorporated into the broader arsenal of targeted radiation cancer therapeutics.

Production of Astatine-211

Astatine is considered Earth's rarest naturally occurring element, and therefore the element must be produced and cannot be naturally sourced. The starting material for astatine-211 is natural bismuth (bismuth-209), which is a rare Earth element that can either be mined directly or obtained as a byproduct from mining other metals, such as lead, tungsten, copper, zinc, and gold. According to the U.S. Geological Survey Mineral Commodity Summaries published in January 2024, there were roughly 20,000 metric tons of bismuth produced through world refinery production and reserves in 2023. The vast majority (80%) was produced in China (one of the only locations where bismuth is produced as a primary product rather than byproduct or coproduct), with small contributions from Laos (10%) and South Korea (roughly 4%); the remaining originates from Japan, Kazakhstan, Bulgaria, and Bolivia. Notably, the United States has not been involved in bismuth production since 1997.

Once obtained, bismuth-209 is irradiated with alpha particles, which can typically be carried out in a cyclotron (exhibit 4). Because of bismuth's relatively low melting point (271°C), cooling apparatuses are key since heat generated from the helium beam can melt the bismuth target. An alpha particle stream with an energy of 28 MeV helps reduce side products, such as astatine-210. Astatine-211 is produced in one step and then purified with dry distillation, which is based on astatine's lower boiling point compared to bismuth; this is the most common purification technique. However, liquid-liquid extraction and liquid-solid extraction can also be used. The radioisotope is then eluted into an appropriate solvent and is ready for radiolabeling.

Exhibit 4
Radiopharmaceuticals
Production Process for Astatine-211



Sources: Adobe Stock, Atley Solutions, and William Blair Equity Research

Compared to some other isotopes, astatine-211 can be produced with inexpensive starting material (and does not rely on nuclear stockpiles) while also generating relatively high radioactive yields. However, astatine-211 is currently produced at a limited number of sites around the world, which we hypothesize could be due to currently limited use-cases. To date, most production has been carried out at academic or medical centers, though production is expanding.

In March 2025, the National Isotope Development Center (NIDC) announced that through the Department of Energy Isotope Program (DOE IP), in partnership with the University of Washington, a biologically active compound radiolabeled with astatine-211 had been successfully transported in the United States and showed no signs of radiolysis upon delivery. In addition, sponsored by the DOE IP, a research group at Texas A&M University has developed a compact fully automated processing device for astatine-211. The device can be remotely controlled and generates a product with more than 99% purity in 20 minutes. Although it does not directly produce the astatine-211 isotope, the device still addresses an important part of the overall manufacturing process.

Suppliers of Astatine-211

Below we summarize current suppliers of astatine-211 in both the United States and abroad. We outline select suppliers in exhibit 6, on the following page, but note that additional facilities and academic centers are likely producing the isotope. We also conducted an analysis to help gauge the potential for astatine-211 production to meet longer-term treatment needs of oncology patients. In our analysis, we assume that each patient will receive four doses of 200 MBq (5 mCi) therapy, equating to 20 mCi per course of treatment. We include two estimates of patients treated per year: one assumes that cyclotrons produce astatine-211 on a 24/7 basis and the other assumes that cyclotrons operate on a typical working-day schedule of 40 hours per week. Our estimate is based only on select suppliers from exhibit 5 that list estimated production capacity with timescale information. Therefore, our analysis is likely an underestimate and is meant to provide a framework for thinking of overall capacity of astatine-211. A summary of our analysis is provided in exhibit 5.

Overall, we believe that current or near-term production of astatine-211 could help generate enough radiopharmaceutical drug product to treat at least 28,000 patients per year. Although not enough to treat the millions of cancer patients living globally today, we believe there is potential to scale production, assuming clinical data warrants the endeavor. We also recognize that astatine-211–based radiopharmaceuticals will likely not be applicable to every cancer treatment. Other modalities will continue to play a role, and even within radiopharmaceuticals, additional isotopes, including lutetium-177 and likely actinium-225 and lead-212, will likely be at play.

Exhibit 5
Radiopharmaceuticals
Production Capacity of Select Suppliers for Astatine-211

Company/Facility	Listed Production Capacity	Production Capacity (Ci/year)	Courses of Treatment[1] (24/7 operation)	Courses of Treatment[1] (modified[2])
Ionetix	125 Ci/year	125	6,250	1,488
University of Washington	4.3 GBq/4 hrs	255	12,726	3,030
Texas A&M	1.5 GBq/9 hrs	39	1,973	470
Alpha Nuclide	4 Ci per day	1,460	73,000	17,381
IPCR Riken	1.3 GBq/1 hr	308	15,389	3,664
Rigshospitalet	3.4 GBq/4 hrs	201	10,062	2,396
Patients treated per year			***119,400***	***28,429***

[1]Assumes that each patient will receive four doses at 200 MBq (5 mCi) per dose, equivalent to 20 mCi per course of treatment.
[2]Modified operation defined as operational 8 hours a day for 5 days a week.
Source: William Blair Equity Research

Exhibit 6
Radiopharmaceuticals
Select Current or Future Suppliers of Astatine-211

Company/Facility	Headquarters	Supply Agreements/ Collaborations	Equipment/Technology	Currently Producing?	Estimated Production Capacity
Domestic					
Ionetix	Lansing, MI	NAYA, Atonco, Z-Alpha	30 MeV cyclotron	Yes	125 Ci/year
Nusano	Salt Lake City, UT	dGenThera, Curadh	Heavy ion linear accelerator (~36 mA)	No	*Not reported*
DOE NIDC	Oak Ridge, TN*	*Not reported*	UW: 29 MeV Scanditronix MC-50 cyclotron A&M: 28.8 MeV K150 variable energy cyclotron	Yes	UW: 4.3 GBq in 4 hr A&M: 1.5 GBq in 9 hr
UC Davis	Sacramento, CA	Atley	Custom-built cyclotron	Yes	*Not reported*
International					
Alpha Nuclide	Jiaxing, China	NAYA, dGenThera, Asta Bio	30 MeV cyclotron	Yes	Up to 4 Ci per day
Arronax	Nantes, France	Oncodesign services (CRO)	IBA Cyclone 70 (28 MeV)	Yes	0.5-1 GBq
IPCR Riken	Wako Saitama, Japan	*Not reported*	AVF cyclotron (29 MeV)	Yes	1.3 GBq in 1 hr
RCNP (at Osaka University)	Osaka, Japan	*Not reported*	K140 AVF cyclotron (28.2 MeV)	Yes	Up to 3 GBq
Rigshospitalet	Copenhagen, Denmark	Atley, Gothenburg University, Minerva, TetraKit	Scanditronix MC32	Yes	3.5 GBq in 4 hr 2-4 irradiations per week
TAT Cyclotron Building (Osaka University)	Osaka, Japan	Alpha Fusion	Sumitomo MP30X	No (expected start: 1Q 2027)	*Not reported*
Forschungszentrum Jülich	Julich, Germany	*Not reported*	IBA Cyclone30XP	Yes	*Not reported*
University of Birmingham	Birmingham, UK	*Not reported*	Scanditronix MC40	Yes	*Not reported*

*Production of isotope occurs at the University of Washington (UW) or Texas A&M.

AVF=Azimuthally Varying Field.

Sources: Feng, Y. and Zalutsky, M. *Nuclear Medicine and Biology* (2021), company reports, facility websites, and William Blair Equity Research

Domestic supply

Astatine-211 is available by the mCi from the DOE's National Isotope Development Center (produced at either the University of Washington or Texas A&M). The quoted radionuclide purity and radioisotopic purity are both more than 99%, while radiochemical purity is quoted as being 85% or greater and up to 99%, depending on the source. Beyond the University of Washington and Texas A&M (which partner with the DOE), Duke University, University of Pennsylvania, and the National Institute of Health (Bethesda, Maryland) have all reported astatine-211 production. Both Duke and the NIH are equipped with CS-30 cyclotrons that incorporate internal target systems.

A few dedicated isotope suppliers are actively pursuing astatine-211 as one of their product offerings. Within the United States, these include Ionetix and Nusano. Ionetix employs a 30 MeV cyclotron, while Nusano combines heavy ion source technology and a linear accelerator. Ionetix announced in early September of this year that it had started routinely shipping astatine-211 in North America and estimates production capacity at scale of 125 Ci/year. Nusano envisions a network of production facilities across the United States, similar in concept to the fluorine-18 facilities that dot the country.

Although not involved in the production of astatine-211, Atley Solutions is becoming an increasingly important player in enabling access to the isotope. Atley's key product offering is the Atley C100 system, which purifies astatine-211 from irradiated bismuth material and performs automated synthesis of astatine-211-labelled radiopharmaceuticals. The process of producing astatine-211 starts with naturally occurring and nonradioactive bismuth-209, a cheap and highly abundant material. The bismuth-209 is irradiated in a cyclotron, and then the Atley C100 is used to purify the irradiated material. This produces purified astatine-211, which in a sequential process on the Atley C100 can then be incorporated into the drug product using the modules for automated synthesis functionality. Beyond purification and automated synthesis, Atley supplies bismuth-209 targets in various forms to accommodate the customer's specific accelerator. Logistically, the irradiated bismuth material is typically shipped in an unpurified form, which increases stability during transport. Upon arrival at the destination, purification of the bismuth target, synthesis of the radiopharmaceutical, and purification of the final product occur in quick succession within the Atley C100. Atley has established partnership and collaboration agreements with several companies operating in the astatine-211 space, including Telix, NAYA, and Nusano.

The DOE has also reported a device that automates purification of astatine-211 by dissolving an irradiated target and using chromatography to extract the astatine-211. Although instrumentation (likely a cyclotron) is still required to irradiate the target, the DOE notes that the automation limits exposure of personnel to radiation, and it reduces sample preparation time to under 20 minutes while maintaining an elution yield of 95%. The expedited sample preparation is especially relevant given astatine-211's short half-life.

International supply

Outside the United States, Japan stands out as a hub for astatine-211 production and development with at least five centers (including Osaka University and Fukushima Medical University) using cyclotron accelerators to make the isotope. The RIKEN research institute uses a particle accelerator to produce astatine-211, and one of the key aspects of its technology is a cooling system that prevents the bismuth target from melting (as discussed earlier in the report). The group is continuing to innovate its technology to increase efficiency and production capacity, and as of April 2024, RIKEN supported roughly 20 research groups in Japan, including Osaka University Hospital, which has carried out the majority of clinical work for astatine-211. The Research Center for Nuclear Physics at Osaka University hosts a cyclotron that can produce the isotope and has helped manufacture TAH-1005 from Alpha Fusion.

Europe is also building out its astatine-211 production capabilities through several initiatives. From 2020 to 2024, the COST European Cooperation in Science and Technology supported an action to bring together multiple entities across Europe with the long-term goal of enabling greater access to astatine-211 technology. The initiative, referred to as Network for Optimized Astatine labeled Radiopharmaceuticals, was enabled in recognition of the potential for astatine-211-based radiopharmaceuticals to impact cancer treatment. Although the action has ended, Europe remains involved in astatine-211 production, and in early 2025, a partnership between Framatome (an international nuclear energy company) and IBA (which develops particle accelerators) to develop a cyclotron network for astatine-211 production across and Europe and the United States was announced. A pilot facility is slated to be installed in 2027 or 2028.

In June of this year, IBA announced the launch of Cyclone iKure, which is a cyclotron designed to enable production of astatine-211 at an industrial scale. The cyclotron operates at 28.5 MeV to 29.5 MeV and incorporates automated processes. It is described as compact, requiring a limited infrastructure footprint, with cyclotron dimensions of 3 meters by 3 meters and vault dimensions of 6.5 meters by 6.5 meters by 3 meters.

In the fall of 2024, financing for the Accelerate.EU project was approved by the European Commission. The Accelerate.EU initiative is led by IBA and the Jules Bordet Institute and received funding of €16 million. The project is five years in length and aims to expand Europe's access to targeted alpha therapy by creating a path to manufacture and clinically evaluate astatine-211. IBA will provide the cyclotron for producing the isotope, and the Jules Bordet Institute will focus on the clinical aspects of the project. A total of 17 institutes and companies across 9 European countries are involved in the project.

In addition, China-based Alpha Nuclide supplies a number of medically relevant radioisotopes, including astatine-211. The company currently operates a center in East China that is equipped with two 30 MeV cyclotrons. One of these cyclotrons is dedicated to astatine-211 production up to a scale of 4 Ci per day. The other cyclotron is dedicated to production of other radionuclides, including the imaging isotopes fluorine-18, copper-64, and zirconium-89. A 3,000-square-meter GMP processing facility, which will enable production of GMP grade radiopharmaceutical products for both clinical and commercial application, is also located at the East China centers. Alpha Nuclide is building out a second facility in North China that is expected to resemble the East China center and be operational in 2028. In mid-2024, Alpha Nuclide and Radnostix (a U.S.-based manufacturer and supplier of nuclear medicine products, calibration and reference standards, and medical devices and equipment) entered a 50/50 joint venture to distribute Radnostix's products from Alpha Nuclide's facility in Jiaxing. There is also an agreement for Alpha Nuclide to supply raw material isotopes to Radnostix's Idaho Falls facility. In addition, Alpha Nuclide has noted supply agreements with multiple therapeutics companies, including NAYA, dGenThera, and Astra Bio.

In Denmark, Copenhagen University Hospital (Rigshospitalet) produces astatine-211 with a Scanditronix MC 32 cyclotron at a purity of 99.9% or higher. Impurities, though limited, include astatine-210, sodium-24, magnesium-27, and aluminum-29. In June of this year, the Technical University of Denmark announced a collaboration with Rigshospitalet to focus on production and application of astatine-211 with the longer-term goal of increasing production capacity for Rigshospitalet. Over the years, Rigshospitalet has established supply agreements with Atley, Minerva Imaging, and TetraKit Technologies.

Companies Investigating Astatine-211

Below, we highlight companies with pipelines investigating astatine-211–based radiopharmaceuticals. Although most have yet to enter the clinic, Alpha Fusion's pipeline includes several clinical programs, NAYA appears to be in very early clinical development, and Telix is slated to enter the clinic this year. A summary of the companies discussed below is provided in exhibit 7, on the next page.

When it comes to manufacturing, companies typically appear to be incorporating decentralized approaches. Given the short half-life, decentralized manufacturing is somewhat of a breakthrough, and we speculate that companies recognize that this aspect of production may be critical to realizing the full clinical potential of astatine-211.

Alpha Fusion
Alpha Fusion is based in Japan, and two of its pipeline programs are under Phase I investigation in thyroid cancer. TAH-1005 (also known as af-001 or ^{211}At-NaAt) targets the sodium iodide symporter with a small molecule. The asset is being evaluated in both radioactive iodine (RAI)-refractory and RAI-naive disease. A Phase I refractory trial sponsored by the University of Osaka has been completed, while a second Phase I trial in both refractory and naive patients is currently enrolling patients. To our knowledge, the ongoing study is the first company-sponsored trial of an astatine-211–based radiopharmaceutical. The second clinical asset is PSW-1025 (also known as af-002 or ^{211}At-PSMA-5), which targets PSMA with a small molecule and is being evaluated in refractory prostate cancer in the Phase I Alpha-PS1 trial (sponsored by the University of Osaka). A third asset, called af-003, targets LAT1 with a small molecule and is under IND-enabling studies for a pan-cancer indication. Two additional programs are in screening phases with undisclosed targets and are employing either a peptide or small-molecule targeting moiety.

For supply of astatine-211, Alpha Fusion has established partnerships with Japanese cyclotron facilities and the Kobe City Medical Center (KCGH). KCGH is already established in manufacturing investigational drugs that incorporate short-lived isotopes for the purposes of PET-based imaging. Therefore, the hospital's expertise and GMP manufacturing facility will be applied to astatine-211. As discussed above, the Research Center for Nuclear Physics at Osaka University has also been involved in producing astatine-211 for TAH-1005.

Atonco
Atonco is based in France and is focused on treating bladder cancer through intravesical administration of astatine-211 based radiopharmaceuticals. The company's lead program is ATO-101, which incorporates carbonic anhydrase IX-targeted girentuximab, an antibody licensed from Telix. The asset is entering Phase I development in non-muscle-invasive bladder cancer through the investigator-initiated PERSEVERANCE study, which is estimated to start early 2027. The radiolabeling technology, developed in France, is described as proprietary. Atonco appears to be involved with the Framatome and IBA partnership, and we speculate this may serve as Atonco's source of astatine-211. Atonco also has an agreement with GIP Arronax to help establish a GMP production process for ATO-101.

NAYA
NAYA is investigating both astatine-211–based radiopharmaceuticals and bifunctional antibodies. Its radiopharmaceuticals pipeline consists of two assets: NY-738 and NY-703. NY-738 targets CD38 for treating multiple myeloma with clinical data from the first-generation version expected this year. The second-generation version is slated to enter the clinic before year-end. NY-703 targets GPC3 with a F(ab')2 antibody fragment for treating hepatocellular carcinoma. Initial China-based data are expected before year-end, with Phase I/II initiation in the United States and Europe slated for the first half of next year. NAYA has established partnerships with several manufacturers to enable a scalable and decentralized supply chain. This includes Atley, Ionetix, and Alpha Nuclide.

Exhibit 7
Biotechnology
Companies with Astatine-211 Radiopharmaceuticals in Development

Company	Location	Drug Name	Format	Target	Indication	Stage
Alpha Fusion	Tokyo, Japan	af-001 af-002 af-003 Undisclosed Undisclosed	Small molecule Small molecule Small molecule Peptide Small molecule	Sodium iodide symporter PSMA LAT1 Undisclosed Undisclosed	Thyroid cancer Prostate cancer Pan-cancer Undisclosed Undisclosed	Phase I Phase I IND-enabling Screening Screening
NAYA Therapeutics	Miami, FL	NY-703 NY-738	F(ab')2 antibody fragment	GPC3 CD38	HCC Multiple myeloma	Early clinical in China Early clinical
Atonco	Saint-Herblain, France	ATO-101	Antibody[1]	CAIX	Bladder cancer	Phase I (IST)
Telix	Melbourne	TLX102-Tx	Small molecule	LAT1	Recurrent GBM and leptomeningeal disease	Phase I starting this year
dGenThera	Durham, NC	DGT-77 DGT-207	Small molecule Bioligand	Undisclosed transporter Undisclosed receptor	Breast cancer Undisclosed	Preclinical[2]
Trevarx	Philadelphia, PA	AlphaPARP	Small molecule	PARP	Ovarian cancer	Preclinical
Asta Bio	Boston, MA	Undisclosed	Single-domain antibodies	Undisclosed	Solid tumors[3]	Preclinical
Z-Alpha	San Diego, CA	PMI21 PMI31 PMI41	Undisclosed Undisclosed Undisclosed	PSMA FAP CAIX	Prostate cancer Undisclosed Undisclosed	IND-enabling[4] Undisclosed Undisclosed

GBM=Glioblastoma. HCC=Hepatocellular carcinoma. IST=Investigator-sponsored trial.

[1]Administered intravesically.

[2]Other undisclosed cancer types are also under earlier investigation.

[3]Initial focus on lung, breast, colon, head and neck, liver, and gastrointestinal cancers.

[4]Exact development status of PMI21, along with remaining pipeline assets, is not certain.

Source: Company reports

Telix
Telix is advancing a broad therapeutic and diagnostic radiopharmaceutical pipeline across a range of isotopes, targets, and indications. One of the programs, TLX102-Tx, incorporates astatine-211 and targets LAT1 with a small molecule. Phase I development is slated to commence this year in recurrent glioblastoma and leptomeningeal disease. Telix believes that for applications that require crossing the blood-brain barrier (including treatment of neuro-oncology indications), radiohalogens are better suited than radiometals requiring a chelator. In February 2026, a collaboration was announced among Atley Solutions, the Cyclotron & Radiochemistry Facility at Standford University, and Telix to establish a supply chain for astatine-211 in California. Production of astatine-211 will take place at the Crocker Nuclear Laboratory at UC Davis and possibly other cyclotrons and accelerators.

dGenThera
Focused on radioactive halogens, including astatine-211 and iodine-131 for therapy and fluroine-18 for diagnosis, dGenThera incorporates stabilization technology to reduce the risk of dehalogenation for both astatine and iodine. Both small molecules and small bioligands are being examined across various undisclosed cancer types, though breast cancer is noted as of interest for the small-molecule program. The small molecules target transporters, while the bioligands target receptors. The six listed programs span from discovery to preclinical stages. Small-molecule ^{211}At-DGT-77 has been tested in mice with breast cancer xenografts and demonstrated nearly 100% tumor growth inhibition at four weeks after a single 2 MBq dose. Meanwhile, bioligand ^{211}At-DGT-207 demonstrated potentially encouraging biodistribution data in mice with undisclosed human cancer xenografts. DGenThera has disclosed an intended supply agreement with Nusano for access to astatine-211.

Trevarx
Trevarx is focused on building DNA-directed radiopharmaceuticals with lead asset AlphaPARP targeting PARP1 and incorporating astatine-211. The company believes that targeting a nuclear protein that is one of cancer's repair mechanisms could be particularly effective. Another potential advantage of targeting PARP1 is that DNA damage can amplify PARP1 expression, which could lead to increased efficacy with continued treatment and could allow a fractionated dosing schedule to be particularly effective. AlphaPARP is under IND-enabling studies in ovarian cancer; in preclinical evaluation for prostate cancer, breast cancer, and neuroblastoma; and in exploratory phases for pancreatic cancer and small-cell lung cancer. The company's pipeline also includes PARPTrace, which incorporates fluorine-18 for diagnosis. The asset is being investigated in multiple tumor types and is completing a Phase II study in breast cancer.

Asta Bio
Asta is a preclinical-stage company using multivalent single-domain antibodies and astatine-211 to develop cancer treatments. Although the specific indication of interest is still evolving, the company has indicated interest in lung, breast, colon, head and neck, liver, and gastrointestinal cancers. Last year, Asta formed a collaboration with Alpha Nuclide to advance Asta's programs in China. Dr. Oliver Sartor sits on the medical advisory board for Asta.

Z-Alpha
In 2022, U.S.-based Z-Alpha was formed through a joint venture between Precision Molecular and Zentera Therapeutics. Although limited information is available about Z-Alpha's pipeline, it appears to be composed of three assets originally developed by Precision Molecular (formerly a subsidiary of D&D Pharmatech): PMI21, PMI31, and PMI41. Based on our research, PMI21 targets PSMA and might be in IND-enabling stages, while PMI31 targets FAP and PMI41 may target carbonic anhydrase 9. According to a press release from early 2022, Precision Molecular disclosed plans to enter the clinic with PMI21 in prostate cancer patients later that year, but to our knowledge, this has not yet occurred. The same press release described a supply agreement between Precision Molecular and Ionetix, and thus we speculate that Ionetix may be supplying Z-Alpha with astatine-211.

Astatine-211 in the Clinic: Trials and Data

Clinical Trials

Although minimal overall, some clinical trials are evaluating radiopharmaceuticals that incorporate astatine-211. Beyond the trials listed in exhibit 8, additional trials with astatine-211-based agents are evaluating bone marrow conditioning regimens. However, we have chosen to focus on trials designed to directly treat various tumor types. All are in early phases with enrollments of less than 40 patients. A range of different tumor types are being tested, and there are multiple trials for both prostate cancer and thyroid cancer. Several studies have been completed (available data is described below), though the majority are either recruiting or posted but not yet recruiting. From a location perspective, Japan appears to be particularly active, likely owing to the concentration of production sites in that geography. Overall, we believe it is encouraging that astatine-211–based radiopharmaceuticals are already in the clinic, and we expect that the number of trials will increase over time.

Exhibit 8
Biotechnology
Clinical Trials Evaluating Astatine-211 Radiopharmaceuticals[1]

Study ID	Phase	Indication	Drug Name	Target	Trial Name	Enrollment	Sponsor	Region	Status
NCT06441994 (Alpha-PS1)	I	Prostate cancer	[At-211]PSMA-5	PSMA	Clinical Trial of Targeted Alpha Therapy Using [At-211]PSMA-5 for Prostate Cancer (Alpha-PS1)	15 patients	Osaka University	Japan	Recruiting
NCT07287748	I	Thyroid cancer	TAH-1005/af-001	Sodium transporter	A Phase I Trial of Af-001 in Patients With Differentiated Thyroid Cancer	38 patients	Alpha Fusion	Japan	Recruiting
NCT07661420	I	Neuroendocrine cancers	211At-MABG	Norepinephrine transporter	211At-MABG in Adults With Advanced Neuroendocrine Cancers	16 patients	University of Pennsylvania	United States	Not yet recruiting
NCT07260162	I	Non-muscle-invasive bladder cancer	ATO-101	CAIX	Evaluation of ATO-101™ in Patients With Non-Muscle-Invasive Bladder Cancer (PERSEVERANCE EU) (PERSEVERANCE)	24 patients	Institut Cancerologie de l'Ouest	France	Not yet recruiting
NCT05275946 (Alpha-T1)	I	Thyroid cancer	TAH-1005/af-001	Sodium transporter	Targeted Alpha Therapy Using Astatine (At-211) Against Differentiated Thyroid Cancer	11 patients	Osaka University	Japan	Completed (2025)
NCT06359821	Early Phase I	Prostate cancer	ZA-001	PSMA	Evaluate Safety, Whole-Body Distribution and Radiation Dosimetry in Metastatic Castration Resistant Prostate Cancer	4 patients	Sichuan University	China	Completed (2024)
NCT04461457	Early Phase I	Ovarian cancer	211-astatine-MX35 F(ab')2	NaPi2b	Targeted Radiation Therapy for Ovarian Cancer: Intraperitoneal Treatment With 211-astatine-MX35 F(ab')2	12 patients	Vastra Gotaland Region	Sweden	Completed (2012)

[1]Trials involving bone conditioning regimens have not been included.
Source: clinicaltrials.gov

Clinical Data

Below, we summarize clinical trial data generated to date that incorporate astatine-211–based radiopharmaceutical treatment, based on our research. Although they all focus on therapies for oncology, we note that preclinical investigations for potential Alzheimer's disease treatment have also been carried out.

Phase I results of ^{211}At-MX35 F(ab′)$_2$ in ovarian cancer

To our knowledge, one of the earliest studies of astatine-211 as a treatment for cancer was published in 2009. The Phase I study evaluated ^{211}At-MX35 F(ab′)$_2$, which targets NaPi2b with a monoclonal antibody, in relapsed ovarian cancer patients, and administration of the drug was carried out intraperitoneally rather than systemically. Initial data were reported in nine patients, and based on dosimetry data, absorbed dose ranges were 0.0020 Gy-0.107 Gy for bone marrow, 0.02 Gy-0.82 Gy for thyroid, 0.28 Gy-1.59 Gy for peritoneal lining, and 0.013 Gy-0.044 Gy for urinary bladder epithelium (only evaluated in four patients). No toxicities related to the treatment were noted, and after a medium of 23 months of follow-up, there were no observations of hematologic, renal, or thyroid abnormalities. At the time of the data publication, three patients were in clinical and CA-125 remission. The remaining patients experienced CA-125 elevations and one patient passed away from the cancer.

In 2015, additional dosimetry and risk estimates were published from six patients in the study. The data was aimed at estimating the radiation absorbed dose using SPECT/CT imaging. SPECT/CT analysis determined organ-to-blood concentration ratios that ranged from 0.27 in breasts to 3.1 in the lungs. The ranges for absorbed dose in red bone marrow, thyroid, peritoneum, and urinary bladder epithelium (only evaluated in two patients) were as follows, respectively: 9.1 mGy-44 mGy; 20 mGy-1,200 mGy; 690 mGy-2,800 mGy; and 300 mGy-480 mGy.

A long-term follow-up analysis was published 10 years after the initial publication and included mature data from 12 patients. The ^{211}At-MX35 F(ab′)$_2$ treatment was administered at escalating doses from 20 MBq/L to 215 MBq/L. The majority of patients (58%) had high-grade serous ovarian cancer, though all patients had a good performance status based on Karnofsky scoring criteria.

Median overall survival was 35 months, and survival rates for 1 year, 2 years, 3 years, 5 years, and 10 years were 100%, 83%, 50%, 33%, and 25%, respectively. At the time of the follow-up analysis (147 months, or roughly 12 years), three patients (25%) were alive while the remaining had succumbed to the disease.

No dose-limiting toxicities were observed during dose escalation. Most reported toxicities in the intent-to-treat population (17 patients total, 14 with an implanted catheter) were grade 1 or 2, with only one report of grade 3 fatigue and one case of grade 4 small-intestine perforation. There were no renal or hematologic toxicities noted during follow-up.

Alpha-T1 trial of TAH-1005 in thyroid cancer

The Japan-based Phase I Alpha-T1 trial evaluated TAH-1005 (developed by Alpha Fusion), which targets sodium iodide symporters through natural accumulation of astatide ion, in radioiodine-refractory thyroid cancer. The data was published in December 2025 in *The Journal of Nuclear Medicine.*

TAH-1005 was administered at dose levels of 1.25 MBq/kg, 2.5 MBq/kg, or 3.5 MBq/kg (the design included doses up to 5 MBq/kg, 7 MBq/kg, and 10 MBq/kg, though dose-limiting toxicities were observed at 3.5 MB/kg). Across 11 patients, all had received prior total thyroidectomy, 91% had prior thyroid-stimulating hormone suppression therapy, 91% had three or more prior radioactive iodine treatments, and 36% had prior radiation therapy. Sites of metastases included lung (73%) and bone (64%).

Patients were evaluated for response after six months of treatment based on computed tomography (CT) imaging and iodine-131 SPECT. Based on CT, the response rate was 10% (out of 10 patients), while the response rate based on SPECT was 33% (out of 9 patients; included one complete response). Mean absorbed dose ranged from 0.002 mGy/MBq in the lung to 2.75 mGy/MBq in the stomach. In organs of interest, including kidney, bone marrow, and salivary glands, absorbed dose was 0.33 mGy/MBq, 0.57 mGy/MBq, and 1.96 mGy/MBq, respectively. We are not surprised by the high absorbed dose in the stomach given that astatine (along with the other halogen iodine) is known to accumulate in this organ.

Across all three doses, grade 3 or 4 treatment-related adverse events were hematologic in nature: lymphopenia (64%), leukopenia (36%), and neutropenia (18%). Xerostomia (all grade 1 or 2) was reported in 54% of patients, while salivary gland swelling (also grade 1 or 2) was observed in 73% of patients. Hematologic adverse events led to dose-limiting toxicities in half of the six patients who received 3.5 MBq/kg.

TAH-1005 is under ongoing investigation in another Phase I trial in Japan that is currently recruiting with a target enrollment of 38 patients.

SPECT imaging data of ^{211}At-PSMA-5 in mCRPC

Also developed by Alpha Fusion, ^{211}At-PSMA-5 is under Phase I investigation in mCRPC. At the 2025 SNMMI annual meeting, the first-in human SPECT/CT image of the agent (compared to ^{18}F-PSMA-1007) was presented. The patient had mCRPC and was refractory to androgen receptor pathway inhibitors, docetaxel, and cabazitaxel. Imaging was carried out three hours after administration of the agents. Compared to ^{18}F-PSMA-1007 PET/CT, ^{211}At-PSMA-5 demonstrated similar biodistribution, and there was high uptake in prostate lesions. As expected, based on the difference in imaging technique, the SUV_{max} was higher for ^{18}F-PSMA-1007 PET: 60.7 versus 4.9 in soft tissue mass and 143.7 versus 17.6 in the left lymph node metastasis.

The Phase I Alpha-PS1 trial of ^{211}At-PSMA-5 is currently recruiting in Japan with a target enrollment of 15 patients.

Phase I data of ^{211}At-MABG in paraganglioma

Meta-astatobenzylguanidine (MABG), which targets norepinephrine transporters, has been labeled with astatine-211 and is under early clinical evaluation. In the first-in-human Phase I study, 10 patients with unresectable or metastatic paraganglioma received one of three dose levels of ^{211}At-MABG: 0.65 MBq/kg, 1.3 MBq/kg, or 2.1 MBq/kg. One partial response and seven cases of stable disease were reported. The mean plasma elimination half-life was 62 hours, and cumulative urinary excretion was 65% after 72 hours. No dose-limiting toxicities were observed at the tested doses. Grade 3 or higher adverse events were rare, with one patient experiencing grade 3 nausea and anorexia. There were no reported grade 3 or higher hematological toxicities or notable renal or hepatic toxicities.

In addition, ^{211}At-MABG is also under Phase I investigation in patients with advanced neuroendocrine cancers.

Outlook

In our view, there are a number of appealing characteristics of astatine-211, specifically relating to the simplified decay chain, short half-life (allowing fractionated or intensified dosing regimens and enabling the immune system to function unhindered), and ability to visualize directly. On the other hand, we believe significant hurdles remain and must be overcome to enable the isotope to reach its therapeutic potential. These hurdles include centralized manufacturing of a short-lived isotope (though manufacturing of short-lived imaging isotopes, such as fluorine-18, could serve as a blueprint) and covalent-based radiolabeling chemistry (though new chemistries are well underway). Based on our conversations, our viewpoint appears to reflect the general sentiment in the investment community. However, we are encouraged that astatine-211 is being investigated in the clinical trial setting, and we believe that the hurdles associated with astatine-211 can be overcome if supported by clinical data outcomes.

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Telix Pharmaceuticals Limited (Outperform)	$11.09

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