Making more Mo-99

Four U.S. companies continue to lead the way in providing a commercial supply of the widely used medical radioisotope.

On May 9, in a farm field next to a small regional airport in south-central Wisconsin, Department of Energy Under Secretary for Nuclear Security and National Nuclear Security Administration head Lisa Gordon-Hagerty joined local officials and some 90 employees of SHINE Medical Technologies in breaking ground on SHINE's first radioisotope production facility. Once complete, the 43,000-square-foot facility in Janesville, Wis., will be home to eight of the company's accelerator-based medical isotope production systems, capable of producing over one-third of global demand for the life-saving isotope molybdenum-99, according to SHINE.

SHINE is one of four companies that were recently selected by the NNSA to begin negotiations for potential new cooperative agreement awards of up to $15 million each (*NN*, Apr. 2019, p. 47). Since 2009, the NNSA has worked to accelerate the commercial production of Mo-99 in the United States by supporting a variety of technologies that do not use high-enriched uranium. The goal of the NNSA's Mo-99 program is to create a redundant, reliable Mo-99 supply network that avoids a single point of failure—a mission that the administration says is made all the more urgent with the shutdown in 2016 of Canada's National Research Universal reactor, historically the United States' largest Mo-99 supplier.

Photo: SHINE

SHINE employees celebrate the groundbreaking of the company's new Mo-99 production facility in Janesville, Wis., in May.

Along with SHINE, the companies selected for the potential new cooperative agreement awards include NorthStar Medical Radioisotopes, located in nearby Beloit, Wis., Northwest Medical Isotopes (NWMI) of Corvallis, Ore., and Lansing, Mich.-based Niowave. The companies, according to the DOE, were selected based upon the evaluations and recommendations of an independent technical review panel, and each company is using its own technological approach to solving the Mo-99 problem.

NorthStar

With its RadioGenix System (technetium-99m generator) receiving approval from the U.S. Food and Drug Administration in February 2018 (*NN*, Mar. 2018, p. 94), NorthStar is furthest along in the Mo-99 production race. In October 2018, the company was recognized by the NNSA for being the first producer of Mo-99 in the United States in 30 years, winning the administration's Award for Outstanding Achievement.

NorthStar's non-uranium system of creating Mo-99 uses natural occurring molybdenum (nMo) as its starting material. The company manufactures small discs of nMo, containing about 24 percent stable Mo-98, that are irradiated at the University of Missouri Research Reactor (MURR) in Columbia, Mo., to produce Mo-99 through neutron capture. The irradiated targets are then dissolved and placed in source vessels, which upon arrival at a radiopharmacy are mounted into the RadioGenix System to extract the Tc-99m, the Mo-99 daughter isotope that is used for diagnostic imaging.

Early this year, the company announced initiatives to increase its manufacturing and production of Mo-99. The company said that construction is well under way on its 20,000-square-foot facility expansion in Beloit, which will more than double NorthStar's capacity to fill Mo-99 source vessels, once dissolution and filling equipment is installed, qualified, validated, and approved by the FDA. The company also said that it is nearing the final validation of two state-of-the-art source-vessel filling systems at its Columbia facility that, pending FDA approval, will increase the number of Mo-99 source vessels available to ship weekly.

NorthStar is also moving forward on its efforts to produce Mo-99 using electron beam accelerators. The method uses accelerators to induce photo transmutation (neutron knock-out) to produce medically useful Mo-99 from enriched Mo-100. In March, the company announced that it has contracted with Ion Beam Applications S.A. of Belgium for the purchase of as many as eight electron beam accelerators to increase NorthStar's production capacity.

On April 23, the company announced that it has received $100 million in financing from Oberland Capital Management, which NorthStar said it will use to increase its Mo-99 production capacity, as well as to complete programs to improve production efficiency, make additional enhancements to the RadioGenix System, and advance its research and development activities.

Image: NWMI

Renderings show NWMI's planned radioisotope production facility in Columbia, Mo.

NWMI

In May 2018, the Nuclear Regulatory Commission approved NWMI's construction license for a Mo-99 production facility at the Discovery Ridge Research Park in Columbia, Mo., a 550-acre research park owned by the University of Missouri. Once completed, the NWMI radioisotope production facility will fabricate low-enriched uranium targets, which will be shipped to a network of university and test reactors, primarily MURR and the Oregon State University TRIGA reactor, for irradiation. Once irradiated, the targets will be shipped back to NWMI for the dissolution, recovery, and purification of Mo-99. The purified Mo-99 will then be packaged and shipped to a radiopharmaceutical distributor. Like the other Mo-99 producers, NWMI will recycle its used LEU targets to recover usable uranium for further target production.

According to NWMI's pre-license presentation to the NRC, construction of the Discovery Ridge facility is to be completed later this year, with operations beginning in 2020. Once operational, NWMI will have a nominal weekly production capacity of 3,500 six-day curies, with the capability of producing an additional 1,500 six-day Ci during surge demand, according to the company's presentation. The term "six-day curie" represents the number of curies present in a Mo-99 shipment six days after it leaves the production facility.

Photo: Niowave

Two Niowave employees load a subcritical uranium target assembly for irradiation.

Niowave

Founded in 2005 as a spin-off from Michigan State University's Facility for Rare Isotope Beams, Niowave is involved in the research, design, manufacturing, and operation of superconducting electron linear accelerators. Currently, the company is building production facilities in the Lansing area in hopes of capturing a significant fraction of the existing medical imaging market.

The company's process of producing Mo-99, known as the LEU-Modified Cintichem Process, uses accelerator-based neutron generation to fission uranium from LEU targets, without the need for nuclear reactors or HEU. Niowave has produced small quantities of Mo-99 and other isotopes under its NRC materials license, and the company said it will seek additional amendments to its license as it scales up production and expands to other facilities. Niowave plans to have only 99 kilograms of LEU enriched to 9.75 percent U-235 at its production facility. By keeping the quantity and enrichment of LEU below this threshold, the company said it avoids the NRC's stricter physical protection and nuclear material control and accounting system requirements. The company is aiming at beginning commercial production by 2025 in a facility that can produce 1,550 six-day Ci per week, with a second facility with the same capacity to open by 2027.

In addition to Mo-99 production, Niowave will harvest other beta-emitting radioisotopes for sale to medical, research, and pharmaceutical organizations, including strontium-89, praseodymium-143, neodymium-147, promethium-149, and iodine-131. The company is also able to produce alpha emitters using radium targets. Niowave said that its NRC license and its expertise in superconducting electron linear accelerators will position the company to take the lead in producing alpha- and beta-emitters for cancer therapies. Sales of the additional isotopes are expected to support Niowave's operating and expansion costs.

SHINE

Similar to Niowave, SHINE Medical Technologies' method of Mo-99 production uses accelerator-based neutron generation to induce a subcritical reaction in LEU targets. Instead of using solid targets, however, SHINE's system uses an aqueous target solution (enriched to 19.75 percent U-235). According to SHINE, using liquid LEU targets simplifies the production process, allowing the company to collocate its irradiation and processing facilities. SHINE's neutron generators—what it calls the heart of its system—are being supplied by Phoenix (formerly Phoenix Nuclear Labs), the company SHINE was spun off from. SHINE said that it expects to produce around 4,000 six-day Ci per week once operations start in 2020, although the company's operating license is based on producing 8,000 six-day Ci per week (*NN*, June 2018, p. 32).

Also like Niowave, SHINE is hoping to expand into the production of other medical radioisotopes in addition to Mo-99. On May 15, the company announced that it has signed a licensing agreement with the Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences (IOCB), giving SHINE the exclusive rights to a separation technique for producing lutetium-177, which is used in cancer therapies, from rare earth metals. According to SHINE, the IOCB separation method will allow SHINE to rapidly and efficiently separate Lu-177 from irradiated ytterbium-176 targets, producing a highly concentrated Lu-177 product known as "non-carrier-added" or "high-specific-activity" Lu-177. In addition to irradiation and separation capabilities, SHINE is also pursuing the ability to create its own Yb-176 starting material. **NN**