Improve the regulation policies and standards to promote a quality development of innovative radiopharmaceuticals industry

Novartis

Executive Summary

Nuclear technology, as a modern cutting-edge high technology, is widely applied across various sectors of the national economy. In healthcare, nuclear medicine, which uses radionuclide to diagnose, treat and research diseases, plays an irreplaceable role in the diagnosis, treatment and prognosis of various diseases. Radiopharmaceuticals, as a special category of drugs and a cornerstone of modern nuclear medicine, enable effective diagnosis and treatment for various diseases with the radiation emitted by the contained radioisotopes.

Clinical trials have shown that radioligand therapy benefits patients with gastroenteropancreatic neuroendocrine tumors and metastatic castration-resistant prostate cancer. Ongoing clinical research on more indications suggests that it shows promise in potentially treating other cancers, including brain malignant tumors (glioblastoma), breast cancer, lung cancer, and digestive tract tumors. The country attaches great importance to cancer prevention and treatment, and has set up the Cancer Prevention and Treatment Action in the special actions of the *Healthy China Action (2019-2030)*. Radioligand therapy offers a promising opportunity to advance the Healthy China Initiatives.

Over the past decades, China has made significant strides in the research, development and clinical application of radiopharmaceuticals. Thanks to the release of supportive policies constantly in recent years, the industry has been developing fast. In October 2024, the China Atomic Energy Authority, along with eleven other ministries, issued the *Three-year Action Plan for Quality Development of Nuclear Technology Application Industry (2024-2026)*, further boosting industry confidence. Despite advances in radiopharmaceuticals and growing clinical demand, China's pharmaceuticals industry faces several challenges: (a) improving the clinical application system of nuclear medicine and recognizing the technical service value of nuclear medicine departments, (b) balancing radiation safety regulations with practical clinical applications and transportation, (c) enhancing the specifications for new radionuclide radiopharmaceuticals and protection standards in medical institutions, and (d)

clarifying policies and regulations for research, management, and approval of radiopharmaceuticals and their components.

The nuclear medicine industry has emerged as a key area for developing new quality productive forces. The government has already identified the radiopharmaceutical industry as one of the strategic emerging industries and foundations for quality development of China's healthcare sector. In support of the accomplishment of these goals, Novartis would like to propose the below recommendations, to foster a sustainable environment that enables the development of radiopharmaceuticals industry, with all relevant stakeholders.

1. Strengthen coordination and optimize the clinical application system of nuclear medicine

- Keep promoting the establishment of nuclear medicine departments in tertiary hospitals. Include the development of nuclear medicine departments as one of the key assessment indicators for evaluation and review of new tertiary hospitals. Select several tertiary hospitals in major cities and upgrade their infrastructures of nuclear medicine department, or establish nuclear medicine specialized hospitals equipped with first-class infrastructure in key regions, to improve the basic layout of clinical application of new radioligand therapy.
- Optimize the application and creation of medical service fees of new technologies, such as cutting-edge radiopharmaceuticals therapies.

2. Scientifically differentiate radiopharmaceuticals from other radioactive substances, balancing radiation safety with clinical needs

- Dynamically adjust the radionuclide quota in medical institutions based on clinical needs, optimize the resources allocation of clinical radionuclide therapies, and flexibly reduce the restriction of radionuclide quota for radiopharmaceuticals use.
- Standardize radiopharmaceutical transportation regulations nationwide, creating unified rules and exploring exemptions within safe and controllable radioactive activity level.

3. Optimize relevant standards of clinical application for radiopharmaceuticals to lead quality development of the industry

- Develop radiation safety guidelines for clinical use of new therapeutic radionuclide (e.g., ^{177}Lu), including patient discharge standards, to

promote a standardized clinical application of these new radionuclide solutions.

- Improve radiation safety regulation standards for waste management in nuclear medicine, aligning with clinical practice and current needs, to continuously improve the optimal level of radiation protection and safety in nuclear medicine departments.

4. Improve the relevant guidelines for radiopharmaceuticals registration to further encourage radiopharmaceuticals research and development

- Revise the *Administrative Measures for Radiopharmaceuticals* and release registration related supporting documents to clarify the definition, management attribute, registration pathway, and technical requirement of radiopharmaceuticals and components.
- Promote the formulation of implementation regulations and technical guidelines to better implement supporting policies of radiopharmaceuticals review and approval.

Novartis looks forward to working more closely with the government and other key stakeholders to proactively address existing and emerging challenges, and creating a more dynamic policy environment. We are dedicated to promoting the development of innovative radiopharmaceuticals industry by improving the regulation and standards, to ultimately better respond to patients' unmet medical needs.

1. Situation Analysis

Despite significant advancements in cancer diagnosis and treatment technologies in recent years, treatment options remain limited for many patients, especially for those with metastatic or rare cancers.[1] Cancer, a serious global public health issue, needs new treatment to improve survival rate and quality of life.[2] In the past decade, China has witnessed an increase in the number of cancer incidences and deaths, leading to an elevated cancer burden.[3] According to data released by the China National Cancer Center, in 2022, there were 4,824,700 new cancer cases in China, with an incidence rate of 206.01 per 100,000, and the total number of cancer deaths was 2,574,200, with a mortality rate of 96.47 per 100,000.[4]

China has attached great importance to cancer prevention and treatment, and has established the Cancer Prevention and Treatment Action as one of the 15 special actions under the *Healthy China Action*, aiming to achieve original breakthroughs in cancer prevention and treatment technologies.[5] With an increase in health awareness and healthcare spending, as well as an acceleration in population aging and rising incidence rate of cancer, heart diseases and neurodegenerative diseases, there is a growing need for diagnosis and treatment services among residents. As a result, the demand for innovative technologies, therapies and drugs is also expected to increase. Radioligand therapy (RLT), an emerging treatment method, has demonstrated remarkable clinical benefits in cancer diagnosis and treatment, with exciting prospects and significance in promoting the *Healthy China Initiatives*.

1.1 Innovative radiopharmaceuticals play an irreplaceable role in cancer diagnosis and treatment.

Nuclear technology, a modern, cutting-edge high technology, has been extensively applied across various sectors of national economy, including industry, agriculture, environmental protection, public security, and healthcare, significantly contributing to the development of science and technology, economy and society.

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1 Rahbar K, Bode A, Weckesser M, et al. Radioligand Therapy With 177Lu-PSMA-617 as A Novel Therapeutic Option in Patients With Metastatic Castration Resistant Prostate Cancer. Clin Nucl Med, 2016, 41(7):522-8

2 Khan S, Krenning EP, van Essen M, et al. Quality of life in 265 patients with gastroenteropancreatic or bronchial neuroendocrine tumors treated with [177Lu-DOTA0,Tyr3]octreotate. J Nucl Med, 2011,52(9): 1361-8

3 Rongshou Zheng, Siwei Zhang, Hongmei Zeng, et al. Cancer incidence and mortality in China, 2016. Journal of the National Cancer Center, 2022, 2(1):1-9

4 Bingfeng Han, Rongshou Zheng, Hongmei Zeng, et al. Cancer incidence and mortality in China, 2022. Journal of the National Cancer Center (2024), doi: https://doi.org/10.1016/j.jncc.2024.01.006

5 National Health Commission. Notice on Printing and Distributing Healthy China Action - Cancer Prevention and Treatment Action Implementation Plan (2023-2030). http://www.nhc.gov.cn/ylyjs/pqt/202311/18bd5bb5abc74ebc896f9d5c9ca63422.shtml

In the field of healthcare, nuclear medicine, utilizing radionuclide to facilitate the diagnosis, treatment and research of various diseases, has been widely applied in cancer diagnosis and treatment, myocardial imaging and heart disease diagnosis, and the monitoring of neurodegenerative diseases, providing new means and more effective ways for early disease diagnosis and precise treatment.[6] Radiopharmaceuticals are fundamental to the development of nuclear medicine, leveraging the radiation emitted by radionuclide to diagnose and treat diseases. These radiopharmaceuticals are predominantly classified into diagnostic ones and therapeutic ones based on their intended usages. RLT, innovative targeted therapeutic radiopharmaceuticals with safe dosage, will barely be affected by conventional tumor drug-resistance mechanisms.[7] In contrast to conventional tumor treatment methods (chemotherapy, radiotherapy, and surgery), RLT can selectively target and bind to corresponding tumor cells, killing them with radiation energy. In this way, due to the appropriate radiation distance, it can minimize damage to healthy cells, achieving the goal of precise treatment.[8] Therefore, RLT exhibits the characteristic of precise targeting, potent killing, and limited damage.[9]

Evidence from clinical trials has demonstrated the benefits of RLT to patients with gastrointestinal pancreatic neuroendocrine tumors[10] and metastatic castration-resistant prostate cancer.[11] Its special mechanism of action is also applicable to other cancers, improving the survival rate and quality of life for cancer patients.[12] Ongoing clinical research on more indications suggests that RLT shows promise in providing alternative treatment options for patients with other cancers, including brain malignant tumors (glioblastoma), digestive tract tumors, lung cancer, and breast cancer.[8,13]

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6 Czarniecki M, Mena E, Lindenberg L, et al. Keeping up with the prostate-specific membrane antigens (PSMAs): an introduction to a new class of positron emission tomography (PET) imaging agents. Translational Andrology and Urology, 2018, 7(5):831-843

7 George Sgouros, Lisa Bodei, Michael R. McDevitt, et al. Radiopharmaceutical therapy in cancer: clinical advances and challenges. Nature Reviews, 2020,19:589-608

8 Society of Nuclear Medicine & Molecular Imaging. Fact Sheet: Radiopharmaceutical Therapy and Prostate Cancer.

9 Sartor O, De Bono J, Chi KN, et al. Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer [J]. New England Journal of Medicine, 2021, 385(12): 1091-1103.

10 Navalkissoor S, Gnanasegaran G, Grossman A. Optimisation of radioligand therapy in neuroendocrine tumours: Current and evolving evidence. J Neuroendocrinol. 2022, 34(11):e13208

11 Mike Sathekge, Frank Bruchertseifer, Mariza Vorster, et al. mCRPC Patients Receiving 225Ac-PSMA-617 Therapy in the Post-Androgen Deprivation Therapy Setting: Response to Treatment and Survival Analysis. Journal of Nuclear Medicine. 2022, 63 (10): 1496-1502; DOI: 10.2967/jnumed.121.263618

12 Malandrino P, Mazzilli R, Puliani G, et al. The Effects of Radioligand Therapy on Quality of Life and Sexual Function in Patients with Neuroendocrine Neoplasms. Cancers. 2023,15(1):115

13 M. J. M. Uijen, Y. H. W. Derks, R. I. J. Merkx, et al. PSMA radioligand therapy for solid tumors other than prostate cancer: background, opportunities, challenges, and first clinical reports, European Journal of

1.2 Supported by government policies, China's radiopharmaceuticals industry has developed rapidly with abundant pipelines and continuous investment.

China's radiopharmaceuticals industry has developed rapidly driven by supportive government policies. In 2021, the China Atomic Energy Authority (CAEA) and seven other ministries jointly issued the *Medium- and Long-Term Development Plan for Medical Isotopes (2021-2035)* [14] (the "Development Plan"), proposing to achieve full coverage of nuclear medicine departments in tertiary comprehensive hospitals by 2025, which has accelerated the quality development of the radiopharmaceuticals industry based on medical isotopes. In 2024, the CAEA and eleven other ministries issued the *Three-year Action Plan for Quality Development of Nuclear Technology Application Industry (2024-2026)*[15], encouraging the establishment and improvement of characteristic nuclear medical institutions in areas with mature conditions and supporting regions with sound infrastructures in the nuclear technology application industry to take the lead in piloting and building high-level nuclear technology application industry clusters. To encourage radiopharmaceuticals research and development (R&D) and application, in 2023, the National Medical Products Administration (NMPA) issued the *Opinions on Reforming and Improving the Review and Approval Management System for Radiopharmaceuticals* (GUOYAOJIAN YAOZHU [2023]No.20) [16], and the National Health Commission and ten other ministries jointly issued relevant breakthrough plans to promote radiopharmaceuticals R&D and application. In December 2024, the State Council issued the *Opinions on Comprehensively Deepening the Reform of Drug and Medical Device Regulation to Promote the Quality Development of the Pharmaceutical Industry* (GUOBANFA [2024]No.53) [17] to encourage clinical-value-oriented radiopharmaceuticals innovation and grant prioritized review and approval to radiopharmaceuticals registration as an enhancement to the radiopharmaceuticals review system. Some provinces have proactively adopted the *Development Plan*, treating nuclear medicine industry as a crucial part for developing new quality

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Nuclear Medicine and Molecular Imaging, 2021,48(13): 4350-4368

14 China Atomic Energy Authority. Notice on Issuing the *Medium- and Long- Term Development Plan for Medical Isotopes (2021-2035).* http://www.caea.gov.cn/n6758881/n6758890/c6812195/content.html

15 China Atomic Energy Authority. Notice on Issuing the *Three-year Action Plan for Quality Development of Nuclear Technology Application Industry (2024-2026).* https://www.caea.gov.cn/n6760339/n6760347/c10625020/content.html

16 National Medical Products Administration. Opinions on Reforming and Improving the Review and Approval Management System for Radiopharmaceuticals. https://www.nmpa.gov.cn/directory/web/nmpa/zhuanti/ypqxgg/ggzhcfg/20230425160128160.html

17 General Office of the State Council. Opinions on Comprehensively Deepening the Reform of Drug and Medical Device Regulation to Promote the Quality Development of the Pharmaceutical Industry. https://www.gov.cn/zhengce/zhengceku/202501/content_6996117.htm

productive forces. Implementation guideline opinions on the quality development of the medical isotope industry and the radiopharmaceuticals industry at provincial level[18,19]as well as supporting implementation plans[20] have been formulated, aiming to build national leading demonstration highlands for the nuclear medicine industry.

The release of a series of favorable policy documents has provided effective guidance and best practices nationwide, leading to the acceleration of China's radiopharmaceuticals industry layout. Several national-level platforms have been approved and established. The layout of nuclear technology application has been prioritized, with industry clusters taking shape[21] one after another in the growth pole areas, such as the Yangtze River Delta, the Pearl River Delta, the Bohai Rim, and the Chengdu-Chongqing Economic Zones. National and regional medical isotope industry alliances[22] and nuclear medicine alliances[23] have been established, and ecosystems[24] have been built. Foreign-funded pharmaceutical companies are accelerating their domestic pipelines and continuous investment, commencing the construction of radiopharmaceuticals manufacturing bases, and expediting the introduction of innovative RLT[25]. The nuclear medical and health industry is steadily moving forward with accelerating radiopharmaceuticals R&D and application. Over the past two years, there has been a gradual increase in R&D and registration applications of radiopharmaceuticals. Beginning in 2025, China will witness the launch of several new radiopharmaceuticals, which will significantly benefit the large population of cancer patients and contribute to the realization of a 46.6% 5-year survival rate for cancer cases by 2030.

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18 Sichuan Provincial People's Government. Opinions on Promoting the Quality Development of Nuclear Medical Industry.
https://www.sc.gov.cn/10462/zfwjts/2024/7/25/01472cc977b94a2293c6e58018ac6d04.shtml

19 Defense Mobilization Office of Zhejiang Province. Announcement on Public Solicitation of Opinions on the *Implementation Opinions on Promoting the Development of Medical Isotope Industry in Zhejiang Province (Exposure Draft)*. http://rfb.zj.gov.cn/art/2025/1/3/art_1229732596_58943067.html

20 Sichuan Province National Defense and Science and Technology Office. Implementation Plan for the Critical Project of Nuclear Medicine Industry Chain of Sichuan Province.
https://www.scjg.gov.cn/news/5493.html

21 CNR News. Chinese Think Tank Report: Where is the trillion market of China's nuclear technology application? https://china.cnr.cn/gdgg/20230529/t20230529_526268180.shtml

22 Chinese Academy of Engineering. The Founding Meeting of National Medical Isotope Industry Alliance Was Held in Chinese Academy of Engineering.
https://www.cae.cn/cae/html/main/col84/2023-05/11/20230511145552665910831_1.html

23 China Isotope & Radiation Corporation. China Isotope & Radiation Corporation Supported the Launch of the Shandong Nuclear Medicine Alliance in China.
https://mp.weixin.qq.com/s/5jAX02H-9DuZDgYgHs3aWA

24 Novartis Group. From Leadership to Collaboration - Novartis works with multiple industry partners to build the Radioligand Therapy (RLT) ecosystem. https://mp.weixin.qq.com/s/74Tsi-pK_yJ5oQVQs9mR6Q

25 Novartis Group. Novartis' Radiopharmaceuticals Production Project in China Has Broken Ground.
https://mp.weixin.qq.com/s/i8Xxu2Ugc9yKiT0t877utQ

1.3 The radiopharmaceuticals industry has enormous development potential.

The nuclear medicine in China can be traced to 1956, and since then, with the rapid development of the national economy, the radiopharmaceuticals market in China has undergone significant expansion in recent years. After more than 60 years of development, notable progress has been made in China in radiopharmaceuticals R&D and application. The enthusiasm for investment and financing activities has also been increasing. According to statistics, in 2024, there were 11 financing events in China's radiopharmaceuticals industry, accounting for approximately half of the global radiopharmaceuticals financing events, with a total scale of over $350 million. The radiopharmaceuticals market has witnessed rapid growth in recent years and is expected to maintain a high growth rate in the next decade. According to industry reports, the compound annual growth rate (CAGR) of the radiopharmaceuticals market size from 2025 to 2030 is projected to reach 22.7%, with forecasts indicating a potential increase to $3.6 billion by 2030.[26] Given the rapid expansion of the market, the global radiopharmaceuticals market size is expected to exhibit a CAGR of 19.4%, growing from $10.2 billion in 2024 to $42 billion by 2032.[27]

However, the radiopharmaceuticals industry in China still requires further development in comparison with that of the United States and European countries. There is considerable room for improvement with regard to the clinical application and popularization of nuclear medicine, which stands in contrast to the vigorous development of China's nuclear energy sector. There are more diverse types of radiopharmaceuticals undergoing clinical or pre-clinical research abroad than in China.[28] In the United States, the number of patients receiving radiopharmaceuticals diagnoses and treatment exceeds 20 million annually, while in Europe, the figure stands at approximately 10 million.[29] In China, however, the number is less than 3.5 million, representing only about 30% of the global average. The radiopharmaceuticals used clinically in China are primarily domestic drugs, and many original new radiopharmaceuticals already in use abroad have not yet been introduced in China.[30] As of August 2024, the FDA had approved 67

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26 Frost & Sullivan, Blue Book on the Status and Future Development of China's Radiopharmaceuticals Industry.

27 Fortune Business Insights, Nuclear Medicine Market Size & Global Growth Report (2032), https://www.fortunebusinessinsights.com/industry-reports/nuclear-medicine-radiopharmaceuticals-market-101812

28 National Institutes of Health. Clinicaltrials database. https://clinicaltrials.gov.

29 World Nuclear Association. Radioisotopes in Medicine, https://www.world-nuclear.org/information-library/non-power-nuclear-applications/radioisotopes-research/radioisotopes-in-medicine.aspx

30 Shuming Peng, Yuchuan Yang, Xia Yang. Medical Radioisotopes and Drugs. Beijing: Science Press, Nov

radiopharmaceuticals, including 13 therapeutic radiopharmaceuticals, all of which were indicated for cancer treatment.[31] In China, a total of 106 radiopharmaceuticals have been approved for marketing, with domestic products accounting for 98.39%, and nearly 70% of the marketed radiopharmaceuticals were approved before 2000.[32]

As the number of RLT in the pipelines continues to increase and their approval for marketing is imminent, the clinical applications of these innovative radiopharmaceuticals for treating more patients will also increase rapidly. Therefore, it is imperative for the radiopharmaceuticals industry ecosystem in China to keep up with this innovative development trend and to build an environment that ensures the healthy and rapid development of the innovative radiopharmaceuticals industry so as to bring benefits to the patients timely.

2. Challenges

As innovative radiopharmaceuticals continue to emerge and the clinical demands of patients persistently increase, various challenges must be addressed for their comprehensive clinical application. At present, the development of radiopharmaceuticals still faces problems such as the regulatory system lagging behind technological innovation and the existing regulatory policies and technical standards being immature.[33] These challenges limit the promotion of radiopharmaceuticals clinical applications to some extent, making it difficult for radiopharmaceuticals to give full play to their advantages in the diagnosis and treatment of malignant tumors and other diseases. They also hinder the sustainable and quality development of the innovative radiopharmaceuticals industry and, to a certain extent, affect the healthy development of the national healthcare undertaking.

2.1 The need for an improved clinical application system of nuclear medicine

2.1.1 The nuclear medicine departments in tertiary hospitals are in need of further development, as infrastructure facilities require upgrades and

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2022.

31 Zhang, S., Wang, X., Gao, X. et al. Radiopharmaceuticals and their applications in medicine. Sig Transduct Target Ther 10, 1 (2025). https://doi.org/10.1038/s41392-024-02041-6

32 Moentropy Consulting. Chinese Radiopharmaceuticals Industry White Paper. https://yaorongyun-public.oss-cn-shanghai.aliyuncs.com/%E6%91%A9%E7%86%B5%E5%8C%BB%E8%8D%AF/%E3%80%90%E6%91%A9%E7%86%B5%E5%92%A8%E8%AF%A2%E3%80%91%E4%B8%AD%E5%9B%BD%E6%94%BE%E5%B0%84%E6%80%A7%E8%8D%AF%E7%89%A9%E4%BA%A7%E4%B8%9A%E7%99%BD%E7%9A%AE%E4%B9%A6-20241017%20%E6%B0%B4%E5%8D%B0%E7%89%88_%E7%BA%AF%E5%9B%BE%E7%89%88.pdf

33 Tran, H.H., Yamaguchi, A. & Manning, H.C. Radiotheranostic landscape: A review of clinical and preclinical development. Eur J Nucl Med Mol Imaging (2025). https://doi.org/10.1007/s00259-025-07103-7

clinical treatment capabilities must be enhanced.

The development of radionuclide therapy in China's nuclear medicine departments is currently marked by disparities, as evidenced by the relatively underdeveloped status of the discipline, which continues to encounter substantial difficulties and challenges in the establishment and improvement of nuclear medicine departments. According to data from the national survey of nuclear medicine in 2024,[34] among all tertiary hospitals in China, 1,069 (27.7%) have a nuclear medicine department, and 801 medical institutions equipped with 2,993 dedicated hospital beds in total can conduct nuclear therapy, with ^{131}I used the most, while the proportion of novel radiopharmaceuticals treatment is less than 1%. The unique nature of nuclear medicine departments necessitates high requirements on hardware infrastructure, equipment and space. The receptions and operations of radiopharmaceuticals must be conducted by HCPs in designated locations that adhere to national regulations. Certain administration processes must be carried out and observed in isolation in radionuclide therapy wards or specialized treatment rooms within the nuclear medicine department. However, the limited availability of qualified hospitals and hospital beds often results in prolonged waiting periods (weeks or months) for patients, potentially compromising the optimal treatment timing.

2.1.2 The policies to create and revise radiopharmaceuticals related medical service fees are yet to be improved.

The long-term low pricing of radiopharmaceuticals related medical services in China fails to reflect their disciplinary characteristics and the technical service value of medical personnel, affecting the accessibility of medical services. For instance, the absence of a price information sharing mechanism and variations in price adjustment cycle, range and amplitude have led to substantial price differences in radiopharmaceuticals based medical services among hospitals in different provinces and cities. The medical service fees in the nuclear medicine department, unlike conventional ones, are technically complex and highly risky, but the mechanism for their pricing remains ambiguous. The establishment of reasonable prices for new medical service fees in the nuclear medicine department, based on the characteristics of the *National Technical Specifications for Medical Service Fees*[35] and requirements from relevant documents, has become an issue in price-setting for nuclear medicine in various provinces.

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34 Chinese Society of Nuclear Medicine. A Brief Report on Results of National Survey of Nuclear Medicine in 2024. Chinese Journal of Nuclear Medicine and Molecular Imaging, 2024,44(10): 617-618

35 National Health Commission, National Bureau of Traditional Chinese Medicine, National Bureau of Disease Control. Notice on Issuing Technical Specifications for National Medical Service Projects (2023 version). http://www.nhc.gov.cn/caiwusi/s7785t/202309/914aec9618944ee2b36621d33517e576.shtml

2.2 Radiopharmaceuticals are regulated as radioactive substances in clinical use and transportation, overemphasizing their radiation safety

The present regulatory framework for radiopharmaceuticals exhibits an excessive emphasis on radiation safety, resulting in a substantial overestimation of the associated risks. Radiopharmaceuticals are managed as radioactive substances during the circulation and utilization, thus disregarding their inherent characteristics of radiopharmaceuticals as medicines that necessitate assurance of both safety and efficacy, as well as their limited shelf-life and stringent requirements for logistics and distribution.

2.2.1 Radionuclide quota restrictions fail to meet the growing needs of patients.

Medical institutions engaging in radionuclide therapy are obligated to submit an application to the relevant authorities for licenses of a certain Class, including the *Radiopharmaceuticals Use License* (Classes III and IV) and the *Radiation Safety License*, which must specify specific treatment radionuclide. This process entails multiple administrative approval procedures with protracted cycles, making it arduous to obtain. The radionuclide dosage is constrained by the workplace level (typically Class B), with limitations on the maximum daily equivalent operating amount and maximum equivalent annual amount of a single radionuclide, as specified in the *Radiation Safety License*. The application for new radionuclide or the augmentation of existing radionuclide's dosage necessitates additional approval, which can sometimes require the renovation of existing hardware facilities in the department, all of which hinders the expansion of clinical research and utilization of radiopharmaceuticals in medical institutions. According to investigations, as of January 2025, only less than 40 hospitals in China had ^{177}Lu quota of 30-curie.

2.2.2 Over-regulation of radiopharmaceuticals road transportation significantly increases the time and cost for patients to access these drugs.

Radiopharmaceuticals are transported and managed as Class VII dangerous goods - radioactive substances. However, the existing regulations for the transportation of dangerous goods primarily apply to the road transportation of bulk dangerous goods. Transportation regulations for radioactive substances[36] clarify the transportation qualifications and requirements; nevertheless, it is difficult to implement these requirements in practice. For instance, some cities impose

36 Ministry of Transport. Decision on Amending the *Regulations on the Administration of Road Transport of Radioactive Materials* (Decree No. 17 of 2023 of the Ministry of Transport of the People's Republic of China). https://xxgk.mot.gov.cn/2020/jigou/fgs/202312/t20231204_3961953.html

restrictions on the operating hours of special vehicles within city centers[37], while the short shelf-life of some radiopharmaceuticals poses a heightened time sensitivity in terms of transportation when compared to conventional goods. Consequently, the consistent provision of medication to patients becomes uncertain, potentially resulting in missed opportunities for optimal diagnosis and treatment. Furthermore, the number of qualified transportation organizations is limited since numerous provinces and cities have not issued new Class VII dangerous goods transportation license for years, therefore, making costs associated with radiopharmaceuticals transportation and management constantly stay at a high level. For instance, the cost of transporting a dose of ^{177}Lu radiopharmaceutical product from Beijing to Xi'an exceeds $2,000[38]. It is evident that China has not yet developed specific radiopharmaceuticals related safety transportation measures with its uniqueness. The focus of the current regulatory framework is not on radiopharmaceuticals, and there is an absence of a scientific and rational, hierarchical and classified regulatory system for radiopharmaceuticals transportation safety, which poses a potential threat to patients' health and increases economic burden on patients, families, and medical institutions seeking radiopharmaceuticals treatment.

2.3 The standard system for scientific application of new radiopharmaceuticals needs to be improved

2.3.1 Regulations and specifications for the clinical application of new radiopharmaceuticals need to be formulated.

The clinical application of ^{177}Lu RLTs in China remains at start-up stage, with clinical practice predominantly informed by experiential knowledge. A normalized diagnosis and treatment pathway and relevant radiation protection guidelines (including patient discharge standard) have not yet been established based on scientific methods. The absence of radiation protection standards for patients discharged after receiving ^{177}Lu new radionuclide treatments has led to a tendency among medical institutions to refer to the standards applicable to ^{131}I-based thyroid cancer treatment, which necessitates hospitalization for three to four days, the safety characteristics of the new radionuclide ^{177}Lu not been scientifically considered. This has resulted in a waste of medical resources, as many patients are unable to receive timely treatment due to the limited availability of nuclear medicine resources in China.

2.3.2 The criteria for radioactive waste management in medical institutions

37 Yeehong Business School. Research Project Report on the Regulatory System of Radiopharmaceuticals in China.

38 Data from private market research.

need to be optimized.

The *Radiation Protection and Safety Requirements for Nuclear Medicine* (HJ 1188-2021), promulgated in 2021, establishes stringent criteria on monitoring radioactive liquid waste discharge within medical institutions. To address industry concerns regarding nuclear medicine radiation protection standards, the Ministry of Ecology and Environment issued the *Reply Letter on Consultation of Relevant Provisions of Nuclear Medicine Standard*[39](the "Reply Letter"), clarifying the issues in HJ 1188-2021, such as the discharge of radioactive wastewater containing ^{131}I, and outlining three optional methods for the disposal of such wastewater. However, in practice, ecological and environmental departments at various levels have divergent interpretations of this policy, and many of them do not even fully comply with the Reply Letter during environmental impact assessment, which have, to some extent, restricted the establishment and development of nuclear medicine departments. Moreover, the discharge requirements for radioactive wastewater containing ^{131}I, as stipulated in HJ 1188-2021, are derived from monitoring data and calculated with reference to the requirement of total $\beta \leq 10$ Bq/L in the national standard, *Integrated Wastewater Discharge Standard* (GB 8978-1996), since 1998, with consideration given to other comprehensive factors. In light of the continuous emergence of new therapeutic radionuclide and the rapid advancement in nuclear medicine, it is imperative to optimize the monitoring indicators for radioactive liquid waste discharge in accordance with the development of clinical applications.

2.4 The regulations and guidelines pertaining to radiopharmaceuticals registration require enhancement

2.4.1 The definition, management attribute, registration pathway, and technical requirement of radiopharmaceuticals and related components haven't been clarified.

In China, the definition, management attribute, registration pathway, and technical requirement of radiopharmaceuticals and related components (radionuclide, chemical precursors, cold kits, radionuclide generators, etc.) haven't been clarified and there is a paucity of radiopharmaceuticals related specific technical guidelines, bringing about many challenges and uncertainties with respect to radiopharmaceuticals full-life-cycle management, to address which, the *Administrative Measures for Radiopharmaceuticals* requires further revision and supporting documents and guidelines related to radiopharmaceutical registration

39 Ministry of Ecology and Environment. The Reply Letter on Consultation of Relevant Provisions of Nuclear Medicine Standard.
https://www.mee.gov.cn/xxgk2018/xxgk/sthjbsh/202309/t20230913_1040761.html

need to be released as soon as possible.

2.4.2 The implementation guidelines for the supportive policies on radiopharmaceuticals review and approval have not been issued, rendering the implementation of these policies unfeasible.

The document issued by NMPA (GUOYAOJIAN YAOZHU [2023] No. 20) explicitly delineates a series of supporting measures specific to radiopharmaceuticals, including the formulation and refinement of the requirement for review acceptance of radiopharmaceuticals during the acceptance stage, and the improvement in guidance during application; the establishment of dedicated radiopharmaceuticals channel during review stage and a separate review sequence; the optimization of working mechanisms for radiopharmaceuticals registration test and verification; the encouragement of launched radiopharmaceuticals to transfer their production from overseas to domestic sites; and the improvement of technical guidance system for radiopharmaceuticals R&D in China. However, it is difficult to implement these supportive policies due to the absence of detailed implementation measures. It is therefore imperative to promote the detailing and implementation of these policies as soon as possible.

3. Suggestions

3.1 Strengthen overall coordination and optimize the clinical application system of nuclear medicine.

3.1.1 Continue to promote the establishment and improvement of nuclear medicine departments in tertiary hospitals.

It is recommended that the establishment plan of nuclear medicine departments be specifically included as one of the key assessment indicators for the evaluation and review of new tertiary hospitals. In order to prospectively benefit more patients as soon as possible with more novel radionuclide-based therapeutic drugs right after approvals, it is necessary to provide financial support to a group of selected tertiary hospitals in major cities to upgrade and renovate their hardware facilities, such as decay pools, wards, and observation areas in their nuclear medicine departments. Furthermore, strategically establish specialized nuclear medicine treatment hospitals equipped with first-class infrastructure in key regions. This could greatly enhance the diagnosis and treatment capabilities for new radiopharmaceuticals and benefit the surrounding areas, improving the basic layout for the clinical application of new RLT. Some provinces in China have already proposed specific measures[18] and implementation plans[20] for establishment and improvement of comprehensive nuclear medicine clinical application system, which can serve as references for the formulation of relevant

documents at provincial and national level.

3.1.2 Optimize the application and creation of medical service fees involving new technologies, such as cutting-edge radiopharmaceuticals treatment.

Encourage the pricing of radiopharmaceuticals treatment's medical service items to be clinical-value-oriented, optimize the filing and approval process for new technologies, and expedite the clinical application of new therapies. The management rules and pathways for converting radioactive diagnosis and treatment services into charging items should be defined, and the boundaries among charging items, clinical diagnosis and treatment technical specifications in nuclear medicine, and the in-hospital use, management, and storage conditions of radiopharmaceuticals should be clarified. Establish a charging system easy to evaluate and regulate and with adaptability to clinical diagnosis and treatment, which could better reflect the disciplinary characteristics, protection requirements and innovation, as well as the technical service value of medical personnel.

3.2 Distinguish radiopharmaceuticals from other radioactive substances in a scientific way, balancing radiation safety with clinical needs.

3.2.1 Dynamically adjust the radionuclide quota in medical institution based on clinical needs, optimize the allocation of clinical resources for radionuclide therapy, and flexibly reduce the limit to the total radionuclide amounts for radiopharmaceuticals use.

With the characteristics of medical radionuclide considered, measures should be taken to optimize the pertinent policies for environmental impact assessment and radiation safety licensing of medical institutions. With the support of regulatory authorities, proactive intervention in the review of relevant license applications should be made and the regulatory approval process for licenses such as the *Radiation Safety License* required for the in-hospital use of radiopharmaceuticals should be streamlined. Additionally, the access threshold for environmental protection assessment should be reduced to assist hospitals in obtaining qualifications. During radiation safety regulation of radionuclide, the restrictions on radionuclide utilization in hospitals as well as the total radionuclide amount limit should be progressively reduced. It is necessary to explore pilot solutions to support the gradual upgrading of workplace level according to the characteristics of radionuclear medicine and increase the quota of new radionuclide by optimizing the allocation of clinical resources for radionuclide therapy.

3.2.2 Make radiopharmaceuticals transportation more scientific and normalized. Establish nationally unified rules for radiopharmaceuticals

transportation and explore gradual exemptions for transporting radiopharmaceuticals with safe and controllable radioactive activity levels.

As Class III radioactive substances, radiopharmaceuticals have a comparatively limited radiation impact on human health or the environment after being released.[40] Their short half-lives mean that delays in transportation can have serious consequences, such as patients not receiving treatment in a timely manner, which varies a lot from other radioactive substances. To address these concerns, it is recommended to: promote the approval process by classification; promote the scientific and normalized management of radiopharmaceuticals transportation; optimize the license and approval procedures for road transportation; establish "green channel" approval model; simplify the requirements for transport vehicles and personnel; encourage more large domestic logistics enterprises to undertake radiopharmaceuticals transportation; gradually improve the transportation and logistics distribution capacity; and give priority to radiopharmaceuticals transportation. It is also necessary to formulate nationally unified regulations specifically for radiopharmaceuticals transportation, simplify the approval for low-risk products, and explore the feasibility of exemptions for radiopharmaceuticals transportation within safe and controllable radioactive activity levels. According to China's 2020 *Classification and Catalogue of Radioactive Substances*[41], a proposal has been made to offer the possibility of exemption from the regulation on the transportation of dangerous goods, if the maximum loading radioactivity of one vehicle is within the limit when delivering radiopharmaceuticals to hospitals, which provides an optional solution for transport exemption that can be further detailed and implemented.

3.3 Enhance the standards of clinical application for novel radiopharmaceuticals to drive quality development of the industry.

3.3.1 Develop guidelines for the clinical use of new therapeutic radionuclide (e.g., ^{177}Lu) RLTs to promote standardized and homogenized clinical application of these therapies.

In light of the recommendations outlined in the expert consensus for clinical practice[42,43] on ^{177}Lu-based RLT, there is a compelling rationale for expeditiously

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40 Regulations on the Safety Management of Radioactive Substance Transportation (Decree No. 562 of the State Council), https://www.mee.gov.cn/ywgz/fgbz/xzfg/200909/t20090923_161437.shtml

41 Ministry of Ecology and Environment. Notice on Publicly Soliciting Opinions on *Classification and Catalogue of Radioactive Substances* (Revised draft for comments). https://www.mee.gov.cn/xxgk2018/xxgk/xxgk06/202005/t20200506_777840.html

42 Cancer Nuclear Medicine Committee of China Anti-Cancer Association. Expert Consensus of 177Lu-labeled PSMA Radioligand Therapy for Clinical Practice of Prostate Cancer (2024 edition). China

formulating industry guidelines. This is poised to further propel the formulation of standards for standardized diagnosis and treatment centers of RLT, ensuring their equitable distribution and driving the normalization and homogenization of treatment across surrounding medical institutions. Research on ^{177}Lu-PSMA drugs conducted in many countries[44,45] suggests that outpatient treatment is feasible. Given the recognized safety benefits of the ^{177}Lu over ^{131}I with respect to physical properties, it is recommended that policy pilots be conducted in selected regions to assess solutions to shared challenges in promoting clinical application, such as considering the radiation dose equivalent rate measured at a distance of 1 meter from the patient after treatment with ^{177}Lu medication for 6 hours as meeting the discharge criteria (as recommended in the aforementioned expert consensus). Concurrently, national authority should initiate related monitoring and research activities to scientifically determine the radiation dose rates as the patient discharge standard after treatment. The formulation of pertinent guidelines and standards will help to ensure the efficacy and safety of new radionuclide drugs and ultimately contribute to the advancement of diagnosis and treatment level.

3.3.2 Further improve radiation safety regulation standards for radioactive waste in nuclear medicine to continually improve the optimal level of radiation protection.

In order to enhance its authority, it is recommended that the clarifications stated in the Reply Letter be formally incorporated into the revised version of HJ 1188-2021. It is also necessary to continuously strengthen training and publicity to ensure the consistent interpretation of clauses and the alignment of management requirements among ecological and environmental departments, which will allow the approval procedures of environmental impact assessment in accordance with the requirements of Reply Letter. It is further recommended to promote the adaptive upgrading of relevant indicators to international standards while considering the situation in China. For instance, the monthly average concentration limit for ^{131}I wastewater discharge set by the US Nuclear Regulatory Commission is 370 Bq/L.[46] In addition, the industry anticipates that

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Oncology, 2019,34(7):702-714.

43 Guobing Liu, Weihai Zhuo, Yucan Gu, et. al. Expert Consensus on Clinical Application of 177Lu-Prostate Specific Membrane Antigen Radioligand Therapy in Prostate Cancer. Chinese Journal of Clinical Medicine. 2024,31(5):844-850.

44 Federico Zagni, Luigia Vetrone, Andrea Farolfi, et al. Feasibility of 177Lu-PSMA Administration as Outpatient Procedure for Prostate Cancer. Journal of Nuclear Medicine November 2024, jnumed.124.268062; DOI: https://doi.org/10.2967/jnumed.124.268062

45 Federico Zagni, Luigia Vetrone, Andrea Farolfi, et al. Feasibility of 177Lu-PSMA Administration as Outpatient Procedure for Prostate Cancer. Journal of Nuclear Medicine November 2024, jnumed.124.268062; DOI: https://doi.org/10.2967/jnumed.124.268062

46 Nuclear Regulatory Commission.
https://www.nrc.gov/reading-rm/doc-collections/cfr/part020/appb/iodine-131.html

authority will consider the prospective increase in clinical needs, engage in continuous monitoring to accumulate evidence, and improve the requirements for discharge control indicators of radioactive liquid waste. Moreover, the industry calls for the refinement of HJ 1188-2021, the optimization and improvement of the relevant liquid waste discharge control indicators in GB 8978-1996, and the revision of the total β discharge requirements with reference to international practices. These actions will help ensure the continuous enhancement of the optimal level of radiation protection in nuclear medicine department.

3.4 Improve regulations and guidelines for Radiopharmaceuticals registration and further promote Radiopharmaceuticals R&D

3.4.1 Revise the Administrative Measures for Radiopharmaceuticals to clarify the definition, management attribute, registration pathway, and technical requirement of Radiopharmaceuticals and related components.

At present, both Europe and the United States have instituted explicit management pathway for components such as radionuclide generators and cold kits, and NMPA has clearly articulated its intention to "study and improve the management method and related requirement for generators and cold kits." Therefore, it is recommended that a comprehensive revision of the *Administrative Measures for Radiopharmaceuticals* be undertaken to enhance the management method for generators and cold kits, and to clarify the definition of Radiopharmaceuticals and related components (radionuclides, chemical precursors, cold kits, radionuclide generators, etc.) in conjunction with international practical experience. The regulation of generators as active pharmaceutical ingredients or adjuvant, and cold kits as radiopharmaceuticals preparations, should be pursued to obtain independent marketing authorization.

3.4.2 Promote the formulation of implementation regulations and technical guidelines to better implement supporting policies of radiopharmaceuticals review and approval.

The State Council document (GUOBANFA [2024] No.53) requires greater resource allocation to the review and approval of key innovative drugs with urgent clinical need, and advocates for the formulation of implementation and technical guidelines for radiopharmaceuticals review and approval supporting policies to ensure the consistent implementation of these policies. To benefit more Chinese patients as soon as possible, the review and approval process for novel radiopharmaceuticals applying for marketing authorization (especially those already launched overseas) must be expedited to promote early access to more advanced cancer treatment given the multiple benefits they bring, and optimize the process of transferring radiopharmaceuticals production from overseas to local

sites.

4. Conclusion

As stated in the Report to the 20th CPC National Congress, people's health is an important symbol of national prosperity and power. Biopharmaceuticals are making significant breakthroughs at an unprecedented pace, and innovative treatment solutions have the potential to improve and extend patients' lives. As radiopharmaceuticals play an increasingly prominent role in the diagnosis and treatment of major diseases, multi-level and diverse health needs will show a trend of explosive growth. In this era full of opportunities and challenges, collaboration among academia, industry, and authority is particularly important as the key to unlocking the full potential of radiopharmaceuticals. As a dedicated innovative medicines company, Novartis is a pioneer and leader in the development of radioligand precisely targeted medicines. Leveraging our expertise in such highly specialized technology, we are poised to support the Chinese government in its unwavering commitment to provide comprehensive and full-cycle health services to the people, in particular to promote the healthy development of the innovative radiopharmaceuticals industry and ultimately contribute to improving the health of Chinese people.