NOVARTIS

# 建设有竞争力的创新生态系统，惠及中国患者

## 以放射性药物为例的思考

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# 摘要

在生物医药领域改革和政策引导下，中国正从以仿制药为主迈向越来越注重创新生态系统。这不断吸引着全球领先制药企业加大在中国的投入，促进了创新水平提升，临床试验数量增加，药品可及性提高。

创新不仅是经济增长的引擎，也是应对包括人口老龄化、慢性病增加和未被满足的医疗需求等这些不仅影响医疗卫生领域的挑战的关键解决方案，并且有助于加强全球卫生领导力。

随着创新技术的不断发展，需要持续完善政策以鼓励研发并促进去适应创新。中国已在知识产权保护、监管框架和准入这三个领域取得了很大进展，这些领域的进一步政策完善可以促进创新药产业的快速发展，该产业是新质生产力[1]的一支重要力量。随着先进疗法的出现，特别是针对癌症治疗，这三个领域仍还有进步空间。

近年来癌症是药物创新较为集中的疾病领域，世界各地的科学家们正坚持不懈地开发新的治疗方法，然而仍有很多病人的治疗选择很有限，亟需新的治疗方案。

放射配体疗法是一种新一代创新型药物，已经用于多种不同类型癌症在不同阶段的治疗[2,3]。通过将放射性同位素与配体结合以直接靶向肿瘤细胞，能够杀伤肿瘤细胞，并最大限度减少对健康细胞的损害。放射配体疗法对于推动“健康中国”建设具有积极意义，对此我们倍感兴奋。然而，中国不断发展的放射性药物产业已经并将继续面临一些挑战，这也说明上述提及的三个

[1] 2024 年政府工作报告. https://www.gov.cn/zhengce/jiedu/tujie/202403/content_6936516.htm
[2] Bugani V, Battistelli L, Sansovini M, et al. Radioligand therapies in cancer: mapping the educational landscape in Europe [published online ahead of print, 2023 Apr 14]. Eur J Nucl Med Mol Imaging. 2023;1-7.
[3] Uijen MJM, Derks YHW, Merkx RIJ, et al. PSMA radioligand therapy for solid tumors other than prostate cancer: background, opportunities, challenges, and first clinical reports. Eur J Nucl Med Mol Imaging. 2021;48(13):4350-4368.

优先领域仍需持续提高。

本报告针对知识产权保护、监管框架和准入提供政策完善建议。此外，该报告亦为放射配体疗法这一高度创新治疗方案的发展建言：

**1. 持续加强知识产权保护，完善创新生态系统， 促进持续吸引投资**

可预测的和强健的知识产权保护对于企业持续研发投入至关重要，也是把放射配体疗法等创新治疗方案带给医疗卫生系统和患者的主要驱动力。

我们建议：

- 加强创新产品的知识产权保护，包括优化药品专利纠纷早期解决机制（即专利链接），尤其是使其能够覆盖更多的专利类型并有效地适用于所有药品类型。
- 加快实施新药的药品专利期限补偿制度。
- 制定并实施药品试验数据保护、儿童用药品和罕见病药品市场独占制度。

**2. 优化监管框架**

强健的药物监管体系有助于构建一个健全的生物医药生态系统。为了促进创新疗法的落地，可考虑以下建议进一步优化监管框架：

- 与国际标准保持一致，调整新药定义为在中国未上市的创新药物。
- 完善放射性药物审评审批。促进放射配体治疗药物的多手段患者筛选，建立和明确药物注册和管理的相关路径和要求。

**3. 完善准入政策，在鼓励创新的同时确保可负担性和可及性**

只有当患者能够使用到创新的药品时，创新才真正创造了价值。为了确保中国患者能够从创新中获益，我们呼吁继续改革准入环境，包括：

- 建立多层次医疗保障体系，完善价值评估框架，基于药品全生命周期中的价值维持可持续和可预测的价格。
- 存在重大专利侵权风险的药物不纳入国家集中带量采购。
- 将创新药的支付标准与定价分开，不对企业的药品定价进行干预和限制。

**4. 完善医疗卫生系统以适应创新疗法发展**

中国的医疗卫生系统取得了显著进步。然而，随着放射配体疗法等高度创新和前景广阔的治疗方案的发展，我们发现为了适应创新，医疗卫生系统仍需在以下方面进行改进：

- 优化多部门的监督和管理机制，并强化政策引导和多方合作。
- 加强规范化诊治。
- 增加政府对基础设施的投入，持续改善医疗资源配置。

随着中国发展壮大，创新的重要性怎么强调都不为过。中国政府的政策方向在全球范围都很有影响力。在庆祝以上成就的同时，必须看到仍需要持续改进，中国生物医药产业正在从以跟随式创新为主的时代加速向更加注重差异化创新和源头创新的时代迈进，通过优先完善上述领域，我们相信中国将能保持持续增长并成为全球的领导者。

## 现状分析

### 医药卫生创新的重要性

中国已成为全球制药领域的核心力量，正从以仿制药为主迈向越来越注重创新生态系统。在应对快速发展的医药卫生领域的复杂性时，了解中国的发展对于包括行业领袖、政策制定者和患者等相关方都至关重要。中国的发展是一个由改革和政策推动的战略转变，涵盖了药物从早期研究到患者可及的主要环节，这一战略转变不断吸引着全球领先制药企业的关注和参与，并为中国生物医药产业的发展带来了显著进步。

2024 年政府工作报告提出加速发展新质生产力是一个重点工作任务，其中包括发展前沿产业，如生命科学领域。诺华的战略与之高度一致，诺华具有包括放射配体疗法在内的五大技术平台，致力于为中国患者带来高质量的创新药物。

诺华在中国的新药及新适应症开发已实现 100%与全球保持同步，我们在华投资于药物生产和商业化，并会持续加大投资力度。中国现在是诺华全球第二大市场，也是增长最快的市场。更重要的是现在有更多中国患者能够从创新药物治疗中获益，医疗卫生体系更加高效，长期以来中国市场对外资吸引力不断增强。

**创新可以弥合差距，解决未满足的临床需求。**中国面临着诸多不仅影响医疗卫生领域的挑战，如人口老龄化、慢性病患者持续增加和未被满足的医疗需求。通过促进创新和提高创新疗法的可及性，有助于提高中国人民的健康水平和生活质量，同时建设一个更强大的国家。**创新促进经济增长和创造就业。**一个充满活力的生命科学领域可以创造更多就业机会，吸引投资，并促进 GDP 的增长。中国成为全球生物医药创新中心这一宏伟目标也依赖

于培育一个鼓励创造力、协作和创业的生态系统。**创新助于加强全球卫生领导力。**中国提出推动构建人类卫生健康共同体，倡导创新可以引领应对全球卫生挑战。与国际伙伴合作、知识分享和联合研究活动有助于中国成为负责任的全球参与者，为促进全球健康贡献中国力量。

## 中国推动创新发展的改革举措

中国政府将生物医药创新发展视为国家发展和经济增长的重要目标，《中华人民共和国国民经济和社会发展第十四个五年规划和 2035 年远景目标纲要》[4]将生物医药纳入国家重大创新领域。我们高度赞扬中国政府积极培育有利于创新的生态环境，以下三个领域过去一直是，未来也将是推动中国当前发展和未来发展的关键。在该报告后续部分，我们还以放射性药物（以下简称“放药”）为例概述了针对创新疗法相关产业的挑战和解决建议。

**完善监管框架**。更加优化的监管体系成为创新的催化剂。中国加入国际人用药品注册技术协调会（ICH），积极融入国际药品监管体系。国家药品监督管理局深化药品审评审批制度改革，加快了药品上市注册程序（包括突破性治疗药物程序、附条件批准程序、优先审评审批程序、特别审批程序等）[5]，极大鼓励了国内公司和跨国公司在华加大研发投入。

中国在临床试验数量和新药获批数量方面都取得了显著成效。基于公开数据诺华分析发现，中国的 II 期和 III 期临床试验数量从 2017 年到 2021 年增加了 100%，年复合增长率（CAGR）为 26%，而其他主要市场的 CAGR 则低至 4%-6%，有些甚至为负增长。近五年来，中国的新药上市数量仅次

[4] 中华人民共和国国民经济和社会发展第十四个五年规划和 2035 年远景目标纲要. https://www.gov.cn/xinwen/2021-03/13/content_5592681.htm?eqid=a14468700001730f000000026480655e

[5] 国家市场监督管理总局. 药品注册管理办法. https://www.gov.cn/zhengce/zhengceku/2020-04/01/content_5498012.htm

于美国[6]。中国的成功在于与全球市场的紧密链接，统一监管标准、促进跨境伙伴关系以及与国际通行做法保持一致都会扩大其全球影响。

目前中国对新药定义为在世界任何地方都未上市的新药[7]，而不仅仅是在中国未上市的新药。国家制定多项措施鼓励新药开发和加强 IP 保护，而这些措施通常与药物是否被定义为新药高度相关。因为新药定义的原因，很多国际上获批上市的创新药品却不能在中国享受相关激励措施，这将极大降低企业将国际创新药品引入中国的信心和速度。此外，新药的定义并未与国际制度接轨，如与中国 2021 年申请加入的高水平贸易协定《全面与进步跨太平洋伙伴关系协定》等国际条约并不一致。

**加大研发投入和知识产权保护。**强有力的知识产权保护是创新的基石，中国在该领域取得了实质性进展，增强了创新者的信心。中国建立了药品专利期限补偿制度和专利链接制度，专利期限补偿即将落地实施，用于补偿因药品审评审批而被占用的专利期，专利链接制度目的是于仿制药或生物类似药产品上市之前提供专利纠纷早期解决机制。近期公布的新版《中华人民共和国专利法实施细则》[8]为新药专利期限补偿制度落地实施提供了更具体的指引。

在 2022 年公布的《药品管理法实施条例（修订草案征求意见稿）》[9]中，我们欣喜看到关于儿童用药品市场独占和罕见病药品市场独占制度的框架性条款草案，相信这些制度的细化和落地，将有效地激励儿童用药品和罕见病

[6] IQVIA. Global Trends in R&D 2024: Activity, Productivity, and Enablers.
[7] 国家食品药品监管总局. 总局关于发布化学药品注册分类改革工作方案的公告（2016 年第 51 号）. https://www.nmpa.gov.cn/xxgk/ggtg/ypggtg/ypqtggtg/20160309151801706.html
[8] 国务院. 国务院关于修改《中华人民共和国专利法实施细则》的决定. https://www.gov.cn/zhengce/content/202312/content_6921633.htm
[9] 国家药品监督管理局. 国家药监局综合司公开征求《中华人民共和国药品管理法实施条例（修订草案征求意见稿）》意见. https://www.nmpa.gov.cn/xxgk/zhqyj/zhqyjyp/20220509222233134.html

药品的研发。

药品试验数据保护被许多国家和地区所广泛采用，其对激励创新同样发挥了至关重要的作用，保护了创新者的核心数据，在挑战和市场方面为创新者提供更高的可预测性，有利于推动生物医药产业的健康发展，我们理解中国持续致力于完善药品试验数据保护制度[10]，并且相信有效的药品试验数据保护将积极促进中国生物医药产业的发展。

知识产权执法上的典型案例也突显了政府对保护创新的承诺。我们积极支持中国政府继续完善知识产权保护体系，促进现有政策的落地实施，这将是吸引包括外国资本在内投资的关键驱动力。

中国在研发方面的投入需要与其远大目标相匹配。公私合作、支持风险投资和激励早期研究将共同推动创新，与学术界和初创企业的合作可以产生变革性的结果。

**市场准入改革。**近年来，中国的市场准入政策持续变化，中国医保事业稳定发展，截至 2022 年底，全国基本医疗保险参保人数为 134592 万人，参保率稳定在 95%以上；全国基本医疗保险基金总收入 30922.17 亿元，比上年增长 7.6%[11] 。自 2018 年成立国家医保局以来，已经连续 6 年开展国家医保药品目录调整工作，并建立了常态化、动态化的调整机制。尤其创新疗法的保障得到显著改善：新药从获批上市到纳入国家医保目录的时间，已从原来的 5 年左右降至 1 年多，80%以上的创新药能在上市后 2 年内进入国家医保目录[12]，这是一个巨大进步。而且，医保谈判也正逐步更加注重药品的临床

[10] 国家药品监督管理局. 国家药品监督管理局办公室公开征求《药品试验数据保护实施办法（暂行）》意见. https://www.nmpa.gov.cn/directory/web/nmpa/xxgk/zhqyj/zhqyjyp/20180426171801468.html

[11] 国家医疗保障局. 2022 年全国医疗保障事业发展统计公报. http://www.nhsa.gov.cn/art/2023/7/10/art_7_10995.html

[12] 国家医疗保障局. 国家医保局 2023 年国家基本医疗保险、工伤保险和生育保险药品目录调整新闻发布会实录. http://www.nhsa.gov.cn/art/2023/12/13/art_52_11685.html

价值而非只谈价格。

然而我们发现还是有一些创新药，由于价格谈判时降价幅度不足，无法进入国家医保目录，如近年来通过谈判和竞价新准入的医保药品，价格平均降幅达 60%，对新上市的创新药还是比较大的价格挑战。确保患者能用上不只为患者、更为医药卫生系统及社会带来价值的突破性疗法，同时确保一个可持续的医药卫生体系和有国际竞争力的药品定价，这并非易事。我们相信致力基于临床价值的评估和基于可预测价格的谈判机制对实现这些目标至关重要。

中国的药品集中带量采购（VBP）制度自 2018 年推出以来，经过多年的发展已日趋成熟，切实减轻了就医购药负担。但是出现了有些原研产品专利仍未过期的仿制药也被纳入到了国家集中带量采购。

最近一个关于新上市化学药品首发价格形成机制的文件在征求意见，其目的是鼓励以临床价值为核心的药物研发创新，支持优质创新药物的供应和公平可及，并充分发挥市场的决定性作用。行业期待这一机制能够进一步完善，可以将药品在自费使用阶段时，定价权交还给市场决定。

创新是中国发展壮大的基石。很少有国家能与中国政府政策方向的全球影响力相媲美，其对世界其他国家都产生了影响。在庆祝以上成就的同时，必须看到仍需要持续改进，中国生物医药产业正在从以跟随式创新为主的时代加速向更加注重差异化创新和源头创新的时代迈进，通过继续改革与不断完善，我们相信中国将能保持持续增长并成为全球的领导者。

### 癌症和放射性药物

癌症是药物创新较为集中的疾病领域，在 FDA 和 EMA 的 2023 年获批新药中，癌症是数量最多的治疗领域（分别占了新治疗药物的 21%和新活性

物质的 35%），癌症也在 2023 年国家医保谈判独家品种中占比最大（达到 18%）[13,14,15]。中国和世界各地的科学家们正不懈努力去寻找新的方法来识别、诊断和治疗癌症患者。创新药物已将某些癌症从绝症变为慢性病。

尽管近年来癌症领域的诊疗技术手段取得了极大进展，但仍有很多病人的治疗选择很有限，尤其是患有罕见、转移性的癌症患者[16]。癌症作为一个严峻的全球公共卫生问题，需要新的治疗方案来提高生存率和生活质量[17]。在过去十年时间里，中国的癌症发病和死亡人数持续上升，癌症负担不断增加[18]。根据国家癌症中心最新发布数据，2022 年中国有 482.47 万新发癌症病例，发病率为 201.61/10 万；癌症总死亡人数为 257.42 万，死亡率为 96.47/10 万[19]。

国家高度重视癌症防治工作，在健康中国行动的 15 个专项行动中设立了“癌症防治行动”，明确了到 2030 年要实现的目标，包括癌症防治体系进一步完善，规范诊疗水平稳步提升，癌症发病率、死亡率上升趋势得到遏制，总体癌症 5 年生存率达到 46.6%[20]。

为了实现这些目标，需要继续开展筛查计划，并提高创新治疗方案的可

[13] Baedeker, M, Ringel, M S, Möller, C C. 2023 FDA approvals: unprecedented volume at moderate value. Nature Reviews Drug Discovery, 2024, (23): 98

[14] European Medicines Agency (2023). Human Medicines Highlights 2023.

[15] IQVIA. Summary of 2017-2023 China NRDL Updates. January 8, 2024.

[16] 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

[17] 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

[18] 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

[19] 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

[20] 国家卫生健康委等. 关于印发健康中国行动—癌症防治行动实施方案（2023—2030 年）的通知. http://www.nhc.gov.cn/ylyjs/pqt/202311/18bd5bb5abc74ebc896f9d5c9ca63422.shtml

及。此外，新的治疗技术如放射配体疗法等取得了巨大进展，以治疗包括癌症在内的存在巨大未满足临床需求的疾病领域。

放射配体疗法是新一代创新型靶向治疗放药，其将配体与放射性同位素相结合，配体可靶向特定标志物。配体将放射性同位素引导到表达了特定标志物的肿瘤细胞，即使这些肿瘤细胞已扩散到全身。这种独特的作用机制可以通过物理辐射杀伤肿瘤细胞，同时最大限度减少对附近健康细胞的损害[21,22]。临床试验已证明，放射配体疗法为胃肠胰神经内分泌肿瘤[23]和转移性去势抵抗性前列腺癌[24]患者带来了良好获益，放射配体疗法的特殊作用机制也适用于其他癌症，提高癌症患者的生存率和生活质量[25]，正在进行的覆盖更多适应症或疾病领域的临床研究显示，放射配体疗法还将为其他癌症患者带来更多治疗选择，包括脑恶性肿瘤（胶质母细胞瘤）、消化道肿瘤、肺癌和乳腺癌等[26]。放射配体疗法治疗癌症的应用前景广阔，对推动“健康中国”建设具有积极意义，但也需要持续政策完善以支持不断出现的颠覆性创新。

这一新技术为患者带来了新的希望，但也给世界各地还未调整好其相应政策环境的医疗卫生体系带来了新的挑战。诺华作为包括放射配体疗法在内的先进疗法的先驱者，我们看到那些对变革持开放态度的国家通常在促进这

[21] Aboagye EO, Barwick TD, Haberkorn U. Radiotheranostics in oncology: Making precision medicine possible. CA Cancer J Clin. 2023;73(3):255-274. doi:10.3322/caac.2176
[22] Duan H, Iagaru A, Aparici CM. Radiotheranostics - Precision Medicine in Nuclear Medicine and Molecular Imaging. Nanotheranostics. 2022;6(1):103-117. doi:10.7150/ntno.64141
[23] Navalkissoor S, Gnanasegaran G, Grossman A. Optimisation of radioligand therapy in neuroendocrine tumours: Current and evolving evidence. J Neuroendocrinol. 2022, 34(11):e13208
[24] 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
[25] 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
[26] 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 Nuclear Medicine and Molecular Imaging, 2021,48(13): 4350-4368

一创新疗法可及性方面亦最为成功。

近年来在政策支持下，中国的放射性药物研究、开发和临床应用取得重要进展。八部委于 2021 年印发了《医用同位素中长期发展规划（2021-2035 年）》[27]（简称“《发展规划》”）之后，为以医用同位素为基础的放射性药物行业高质量发展按下了加速键，国家药监局印发了改革完善放药审评审批的相关意见[28]，以进一步鼓励放射性药品研发申报，国家卫健委等十一个部委也联合下发相关攻关方案以推动放药的研发和应用。

然而，医疗卫生系统仍需要进一步完善以适应放射配体疗法这一创新，尤其是在监督管理体系和顶层设计机制，审评审批，临床使用，以及核医学基础设施和能力等方面：（1）在中国放药监管涉及的部门较多，为多部门交叉管理，职责边际不清晰。（2）放射配体治疗药物患者的多手段筛选仍需进一步促进，药品的注册要求和路径有待建立和明确，包括化学/放射性核素前体的注册途径、发生器和冷药盒的监管、多个生产场地的管理方法，以及放药的本地注册检验等。（3）针对病人诊断、转诊和治疗的全流程的放药临床使用规范还尚未建立，规范化诊疗中心的建设标准也尚未形成，医疗机构核素配额还不足，放射性废物管理也待进一步优化。（4）核医学科基础和资源有待提升，还存在发展不平衡的情况，东南地区相对发展更好。虽然基础设施和人才资源短缺也是国际上共性挑战[2930]，中国仍然可以提前应对这一问题以增强其核医学能力。

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[27] 国家原子能机构, 等. 关于印发《医用同位素中长期发展规划（2021-2035 年）》的通知. http://www.caea.gov.cn/n6758881/n6758890/c6812195/content.html

[28] 国家药品监督管理局. 国家药监局关于改革完善放射性药品审评审批管理体系的意见. https://www.nmpa.gov.cn/directory/web/nmpa/zhuanti/ypqxgg/ggzhcfg/20230425160128160.html

[29] The Society of Nuclear Medicine and Molecular Imaging. Uptake: Unrest In the Healthcare Workforce. https://www.snmmi.org/NewsPublications/NewsDetail.aspx?ItemNumber=45589

[30] European Cancer Organisation. A Cancer Workforce in Crisis. https://www.europeancancer.org/workforce-crisis

我国放药产业布局正不断加速，核技术应用在我国长三角、珠三角、环渤海和成渝经济圈等增长极均实现了规模化重点布局；国内也纷纷成立了国家级和区域级医用同位素产业联盟[31]，核医学技术应用联盟[32]，核医学联盟等[33]，中国放药企业投融资活动热度不断增加，外资药企加速在国内的产业布局，投资设立放药生产基地，加快创新型放射配体疗法的引入[34]。多个放射性诊断和治疗药物产品获批开展临床试验，其中不乏在华同步启动的国际多中心临床研究。

## 诺华的建议

创新药产业的发展成为新的经济增长引擎，以下建议有助于推动该行业达到更好的质量、更高的效率和更可持续，促进中国发展，并与政府加快发展“新质生产力”的远大目标保持一致。

### 1. 持续加强知识产权保护，完善创新生态环境，促进持续吸引投资

创新药的研发是一个高投入、高风险的过程，平均而言开发一个新药需要 10 到 15 年时间，花费数十亿美元，进入临床试验阶段的新分子实体约只有 10%最终能获得上市许可[35]。尤其对于放药，除去高研发投入之外，基于其具有放射性、半衰期短、药品有效期短等特点，对产业链的上游、中游和下游提出了更高的要求。

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[31] 中国工程院. “国家医用同位素产业联盟”成立大会在中国工程院召开. https://www.cae.cn/cae/html/main/col84/2023-05/11/20230511145552665910831_1.html

[32] 诺华集团. 诺华进博携手生态伙伴，加速放射配体疗法落地. https://mp.weixin.qq.com/s/m623MmEZvF4rFR3ECWDXjQ

[33] 中国同辐. 中国同辐助力山东省核医学联盟全国首发. https://mp.weixin.qq.com/s/5jAX02H-9DuZDgYgHs3aWA

[34] 诺华集团. 诺华宣布在中国投资设立全新生产基地，加快创新型放射配体疗法引入. https://mp.weixin.qq.com/s/yxq0PwCWehmsRLUE53m3Cw

[35] Pharmaceutical Research and Manufacturers of America. “Progress toward New Medicines and Vaccines.” https://phrma.org/policy-issues/Research-and-Development-Policy-Framework#:~:text=On%20average%2C%20it%20takes%2010,Drug%20Administration%20(FDA)%20approval.

为不断提升市场创新活力，引领生物医药产业的可持续健康发展，中国仍需构建并完善创新生态环境。医药创新发展与知识产权保护的力度密切相关，具体建议包括：

（1）加强创新产品的知识产权保护，包括优化药品专利纠纷早期解决机制（即专利链接），尤其是使其能够覆盖更多的专利类型并有效地适用于所有药品类型。

（2）加快实施新药的药品专利期限补偿制度。

（3）制定并实施药品试验数据保护、儿童用药品和罕见病药品市场独占制度。

**2. 优化监管系统**

（1）重新考虑创新药的定义，与国际接轨，将当前一类创新药从境内外均未上市的创新药调整为境内未上市创新药，并加强部门间政策衔接，将该定义应用于所有相关创新药激励政策的范畴。

（2）完善放药的审评审批。建议增加放射配体治疗药物的多手段患者筛选，不限制使用特定的放射配体诊断药物进行患者筛选。完善放射性核素前体和化学前体的管理方法和相关要求，并将这些前体按照起始物料资料要求提交核素前体技术资料。建立和明确发生器和冷药盒的注册路径，将冷药盒按照药品制剂进行监管，并可获得独立的上市许可。使用 ICH 指南指导原则 Q8 进行样品本地注册检验，特别是当有多个化学/放射性核素前体生产场地时，根据风险评估没有必要对所有不同组合的生产场地进行 3 个批次的样品检验。

**3. 完善准入政策，在鼓励创新的同时确保可负担性和可及性**

（1）建立多层次医疗保障体系，完善价值评估框架，基于药品全生命

周期中的价值维持可持续和可预测的价格。加强多层次医疗保障体系发展，形成稳定可持续的筹资机制，尤其是对于高价值药品。药品已列入国家医保目录的，应当基于药品给患者、医疗卫生体系和社会带来的价值来制定合理的支付标准。

（2）存在显著专利侵权风险的药物不纳入国家集中带量采购。采用明确和统一的标准评估和认定在集中采购中的药品专利侵权风险，优化不同机构间的协作和联动以切实有效地保护知识产权。此外，落入专利保护范围的仿制药在药品采购平台申请挂网为许诺销售，构成侵权，因此不应允许此类药品在采购平台挂网。

（3）将创新药的支付标准与定价分开，不对企业的药品定价进行干预和限制。基于药品全生命周期进行价格管理，当药品处于自费阶段时，由市场决定药品价格，最大限度减少行政干预。

**4. 完善医疗卫生系统以适应创新疗法**

（1）优化多部门的监督和管理机制，并强化政策引导和多方合作。我们欣喜看到曾下发通知召开“核医疗高质量发展部际领导小组第一次会议”[36]（该会议后来延期举行），行业期待核医疗高质量发展部际领导小组尽快确定并对外公布，并在领导小组指导下，进一步加强顶层政策文件出台，加快推动《发展规划》的落地实施，制定《核医学产业中长期发展行动方案》，持续创新体制机制，并完善政企沟通机制，为产业良性发展提供更明确的政策引导 。

（2）加强规范化诊疗。制定临床应用标准，涵盖患者诊断筛查、转诊、治疗给药方式、治疗期间及治疗后的辐射防护、患者出院和随访，并在全国

[36] 中国同位素与辐射行业协会. 关于召开核医疗高质量发展部际领导小组第一次会议暨核医疗产业联盟成立大会的通知（第一轮）. https://www.cira.net.cn/news/show-873.html

加强统一执行。推动规范化诊疗中心标准制定，并在国内均衡布局建设规范化诊疗中心。完善放射性废液排放控制指标要求，持续提升核医学辐射防护与安全的最优化水平。

（3）增加政府对基础设施的投入，改善包括人才在内的医疗资源配置，以减少医疗卫生系统中的不平等情况。在主要城市布局建设配备有先进技术、基础设施和足够核素配额的核医学科，提前做好人才储备工作，加大核医学专业人员在最新先进疗法领域的培训，不断提高其数量和专业水平。

我们相信，只有不断加强知识产权保护、优化监管框架、改革准入和完善医疗卫生系统，才有助于真正确保和加快中国患者从包括放射配体疗法在内的先进疗法中获益，并促进经济增长。

这些建议是为了应对中国生物医药产业发展中面临的挑战，随着高质量发展路线图的进一步清晰，还会不断出台鼓励创新的新措施，对此我们也充满信心。我们期待与政府和多方共同携手，迎接一个鼓励创新的生态系统的新时代的到来。

## 结语

中国的发展证明了其远见卓识和强大韧性。党的二十大报告指出，人民健康是民族昌盛和国家强盛的重要标志。生物医药正在以前所未有的速度取得重大突破进展，获得革命性的创新治疗方案可以帮助患者过上更健康和长寿的生活。在庆祝所取得成就的同时，让我们继续共同推动创新以促进新质生产力的发展，建设一个支持创新蓬勃发展的环境，以造福患者、造福社会和造福全世界。

NOVARTIS

# Advancing a competitive ecosystem in China that fosters innovation and improves patient outcomes – considerations for radiopharmaceuticals

FINAL: March 2024

## Executive Summary

The strategic shift in reforms and policies in the pharmaceutical sector has transformed China from a system primarily focused on generics to an increasingly innovation-focused ecosystem. The change has attracted increased investments in China from leading pharmaceutical companies, resulting in improvements in several important indicators of innovation such as number of clinical trials and improved access to medicines.

Innovation fuels economic growth and will be a key success factor in addressing several existing challenges with impact beyond the healthcare sector – aging demographics, rising prevalence of chronic diseases, and unmet medical needs – as well as enhancing the global health leadership for China.

As innovation evolves, it stresses the need for continued improvement of policies to incentivize research and to drive the uptake of existing innovations. China has seen significant progress in the three areas of *IP*, *regulatory framework*, and *access*. Further policy improvements in these areas can promote the fast development of the innovative-oriented drugs sector which can be a strong contributor to the "new quality productive forces" announced by the Chinese government.[1] While the progress is remarkable, advanced therapies, particularly in the treatment of cancer, underscore the need for continued efforts.

In recent years, oncology has seen significant emerging innovation, with researchers across the world working relentlessly to develop new treatments. However, many patients still have limited treatment options and new treatments are urgently needed.

Radioligand therapy (RLT) is an innovative modality with multiple use cases in different types and stages of cancers.[2,3] Combining a radioisotope with a ligand to directly target the cancer cells has the potential to damage or even destroy the cancer cells while limiting damage to healthy cells. Following this, we are excited about the potential that RLT can bring in addressing the Chinese government's ambitions in the Healthy China Plan. However, the emerging radiopharmaceutical industry in China has encountered and continues to face several challenges, which serve as compelling examples of ongoing work required in the three priority areas mentioned above.

This paper provides suggestions for policy improvements in the areas of IP, Regulatory an Access. In addition, it provides specific advice for highly innovative

[1] "New quality productive forces" refers to the Chinese government's ambition to fuel economic development through innovation in advanced sectors.

[2] Bugani V, Battistelli L, Sansovini M, et al. Radioligand therapies in cancer: mapping the educational landscape in Europe [published online ahead of print, 2023 Apr 14]. Eur J Nucl Med Mol Imaging. 2023;1-7.

[3] Uijen MJM, Derks YHW, Merkx RIJ, et al. PSMA radioligand therapy for solid tumors other than prostate cancer: background, opportunities, challenges, and first clinical reports. Eur J Nucl Med Mol Imaging. 2021;48(13):4350-4368.

treatment options such as RLT:

## 1. Continuously enhance IP protection to improve the innovation ecosystem in China to attract continued investments

A predictable and robust protection of IP is essential for private entities' ability to continue investing in research and development; this is the main driver of bringing new treatments, such as RLT, to healthcare systems and patients.

The government should:

- Strengthen the protection of IP for innovative products, including optimizing the early resolution mechanism for drug patent disputes (i.e., the patent linkage system), in particular by expanding the coverage to include more patent types, and ensuring effective application across all types of drugs.
- Accelerate the implementation of rules on patent term extension for pharmaceutical patents for new drugs.
- Establish and implement rules for Regulatory Data Protection and exclusivity for pediatric and orphan medicines.

## 2. Optimize the regulatory framework

A strong regulatory system is one of the core components of a viable biopharmaceutical ecosystem. To pave the way to highly innovative therapies like RLT, China can further optimize its regulatory framework by considering the following recommendations:

- Align with international standards and adjust the definition of New Drug as innovative drugs that have not been approved in China.
- Optimize the review and approval for radiopharmaceuticals. Promote the implementation of multimode screening methods for patients who may benefit from RLT. Establish and clarify the requirement and pathway of drug registration and management.

## 3. Advance access policies to ensure affordability and accessibility while rewarding innovation

Innovation creates value when it is accessible to patients. To ensure Chinese patients can benefit from innovation, the government should continue to reform the access environment. This includes:

- Establish a multi-layered medical security system, improve the value framework and ensure that prices are sustainable and predictable throughout the lifecycle of a medicine.
- Exclude drug products with a substantial patent infringement risk from the National Volume-Based Procurement program.
- Separate payment standards from pricing of innovative drugs, refrain from

putting unduly restrictions on companies' right to price their medicines.

## 4. Prepare the healthcare system for innovative therapies

The Chinese healthcare system has made outstanding progress. However, the characteristics of highly innovative and promising therapeutic areas such as RLT, put a spotlight on the remaining barriers in healthcare systems for an appropriate uptake of innovation. We encourage the government to:

- Optimize multi-agency supervision and management mechanisms, strengthen policy guidance and multi-party cooperation.
- Enhance the normalized diagnosis and treatment.
- Increase government investment in infrastructure and improve allocation of medical resources.

As China's ascent continues, the importance of innovation cannot be overstated. The policy direction chosen by the Chinese government has broad impact, with implications beyond China's borders. While celebrating achievements, we must remain forward-looking. China's journey is far from complete. China's biopharmaceutical industry is accelerating its transition from an era of fast follow innovation to an era that places greater emphasis on differentiation and source innovation. By prioritizing the areas above, we are confident that China can sustain growth and be a global leader.

## Situation Analysis

## The Importance of Innovation in Healthcare

China has emerged as a formidable force in the global pharmaceutical arena. Its transformation from a system primarily focused on generics to an increasingly innovation focused ecosystem is nothing short of remarkable. As we navigate the complexities of a rapidly evolving healthcare landscape, understanding China's trajectory becomes essential for all stakeholders—industry leaders, policymakers, and patients alike. China's rise is not one of chance; it is a deliberate strategic shift driven by effective reforms and policy guidance of the Chinese government across major elements of a medicine's journey from early research to patient access. This strategic shift keeps attracting the attention from leading pharmaceutical companies and is resulting in remarkable improvements for biopharmaceutical industry in China.

The acceleration of "new quality productive forces" was proposed as a key priority in the 2024 Two Sessions government work report. This includes cutting edge sectors such as life sciences. Novartis welcomes this initiative, which is highly consistent with our strategy. We are dedicated to bringing high-value medicines from our five innovative technology platforms, such as Radioligand therapy (RLT), to Chinese patients.

We are now running development programs in China simultaneous with global programs, we invest in manufacturing, we invest in commercialization, and we plan to continue investing over time. China is now our second largest market in the world in terms of sales and it is also our fastest-growing market. Importantly, this means that more Chinese patients now can benefit from being treated with innovative medicines, the efficiency of the healthcare system is improved, and China has over a long time period increasingly attracted foreign investments.

**Innovation bridges gaps and addresses unmet medical needs.** China faces a number of healthcare challenges with an impact beyond the healthcare sector—aging demographics, rising chronic diseases, and unmet medical needs. By fostering innovation and access to novel therapies, China can extend and improve the life of Chinese patients, while building a stronger country. **Innovation fuels economic growth and creates jobs.** A vibrant life sciences sector generates jobs, attracts investment, and contributes to GDP. China's ambitious goals—such as becoming a global biopharmaceutical innovation hub—rely on nurturing an ecosystem that fosters creativity, collaboration, and entrepreneurship. **Innovation enhances the global health leadership.** China proposes to work together to build a global community of health for all. By championing innovation, China can lead in tackling global health challenges. Collaborations with international partners, knowledge sharing, and joint research initiatives can position China as a responsible global player and contribute to China's strength to promoting global health.

## Past and Future Reforms

China's government considers the development of innovative biomedicines an important objective for national development and economic growth. The *14th Five-Year Plan for National Economic and Social Development of the People's Republic of China and the Outline of Long-term Goals for 2035* proposes that biopharmaceutical be included as a "national mega-innovation field."[4]

We commend the Chinese government for transitioning towards an environment that is conducive to innovation. Below are three areas that have been, and will continue to be, key in moving China to the current state and beyond. In a later section of this paper, we outline specific challenges and solutions for the innovative therapy industry by taking radiopharmaceuticals as an example.

**Regulatory System.** China recognized that optimization in regulatory processes is a catalyst for innovation. China joined the International Council for the Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), actively integrating into the international regulatory system. The National Medical Products Administration (NMPA) has streamlined approval pathways, expedited the regulatory pathways (including breakthrough approval and conditional approval),[5] reducing timelines for drug evaluation. This optimization plays an important role in encouraging both domestic and multinational companies to invest in research and development (R&D) within China's borders.

Significant progress has been made in terms of number of trials conducted in China as well as in number of regulatory approvals. According to Novartis analysis based on publicly available data for the period 2017 to 2021, the total number of Phase II and III trials conducted in China increased by nearly 100% (CAGR of 26%), with CAGR in other major markets in the low to mid-single digits and in some cases even negative. In the past five years, the number of new drugs launched in China has been second only to that in the United States[6]. China's success lies in seamless integration with global markets. Moving towards harmonizing regulatory standards and aligning with international best practices will amplify the impact.

Currently in China a 'New Drug' is defined as one that is new and un-marketed anywhere in the world, not just new to China.[7] Incentive policies, formulated to encourage the innovative medicine development and IP protection are often linked

[4] The 14th Five-Year Plan for National Economic and Social Development of the People's Republic of China and the Outline of Long-term Goals for 2035. https://www.gov.cn/xinwen/2021-03/13/content_5592681.htm#:~:text=%E4%B8%AD%E5%8D%8E%E4%BA%BA%E6%B0%91%E5%85%B1%E5%92%8C%E5%9B%BD%E5%9B%BD,%E5%85%B1%E5%90%8C%E7%9A%84%E8%A1%8C%E5%8A%A8%E7%BA%B2%E9%A2%86%E3%80%82

[5] State Administration for Market Regulation. Administration Measures of Drug Registration. https://www.gov.cn/zhengce/zhengceku/2020-04/01/content_5498012.htm

[6] IQVIA. Global Trends in R&D 2024: Activity, Productivity, and Enablers.

[7] State Food and Drug Administration. Announcement on the Work Plan for Reform of Chemical Drug Registration Classification. https://www.nmpa.gov.cn/xxgk/ggtg/ypggtg/ypqtggtg/20160309151801706.html

to whether a drug is deemed new. Due to the definition of New Drug, many innovative drugs already approved in international markets cannot enjoy relevant incentive measures in China, which greatly reduces the confidence and speed of enterprises in introducing international innovative drugs into China. It is necessary to reconsider the definition of New Drug to make sure all innovative products can really benefit from the incentive policies for innovative drugs. In addition, the definition of New Drug is not in line with international systems and is inconsistent with international treaties such as the Comprehensive and Progressive Agreement for Trans-Pacific Partnership, which is a high-level trade agreement China applied to join in 2021.

**Investment in R&D and Intellectual Property Protection**. Robust intellectual property protection is the bedrock of innovation. China has made substantial progress in this area, bolstering confidence among innovators. China has established a drug patent term compensation system (Patent Term Extension, PTE), which is to be implemented soon, and a patent linkage system, which has been continuously improved. PTE is used to restore the patent term to compensate for the time required by review and approval for pharmaceutical products. Patent linkage aims to provide an early dispute resolution mechanism before marketing of any generics or biosimilars. The recently released new version of the Implementing Regulations of the Patent Law[8] has provided more detailed guidance for the implementation of the PTE system for new drug patents.

We are pleased to see the proposal on provisions regarding exclusivity periods for pediatric drugs and rare disease drugs in the Regulations for the Implementation of the Drug Administration Law (drafted for comments)[9] released in 2022. The introduction of these systems will have a positive impact on R&D of pediatric and rare disease drugs.

Many countries and regions in the world have systems in place for regulatory data protection (RDP), which plays a crucial role in incentivizing innovation by providing innovators with predictability on challenges and market, protection of innovators' critical data. We understand that China has been putting continuous efforts in improving its RDP system[10], and we consider an effective RDP system to be critical to promote the development of the biopharmaceutical industry of China. High-profile IP enforcement cases underscore the government's commitment to safeguarding innovation. We strongly encourage the Chinese government to continue the efforts to improve the IP protection system, and promote the

[8] State Council. Decision of the State Council on amending the Implementing Regulations of the Patent Law. https://www.gov.cn/zhengce/content/202312/content_6921633.htm

[9] National Medical Products Administration. Regulations for the Implementation of the Drug Administration Law (drafted for comments). https://www.nmpa.gov.cn/xxgk/zhqyj/zhqyjyp/20220509222233134.html

[10] National Medical Products Administration. The Office of the National Medical Products Administration publicly solicits opinions on the Implementation Measures for Regulatory Data Protection (Interim). https://www.nmpa.gov.cn/directory/web/nmpa/xxgk/zhqyj/zhqyjyp/20180426171801468.html

implementation of existing policies, which will be a key driver for attracting investments, including foreign capital.

China's investment in R&D must match its ambitions. Public-private partnerships, venture capital support, and incentives for early-stage research will drive innovation. Collaboration with academia and startups can yield transformative results.

**Market Access Reforms.** Market access policies have undergone significant transformation. The healthcare security system in China has developed steadily, as of the end of 2022, the number of people participating in Basic Medical Insurance (BMI) in China was 1,345.9 million, with a stable participation rate of over 95%; the total revenue of BMI fund was 3092.2 billion yuan, with an increase of 7.6% compared to that of previous year.[11] Since the establishment of National Healthcare Security Administration (NHSA) in 2018, it has been carrying out National Reimbursement Drug List (NRDL) adjustments for six consecutive years, and a normalized and dynamic adjustment mechanism has been continuously improved. China now expedites reimbursement decisions for innovative therapies, ensuring a timelier inclusion in the NRDL. The time from the approval of a new drug to inclusion in the NRDL has decreased from about 5 years in 2017 to 1 year in 2023; more than 80% of innovative drugs can be included in NRDL within 2 years after their launch.[12] These improvements are remarkable and unrivalled. In addition to this, we are following with interest an increased attention to the value of medicines during the negotiations, in contrast to a pure focus on price reductions.

However, a number of innovative drugs are not included in the NRDL due to insufficient price reductions during price negotiations. The average price reduction is 60% for newly listed negotiated drugs in recent years, making for a challenging environment for launching innovative new medicines. Ensuring patients access to innovative therapies that bring value to patients, to the healthcare system, and to society, while ensuring a sustainable healthcare system and internationally competitive pricing is not an easy task. We are convinced that continued work towards predictable pricing negotiations and value-based reimbursement models are key in achieving these goals.

The pharmaceutical volume-based procurement (VBP) system in China has matured over the years since it was introduced in 2018, effectively reducing the cost burden of medication, but concerns have emerged as some products, despite the existence of valid patents for the originator product are also included in VBP.

Recently a policy draft for soliciting opinions on initial price setting mechanism aims to encourage clinical value-oriented drug R&D and innovation, support the

[11] National Healthcare Security Administration. Statistical Bulletin on the Development of Healthcare Security Work in China in 2022. http://www.nhsa.gov.cn/art/2023/7/10/art_7_10995.html

[12] National Healthcare Security Administration. Record of the press conference on the adjustment of the NRDL by the National Healthcare Security Administration in 2023. http://www.nhsa.gov.cn/art/2023/12/13/art_52_11685.html

diversified supply and fair accessibility of high-quality and innovative drugs, and acknowledge the importance of the market in pricing. While direction of travel is encouraging, we still expect further improvements to this this mechanism.

As China's ascent continues, the importance of innovation cannot be overstated. Few countries can match the global impact of the policy direction chosen by the Chinese government, with implications beyond China's borders. While celebrating achievements, we must remain forward-looking. China's journey is far from complete. China's biopharmaceutical industry is accelerating its transition from an era of fast follow innovation to an era that places greater emphasis on differentiation and source innovation. By prioritizing the areas above, we are confident that China can sustain growth and be a global leader.

## Oncology and Radiopharmaceuticals

In recent years, oncology has seen significant emerging innovation. It was the leading therapeutic area in terms of new approvals both by FDA and EMA in 2023 (21% of new therapeutic drugs, and 35% of new active substances, respectively) as well as the area with most listed exclusive drugs via negotiation in the 2023 NRDL process (18% of all newly listed exclusive drugs via negotiation).[13,14,15] Scientists in China, and across the world, are relentlessly searching for new ways to identify, diagnose, and treat patients with cancer. Innovative medicines have transformed certain cancer diagnoses from a death sentence to a chronic condition.

Despite great progress made in cancer diagnosis and treatment in recent years, there are still many patients with limited treatment options, especially those with rare or metastatic cancers.[16] Cancer, as a serious global public health problem, requires new treatment options to improve survival rate and quality of life.[17] Over the past decade, the number of cancer incidence and deaths in China has continued to rise, and the burden of cancer continues to increase.[18] The National Cancer Center of China reported an estimate of about 4,824,700 new cancer cases and 2,574,200 cancer deaths occurred in China in 2022. The age-standardized incidence rate and the age-standardized mortality rate were 201.61 per 100,000 and 96.47 per 100,000,

[13] Baedeker, M, Ringel, M S, Möller, C C. 2023 FDA approvals: unprecedented volume at moderate value. Nature Reviews Drug Discovery, 2024, (23): 98

[14] European Medicines Agency (2023). Human Medicines Highlights 2023.

[15] IQVIA. Summary of 2017-2023 China NRDL Updates. January 8, 2024.

[16] 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

[17] 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

[18] 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

respectively.[19]

China attaches great importance to cancer prevention and control, and has set up the "Cancer Prevention and Treatment Action" among the 15 special actions in the *Healthy China Initiatives (2019-2030),*[20] and sets clear goals to be achieved by 2030, including further improving the cancer prevention and treatment system, steadily improving the standard diagnosis and treatment level, curbing the rising trend of cancer morbidity and mortality, and achieving 46.6% of the overall five-year survival rate of cancer.

To achieve these goals, screening programs need to continue and improved access to innovative treatments are necessary. In addition, new treatment modalities, such as RLT are evolving to treat areas with high unmet need, including cancer.

RLT is a new generation of innovative, targeted therapeutic radiopharmaceuticals. RLT combine a targeting compound, the ligand, which binds to a specific marker, with a radioisotope. The ligand directs the radioisotope to the target cancer cells expressing the specific marker, even when they have spread throughout the body. This unique mechanism of action aims to damage or destroy the cancer cells with physical radiation, while limiting impact on nearby healthy cells.[21,22] Clinical trials of RLT have proven effective to patients with gastrointestinal pancreatic neuroendocrine tumors (GEP-NETs)[23] and metastatic castration-resistant prostate cancer (mCRPC).[24] The special mechanism of action of RLT can also be applied to other cancers to improve survival rate and quality of life for patients.[25] Ongoing clinical studies covering additional indications indicate that RLT may also bring more treatment options to patients with other cancers, including brain cancer (glioblastoma), gastrointestinal tumors, lung cancer, and breast cancer, etc.[8, 26] Oncology treatments, and RLT as a particular example, demonstrate an exciting

[19] 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

[20] National Health Commission of the PRC. Notice on Issuing the Implementation Plan for the Healthy China Initiatives - Cancer Prevention and Control Action (2023-2030), http://www.nhc.gov.cn/ylyjs/pqt/202311/18bd5bb5abc74ebc896f9d5c9ca63422.shtml

[21] Aboagye EO, Barwick TD, Haberkorn U. Radiotheranostics in oncology: Making precision medicine possible. CA Cancer J Clin. 2023;73(3):255-274. doi:10.3322/caac.2176

[22] Duan H, Iagaru A, Aparici CM. Radiotheranostics - Precision Medicine in Nuclear Medicine and Molecular Imaging. Nanotheranostics. 2022;6(1):103-117. doi:10.7150/ntno.64141

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

[24] 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

[25] 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

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

prospect and significance in promoting Healthy China Initiatives. RLT also highlight the ongoing need for policy developments as disruptive innovation emerges.

While these modalities offer new hope to patients, they also pose new challenges to those healthcare systems across the world that are not adapting their health-care related policies. Novartis is a pioneer in bringing advanced therapies, including RLT, to patients across the world. We have seen first-hand that countries open to change have generally been most successful in enabling access to these therapies.

China has made significant progress in the research, development, and clinical application of radiopharmaceuticals, driven by some favorable policies. In 2021, eight ministries and commissions issued the *Medium- and Long-Term Development Plan for Medical Isotopes (2021-2035)*[27], accelerating the development of the medical isotope-based radiopharmaceutical industry. From review and approval perspective, NMPA also issued documents to improve the evaluation and approval mechanisms for radiopharmaceuticals,[28] to encourage the launch of innovative radiopharmaceuticals to meet urgent clinical needs. Another encouraging signal is the plan to promote the R&D and application of radiopharmaceuticals, jointly issued by the National Health Commission and ten other ministries and commissions.

However, the characteristics of RLT highlights remaining barriers for an appropriate absorption of innovation, in several areas, such as supervision and management system and top-level design mechanisms, regulatory approval processes, the clinical application, and nuclear medicine infrastructure and capacity: (1) The supervision and management on radiopharmaceuticals involves several governmental agencies, which in many cases work with overlapping responsibilities and insufficient coordination. (2) Implementation of multimode screening for patients receiving RLT needs further promotion. The drug registration requirement and pathway is not yet clear, including registration pathway of chemical/radionuclide precursors, supervision of generators and cold kits, management approach of multiple manufacturing sites, local registration testing of radiopharmaceuticals, etc. (3) Lack of established standards for the clinical use of radiopharmaceuticals, encompassing diagnosis, referral and treatment. In addition, there is no uniform standard for the establishment of standardized diagnosis and treatment centers. The nuclide quota is insufficient. The management of radioactive waste in hospitals also requires further optimization. (4) Nuclear medicine

[27] China Atomic Energy Authority, etc. Medium and Long-Term Development Plan for Medical Isotopes (2021-2035). http://www.caea.gov.cn/n6758881/n6758890/c6812195/content.html

[28] National Medical Products Administration of PRC. Opinions on Reforming and Improving the Administrative System for Review and Approval of Radiopharmaceuticals. https://www.nmpa.gov.cn/directory/web/nmpa/zhuanti/ypqxgg/ggzhcfg/20230425160128160.html

departments in the hospitals need to be improved, and nuclear medicine resources are still not sufficient. There is also an imbalance in distribution, with more resources in the Southeast region. While infrastructure and staff shortages are common challenges internationally,[29,30] China has an opportunity to address the issues proactively to bolster its nuclear medicine capabilities.

However, China's radiopharmaceutical industry is expanding, with industry clusters taking shape in areas like in Yangtze River Delta, the Pearl River Delta, Bohai Rim and Chengdu-Chongqing Economic Circle. Besides, industrial alliances for medical isotopes[31], application of nuclear medicine technologies[32] and nuclear medicine[33] have been set up on both national and regional levels. The investment and financing activities have also been increasing and foreign pharmaceutical enterprises have invested in new radiopharmaceutical manufacturing sites and accelerated the introduction of RLT[34]. Furthermore, clinical trial applications of various diagnostic and therapeutic radiopharmaceuticals have been approved, some of which are international multi-center clinical studies launched simultaneously in China.

## Suggestions

The pharmaceutical industry has become a new driver of economic growth. The suggestions below can improve the industry's impact on China's prosperity further by moving it to a higher level of quality, efficiency, and sustainability – in line with the Chinese government's ambition to promote "new quality productive forces".

## 1. Continuously enhance the IP protection to improve the innovation ecosystem in China to attract continued investments

The development of innovative drugs is a process with high investment and high-risk. On average, developing a new drug takes 10 to 15 years and costs billions of dollars. Only about 10% of new molecular entities entering the clinical trial stage ultimately obtain market approval.[35] For radiopharmaceuticals, in addition to high

[29] The Society of Nuclear Medicine and Molecular Imaging. Uptake: Unrest In the Healthcare Workforce. https://www.snmmi.org/NewsPublications/NewsDetail.aspx?ItemNumber=45589

[30] European Cancer Organisation. A Cancer Workforce in Crisis. https://www.europeancancer.org/workforce-crisis

[31] Chinese Academy of Engineering. The founding conference of the National Medical Isotope Industry Alliance was held at the Chinese Academy of Engineering. https://www.cae.cn/cae/html/main/col84/2023-05/11/20230511145552665910831_1.html

[32] Novartis Group. Novartis collaborates with ecological partners to accelerate the implementation of radioligand therapy in CIIE. https://mp.weixin.qq.com/s/m623MmEZvF4rFR3ECWDXjQ

[33] China Isotope and Radiation Corporation (CIRC). CIRC assists the first launch of Shandong Nuclear Medicine Alliance in China. https://mp.weixin.qq.com/s/5jAX02H-9DuZDgYgHs3aWA

[34] Novartis Group. Novartis announces its investment in establishing a new production base in China to accelerate the introduction of innovative radioligand therapies. https://mp.weixin.qq.com/s/yxq0PwCWehmsRLUE53m3Cw

[35] Pharmaceutical Research and Manufacturers of America. "Progress toward New Medicines and Vaccines." https://phrma.org/policy-issues/Research-and-Development-Policy-

investment in R&D, higher requirements are placed on the upstream, midstream, and downstream of industry chain due to the special characteristics such as radioactivity, short half-life of radioisotopes that remain effective only for a short time, and short shelf life.

Therefore, in order to continuously enhance market innovation vitality and lead the sustainable and healthy development of the biopharmaceutical industry, China needs to build and improve an ecosystem conducive to innovation. The development of pharmaceutical innovation is closely related to the Intellectual Property protection. Specific suggestions include:

(1) Strengthen the protection of IP for innovative products, including optimizing the early resolution mechanism for drug patent disputes (i.e., the patent linkage system), in particular by expanding the coverage to include more patent types, and ensuring effective application across all types of drugs.

(2) Accelerate the implementation of rules on patent term extension for pharmaceutical patents for new drugs.

(3) Establish and implement rules for Regulatory Data Protection and exclusivity for pediatric and orphan medicines.

## 2. Optimize the regulatory framework

(1) Align with international standards and adjust the definition of New Drug as innovative drugs that have not been approved in China as opposed to not having been approved anywhere in the world to innovative drugs. Strengthen policy coordination between departments, applying this definition to all relevant incentive policies for innovative drugs.

(2) Optimize review and approval for radiopharmaceuticals. Novartis recommends promoting multimode patient screening for RLT, without restricting patient screening to a specific radioligand diagnostic kit. Improve the management methods and related requirements for radionuclide precursors and chemical precursors and consider these precursors as starting materials for the manufacturing process and dossier requirements. Establish and clarify the registration path for generators and cold kits and regulate cold kits as pharmaceutical preparations with independent license. Use ICH Q8 risk-assessment principle for samples for local registration test, especially when there are multiple chemical/radionuclide precursors manufacturing sites, it may not be necessary to conduct sample testing of three batches for all different combinations of manufacturing sites based on risk assessments.

## 3. Advance access policies to ensure affordability and accessibility while rewarding innovation

Framework#:~:text=On%20average%2C%20it%20takes%2010,Drug%20Administration%20(FDA)%20approval

(1) Establish a multi-layered medical security system, improve the value framework and ensure that prices are sustainable and predictable throughout the lifecycle of a medicine. In order to enhance the development of multi-level medical security, form a stable and sustainable financing mechanism, especially for high-value drugs. When drugs have been listed in NRDL, formulate a reasonable NRDL payment standard based on the value of these drugs to patients, healthcare system, and society.
(2) Exclude drug products with a substantial patent infringement risk from the National Volume-Based Procurement program. Adopt a clear and unified standard for assessing and determining the drug patent infringement risks in the centralized procurement process and optimize the collaboration and cooperation among agencies so as to ensure the efficient and effective IP protection. Besides, if a generic drug falls into the scope of a patent, the application for listing on drug procurement platforms is considered as offering for sale, thus constituting infringement, listing of such generic drugs on procurement platforms shall not be allowed either.
(3) Separate payment standards from pricing of innovative drugs, refrain from putting unduly restrictions on companies' right to price their medicines. Establish a sound price management based on the entire life cycle of medicines. Follow the principle of the market having a decisive role in determining the price of medicines when they are in the stage of self-pay, with minimal administrative interventions.

## 4. Prepare the healthcare system for innovative therapies

(1) Optimize multi-agency supervision and management mechanisms, strengthen policy guidance and multi-party cooperation. We are pleased to see the announcement of the first meeting of the Inter-ministerial Leading Group for High-Quality Development of Nuclear Medicine,[36] despite the announcement of it being postponed. The industry anticipates that the leading group could play a decisive role in formulating holistic policies, accelerate implementation of the *Development Plan for Medical Isotopes*, and promulgate the *Medium- and Long-term Action Plan for the Development of Nuclear Medical Industry* to proactively promote the radiopharmaceutical industry development. Innovative institutional mechanism to improve communication between the government and industry is also encouraged.
(2) Enhance the normalized diagnosis and treatment. Formulate clinical application standards, covering diagnosis, screening, referral, administration, radioprotection, patient discharge and follow-ups, and with a unified implementation across the country. Promote the development of Center of Excellence (COE) standard and establish a balanced COE layout in China. Further optimization of radioactive waste

[36] China Isotope & Radiation Association. Notice on Holding the First Meeting of the Inter-ministerial Leading Group for High Quality Development of Nuclear Medicine and the Establishment Conference of the Nuclear Medical Industry Alliance (First Round). https://www.cira.net.cn/news/show-873.html

disposal indicators to continuously improve the optimal level of radiation protection and safety in nuclear medicine.

(3) Increase government investment in infrastructure and improve allocation of medical resources, including talents to reduce the inequalities in healthcare system. Build first-class nuclear medicine departments with advanced technology, infrastructure, and sufficient nuclide quota in hospitals in major cities. Prepare talent reserves in advance, increase the training of nuclear medicine professionals on the latest advanced therapies, and continuously improve the number and professional level of nuclear medicine practitioners.

The achievements of all these actions, including continuously enhancing IP protection, optimizing regulations, reforming access and continuous adaption of the system, can help to ensure and accelerate Chinese patients' benefit from advanced therapies, including RLT. In addition to the direct benefit for patients, it will also help China in terms of economic growth.

These suggestions are addressing the challenges faced by China's biopharmaceutical industry. We believe new measures to encourage innovation will continuously be introduced in China as high-quality development continues to advance. We look forward to working more closely with government and other stakeholders to welcoming the arrival of a new era with an ecosystem conducive to innovation.

## Conclusion

China's ascent is a testament to vision, resilience, and adaptability. The report of the 20th National Congress of the Communist Party of China states that people's health is an important symbol of national prosperity and development. Biopharmaceuticals are making significant breakthroughs at an unprecedented pace, and obtaining access to revolutionary innovative solutions can help patients live healthier and longer lives. As we applaud the achievements so far, let us collectively commit to continuously promoting innovation for the development of "new quality productive forces", and sustaining an environment where innovation thrives—for the benefit of patients, society, and the world.