Paving the way for access to innovative cell and gene therapies in China

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Executive Summary

China has made tremendous strides over several decades in reforming and improving its healthcare system, helping millions of people enjoy longer, healthier lives. As the pace of medical innovation in China and around the world accelerates, however, policymakers could adapt their reform efforts to ensure China remains at the forefront of research and development into new therapies. Reforms could also facilitate access for Chinese patients to the latest innovative treatments.

Among the most dynamic areas of progress in medicine are advances in cell and gene therapies. They are often one-time treatments that target the underlying cause of disease and in some cases have the potential to cure patients, rather than simply treat their symptoms. China has made rapid progress in the research and development of these new therapies.

Novartis sees opportunities for the Chinese government to even further accelerate progress in three areas: strengthen the regulatory framework for cell and gene therapies; devote more attention to the special healthcare needs of patients who can benefit from them; and develop new solutions to help patients gain access to them. Reforms in these three areas would complement the tremendous effort and

impressive achievements already made to strengthen China's healthcare system, and support the country's continued social and economic development. It will help the Chinese government to raise the quality level of medicines in general and of these treatments specifically as well as serve patients' needs and ensure their safety.

A favourable policy environment in this field will also further support investments in China, i.e. more drug researchers with a global vision and experience will come to China to develop cell and gene therapies. In addition, raising standards in the various areas related to cell and gene therapies will support the government's aim to take over an international leading role in this field.

Adapt the regulatory framework

Cell and gene therapies are unlike traditional medicines and can require special facilities to process patients' cells, as well as specially trained technicians. China has done significant work to put in place regulations that would facilitate these revolutionary treatments, but would benefit from further enhancing the regulatory framework to ensure these therapies are manufactured and transported according to high-quality international standards.

Clear procedures for the export and re-import of human cells and related materials would facilitate fast and safe clinical trials of experimental cell and gene therapies, as well as safe treatment of patients with approved therapies. Stronger regulations for clinical trials and a clearer framework following international standards to register cell and gene therapies in China will help ensure a high level of patient safety. They could include mandated risk management plans and post-approval

safety monitoring, as well as accelerated access to medicines for patients with critical conditions, for instance via specialized registration pathways, clinical trial waivers, or early access schemes.

Address special aspects of patient care

Administering cell and gene therapies can involve complex, multi-step processes requiring healthcare professionals with specific skills and experience. Conferring with patients about their medical needs and treatment experiences can support better-informed regulatory decisions. Guidelines laying out specific requirements for healthcare professionals and hospitals engaging in cell and gene therapy, covering aspects such as equipment, skills and training, can help ensure high-quality, safe treatment of patients. And mandating that all patients be included in disease-specific registries would help create transparency and better oversight.

Reshape patient access models

With Chinese patients typically paying a portion of healthcare costs from their own pockets, to ensure they can gain access to these innovative new therapies, there is an urgent need to devise new payment and funding models. Solutions could include flexible payment mechanisms that consider the value of cell and gene therapies for patients and caregivers.

Alternative funding models could include commercial health insurance and pooled funds, such as critical illness insurance.

With its significant experience in the field of cell and gene therapy, Novartis stands ready to support the Chinese government in its efforts and looks forward to discussing our suggestions.

I. Introduction

Improved living standards, significant advances in diagnostic and medical innovation, and better access to healthcare enable people across the globe to live longer and more productive lives. The average life expectancy among member states of the Organisation for Economic Co-operation and Development (OECD) has reached about 80 years, more than a decade longer within a generation, and continues to increase. A significant portion of this success is related to medical innovations that are the result of the continued investment and dedication of pharmaceutical companies, research institutions, and healthcare providers in the fight against disease.

Today, we are witnessing the onset of an exciting wave of medical innovation that is expected to reach doctors and patients in the coming years. Personalized medicine delivered by certain types of cell and gene therapies and immunotherapies could provide essential breakthroughs for patients with unmet needs, including those with rare diseases. The effort to find solutions for these patients must continue and is enormous, as for instance, about 6,000 rare diseases exist, of which only a small fraction have effective treatments today.

The Chinese government has recognized the importance of innovation – generally and specifically within healthcare – as a strong force behind economic growth. The Chinese government is taking great care of its population via the ongoing healthcare reform. Comprehensive programs like Healthy China 2030 have been implemented to address healthcare needs and support the ongoing healthcare reform. China's Ministry of Science and Technology (MOST) issued a special plan for biotechnology innovation with the 13th Five-Year Plan, which targets the

sector contributing more than 4 percent of the country's GDP by 2020. Partly as a result of this effort, a large number of new technologies have emerged, industrial structures have been upgraded, and guidance to reform elements of the regulatory system have been published.

Medicinal innovation is the best way to tackle the combined challenges of unmet medical needs, changing demographics, and the resulting increase in chronic diseases. Yet, medicinal innovation is complex and risks failure, creating unique challenges. Novartis scientists are reimagining the definition of a medicine and are investigating novel approaches to treating diseases. A better understanding of the molecular mechanisms of diseases and new types of therapies, for instance, promise to yield powerful new medicines. One example of our work in the field of cell and gene therapies is the development of the first CAR-T therapy[1] for certain types of leukaemia approved by the US Food and Drug Administration. Cell and gene therapies present a new treatment paradigm, which includes their administration as a one-time treatment and potential cure of the disease. Another example is our gene therapy Luxturna that was listed by the National Medical Products Administration (NMPA) in November 2018 as one of 40 drugs addressing high medical need.

Healthcare systems need to adapt to capture the full benefits of the rapid advances in technology and give patients access to these breakthrough innovations. As patients become more and more engaged in their own healthcare decisions and demand safe treatments and transparent processes, their expectation of greater quality of care from their healthcare systems has increased.

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1 Chimeric antigen receptor T-cell (CAR-T) therapy is generated from a patient's own T cells, which are part of the immune system. After genetic modification the T-cells are able to recognize and eliminate cancerous cells.

To allow for the smooth development and safe use of advanced therapies for patients in China, Novartis suggests three areas in cell and gene therapies that may deserve attention:

i. Adapt the regulatory framework to meet the special features of advanced therapies

ii. Address special aspects of patient care

iii. Reshape patient access models

The recommendations made in this document aim to support China's healthcare policies that foster innovation and seek best treatment options for patients. The strict implementation and enforcement of the suggested frameworks will also enable China to progress towards its goals of becoming a leading biotech nation, to attract further investments in the country's biotechnological sector, and ultimately to provide patients with most innovative medicines.

II. Situational analysis and Novartis suggestions

Though commonly considered together, cell therapies and gene therapies are two distinct innovative treatment methods that can make a difference in patient lives. Cell therapies comprise the administration of modified living cells to patients for the treatment of a disease. Gene therapies focus on a defective gene that causes a disease, adding or replacing that gene with a healthy copy that either turns off the defective gene or turns on a gene that can prevent or modify the course of a disease.

Our analysis for this proposal centres on selected elements in the production, development, application, and patient access to cell and gene therapies, addressing the various complexities that are connected to these novel treatments.

i. Adapt regulatory framework to meet special features of advanced therapies

Cell and gene therapies do not follow conventional production models applicable to other therapies. The production of these therapies presents unique challenges and risks that require a specific infrastructure and the involvement of numerous specifically trained parties, including shipment officials and manufacturers, as well as healthcare providers.

a. Local manufacturing of cell and gene therapies

Situational analysis in China

China's policies encourage local manufacturing of medicines, including cell and gene therapies through technical cooperation, foreign direct investment, and outsourcing research and development (R&D). Multinational companies can

participate in joint R&D, undertake national biopharmaceutical development projects, and play a role in shaping the Chinese biopharmaceutical industry into an open ecosystem of innovation. Depending on the business model and company strategy, establishing manufacturing collaborations between foreign and local companies can provide great opportunities for both sides.

Currently, complex requirements must be fulfilled by the manufacturer and the site to get a commercial manufacturing licence in China. However, no special permission is needed for the production of clinical trial material, i.e. without specific requirements or surveillance, a high quality level of clinical trial material may not be guaranteed.

Novartis suggestions

During clinical trials and following marketing authorization, genetic material to be introduced to a patient's cells must be prepared under strict quality controls to ensure the highest level of purity and integrity. For cell therapies, the quality and integrity of the full supply chain must be ensured at every step, from harvesting the cells to administering them back into the patient, to protect patients from preventable harm. As a result, all internationally recognized pharmaceutical quality standards, like Good Manufacturing Practice (GMP), should apply to ensure adequate control of the manufacturing process, including continual training of personnel.

As regulators are in charge of granting manufacturing licenses, we recommend to them to consider the special features of cell and gene therapies and define specific requirements for production sites. For instance, not all GMP requirements are

technically feasible. Instead, GMP should be adapted to the specifics of cell and gene therapies, for example, by taking into account product variability, small batch sizes, and stability of the product. Risk-based approaches should also be established, allowing for flexibility on a case-by-case basis while ensuring maximum patient safety. For example, the EU has issued Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products.[2]

Based on these considerations, a regulatory framework that strives to encourage multinational companies to engage in local manufacturing of cell and gene therapies should:

- Utilize international standards for all steps in the hospital and at the manufacturing site, ensuring the production of high-quality therapy.
- Mandate measures to maintain these high-quality standards, including after marketing authorization.
- Apply these high standards to all hospitals, laboratories, and production sites that are engaged in cell and gene therapies.
- Provide for meaningful enforcement of intellectual property (IP) rights related to the manufacturing of the medicine.

To conduct clinical trials in China with products that are locally produced, Novartis suggests to the Chinese government to provide manufacturing licenses in two steps: one for the production of medicines used in clinical trials and a second for the commercial production. The requirements for the first steps should be designed in a way that clinical trials can be fast initiated without compromising

[2]https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2017_11_22_guidelines_gmp_for_atmps.pdf

the safety of patients. The United States, European Union, Japan and Australia follow such a model. Regular exchange with regulatory agencies of these countries can help to share experience and best practices.

b. Import of cell and gene therapies

Situational analysis in China

When a specific cell or gene therapy is produced outside of China, a patient's cell or genetic material must be exported to the manufacturing site to prepare the treatment. With CAR-T therapies, one of the manufacturing steps is the manipulation of the cells by introducing genetically modified components into the T-cells. Then these cells must be re-imported to China to treat the patient[3]. Currently, China has no guidelines or procedures for exporting and re-importing of CAR-T-related material. This leads to a number of issues that may cause damage to the human material and delay patient treatment, such as:

- In the export of a patient's blood cells and re-import of the patient's blood cells after genetic modification as well as of related materials, different government authorities, including the Chinese Customs office and Human Genetic Resources Administration Office, are involved. Inadequate communication among these agencies and unclear responsibilities make the procedure confusing and time-consuming. In case of a seriously life-threatening condition, the treatment may arrive too late for the patient.

[3] In allogeneic cell therapy, the donor is a different person than the recipient of the cells. Autologous cell therapy uses a person's own cells, and return them into the same person's body after their modification.

- Chinese health authorities require local quality testing of drug samples before the medicine can reach the patient. For cell and gene therapy medicines, this requirement cannot be fulfilled because of the insufficient amount of material available in the drug product for testing and the speed needed for these treatments to reach the patient.

Novartis suggestions

Clear and transparent mechanisms are needed to enable fast and reliable export and import of ingredients, intermediates, human material, and other types of material. Training for customs and regulatory officers on cell and gene therapies in general and on transport conditions specifically, for example in conducting on-site inspections, would create confidence in handling blood cells on the one hand and accelerate processes to the benefit of patients on the other. A functional export and re-import mechanism for human material and cell and gene therapy products would serve twin goals by a) enabling the treatment of patients in countries outside of China with therapies manufactured in China and b) allowing companies to offer highly innovative products to Chinese patients that are manufactured outside of China.

Moreover, Novartis suggests the nationwide introduction and implementation of exceptional import pathways for non-domestically licenced, but internationally approved therapies. One example comes from Shanghai, where a policy introduced in July 2018[4] suggests the establishment of a "green channel" for

[4] Item No. 38 of the "50 items for Shanghai Healthcare Services" to promote healthcare services and to construct Shanghai as a First-Class Medical Center City in Asia. http://www.shanghai.gov.cn/nw2/nw2314/nw2319/nw10800/nw11407/nw42843/u26aw56500

import and supply of medicines to selected hospitals that have been registered in the United States or European Union. Regulations for this green channel should include mechanisms for routine export and re-import of genetically modified material. Exchange on experiences and best practices between customs offices that release and receive this type of material would be very helpful.

Furthermore, processes that create a reliable supply chain from the hospital to the production site and back are essential to ensure that high-quality treatment reaches patients as quickly as possible.

c. Specific regulatory procedures in line with international standards

Situational analysis in China

China has made rapid progress in cell and gene therapy. Some hospitals began conducting their first clinical trials several years ago, and today more than 100 clinical trials in various diseases using different types of cell and gene therapies are reportedly underway.

However, only recently have specific guidance been made available to regulate the pharmaceutical testing requirements and the conduct of clinical trials for new therapies that could potentially bear many unknown safety risks. For instance, the Chinese authorities issued the Guideline for Research and Evaluation of Cellular Therapy Products only in 2017 as a first step to provide regulatory guidance in this dynamic area. This guideline covers many aspects related to cell therapies, but does not specifically consider gene therapies. It does not provide sufficient details on the needed standards of raw material to be used during manufacturing and transport of those therapies. In addition, the guideline requires all reagents

and consumables be registered, which takes significant time and risks delays in local manufacturing, development, and authorization of the treatment.

Also, no specific registration pathway for advanced therapies has been established in China. Instead, there are two options to register a cell and gene therapy product: either through the National Medical Products Administration (NMPA), which register and manage the therapies as drugs or the National Health Commission, presenting it as a type of medical technology. This situation may risk that products of different quality levels reach the market.

Novartis suggestions

Unique risks are associated with the modification of a patient's genetic material or with the administration of cells into a patient. Therefore, before these therapies are applied, their safety and efficacy should be rigorously studied, and companies should obtain marketing authorization based on a tailored regulatory framework. To ease the judicious development and registration of cell and gene therapies, Novartis suggests that NMPA establishes a specific framework for advanced therapies similar to the Regulation on Advanced Therapy Medicinal Products published by the European Medicines Agency (EMA).

At its core, this framework should:

- Support the conduct of clinical trial programs with scientific advice for sponsors by specialized agency staff to overcome challenges related to the characterization of the investigational product and clinical trial design, including considerations related to small patient populations.

- Include criteria for post-approval risk management plans in line with international standards to allow safety monitoring of treated patients over a long period.
- Mandate continual training of regulators, enabling them to make the best informed decisions for the patients on development programs and registration dossiers.
- Allow for waivers for quality testing of products within China, since a robust quality check has already been performed at the manufacturing product releasing site. EMA and Japan's Pharmaceuticals and Medical Devices Agency (PMDA) allow such waivers.
- Include guidance on qualification of raw material used during preparation or transport of a patient's blood cells in line international standards. Authorities may also consider establishing transitional or accelerated procedures to enable the use of materials that have not yet been registered in China.
- Provide for registration of cell and gene therapy products exclusively by NMPA using a full formal marketing authorization process including high-quality control measures, as well as consider accelerated registration pathways beyond priority review.

As many patients are in a highly critical health condition that requires immediate treatment, Chinese authorities may also consider transitional or bridging measures to make such treatments available more quickly, for instance by making clinical trial waivers or post-approval commitments specifically available for cell and gene therapies. Another option of early patient access would be a system that makes drugs available to patients prior to marketing authorization or reimbursement decisions. In France for instance, the exceptional use of

pharmaceutical products that do not have a marketing authorization and are not used in clinical trials is covered by obtaining a Temporary Authorisation for Use (ATU) in advance[5].

Summary

In creating a sophisticated regulatory framework that addresses the unique characteristics of cell and gene therapies, essential elements include:

- Establish a comprehensive framework that ensures cell and gene therapies are manufactured and transported under high-quality standards.
- Set up clear and transparent procedures for the export and re-import of human cells and related materials to provide for fast and safe clinical trials and treatment of patients.
- Have requirements for clinical trials and registration in place that follow international standards to ensure highest patient safety.
- Mandate risk management plans and post-approval safety monitoring in alignment with international requirements.
- Accelerate access to medicines for patients with critical conditions, for instance via specialized registration pathways, clinical trial waivers or early access schemes.

ii. Address special aspects of patient care

[5]https://ansm.sante.fr/var/ansm_site/storage/original/application/cadfbcf9594614d59c8915670853a28b.pdf

Administering cell and gene therapy may be a highly complex process, comprising a number of critical steps and requiring specific skills and experience. Adding to the difficulties, many healthcare professionals may not have sufficient experience to properly diagnose rare diseases. Drawing on the experience and insight of patients can help address both these challenges.

a. Preparing experts and the infrastructure for cell and gene delivery

Situational analysis in China

In China, patients are rarely engaged in expressing their needs. One exception is patients participating in the Chinese Organization for Rare Disorders (CORD), founded in June 2013, which works to promote exchange and cooperation among patients with rare disease and relevant organizations, medical specialists, pharmaceutical companies, and governmental agencies. In the field of cell and gene therapy strengthened patient involvement could be valuable for improved decision making.

Some cell and gene therapies present demanding requirements from hospital infrastructure, such as the proximity of relevant departments, suitable equipment, availability of certain emergency medication, and skills and training of healthcare professionals in the hospital. Currently, there are no guidelines in China available for hospitals that want to engage in these types of therapies.

Furthermore, experience in the United States and Europe shows that all patients that have been treated with an advanced therapy should be included in a patient registry. In China, there is no mature disease-based patient registry system in place. Instead, a kind of post-approval registry – “Post Approval Intensive Safety

Monitoring" - for all new compounds, including cell and gene therapies – was launched recently. However, this registry only focuses on the collection of safety data and has no specific requirements on the data collection methods or data format.

Novartis suggestions

The EMA recognized more than two decades ago that collaborating with patients is important, especially to gather real-life experiences that help inform scientific discussions on medicines and regulatory decisions. At Novartis, we listen to the patient community throughout the development of our medicines. This collaboration enables us to provide the most impactful therapies and design accompanying support services. Novartis suggests the Chinese authorities consider similar approaches to understand patient needs, for example by supporting the creation of patient organizations and their involvement in regulatory processes. Novartis also works with multidisciplinary teams of clinical experts to build on existing knowledge, accelerate research and development of new medicines and facilitate optimal patient care.

As the safety of patient is of utmost importance, Novartis suggests a number of measures to ensure safe treatment of patients and to cope with potential unwanted side effects:

- Establish an appropriate accreditation system in collaboration with local health authorities to qualify or certify healthcare providers or institutions as appropriate. The system could be based on a guideline that is jointly

developed by all relevant stakeholders, including the medical community, the pharmaceutical industry, and patients.

- Provide sufficient resources for hospitals or clinical care units intending to deliver cell and gene therapies. This should include a sufficient number of well-trained personnel and the equipment and tools needed to conduct all steps relevant to the respective therapy. In addition, a properly equipped emergency department and hospital pharmacy with the adequate emergency medication should be accessible at all times.
- Mandate that cell and gene therapies be administered only by healthcare specialists who are experts in the respective field. Members of the hospital team should also be able to recognize as early as possible any signs of adverse reactions and be able to address them immediately.

Because cell and gene therapy products are often complex to administer, Novartis also suggests the establishment of a mechanism that enables medical experts in China and abroad to exchange information and experiences. A good example for such a mechanism are the European Reference Networks (ERNs),[6] which are virtual networks connecting healthcare providers across Europe. The system aims to ease discussions on complex or rare diseases and conditions that require highly specialised treatment, as well as concentrated knowledge and resources. Such exchange networks could help Chinese specialists to ensure best treatment for their patients. In this context, Novartis welcomes the National Health Commission's intention to formulate the country's first dedicated treatment guidelines for rare disease patients, along with a treatment network and a 'patient registration system'.

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[6] https://ec.europa.eu/health/ern_en

We suggest the planned 'patient registration system' be designed to be disease-specific and to include all patients from all hospitals throughout the country. Data fields beyond safety information – for example, long-term efficacy – should be available. In addition, entry format for the data should be clearly defined, creating data sets for individual patients that allow healthcare providers to track patients for potential follow-up measures. International harmonization and collaboration between societies that run similar registries should be supported.

Summary

An appropriate hospital infrastructure and sufficient resources are crucial for successful cell and gene therapies. Core elements include:

- Discuss with patients about their medical needs to support well-informed regulatory decisions.
- Provide guidance on criteria and requirements for healthcare professionals and hospitals engaging in cell and gene therapy, including necessary equipment, skills and training, to help ensure quality and safe treatment of patients.
- Mandate inclusion of all patients in disease-specific registries that also capture patients treated with cell and gene therapies, helping create better transparency and oversight.

iii. Reshaping patient access models

Diseases that are treated with cell and gene therapies only affect a small patient population, but create a significant burden for those patients and their families. With the increasing development of highly innovative, advanced therapies, such as cell and gene therapies, an urgent need arises to find the most appropriate payment and funding models to make these therapies available to patients.

a. Introduction of flexible payment models

Situational analysis in China

The Chinese government has achieved impressive healthcare reforms in the past decades, especially regarding health insurance coverage. The whole population is now covered by medical insurance, which is mainly composed of basic medical insurance for working urban residents, basic medical insurance for non-working urban residents, and the new type of rural cooperative medical care. According to the 2017 State Council White Paper of Development of China's Public Health as an Essential Element of Human Rights, by the end of 2016 basic medical insurance had more than 1.3 billion recipients nationwide - a coverage of above 95 percent[7]. Despite having achieved nearly universal basic health insurance coverage, out-of-pocket health expenditures for innovative therapies remain high in China. The State Council White Paper also states that in 2017 reimbursement rates from basic medical insurance strongly increased in the past years; they are for urban inpatient care 70-80 percent and for rural inpatient and outpatient care 80 or 50 percent, respectively.

[7] http://english.scio.gov.cn/2017-09/30/content_41672354_6.htm

Recent government efforts to improve patient affordability and accessibility on innovative oncology therapies via price negotiation are well noted and very welcome. Recent national drug price negotiations in China and the subsequent inclusion of select innovative medications on the national reimbursement drug list (NRDL) have opened the door to new marketing and reimbursement possibilities. The negotiations seem to be ushering in a new era in which manufacturers are operating in a larger reimbursed market and Chinese patients are offered cost relief. The Ministry of Human Resources and Social Security (MoHRSS) has updated the NRDL in the past two years, and these updates were based on votes from national expert committees comprising clinical, pharmaceutical, and health- and pharmaco-economics experts. The Chinese government is working on a new framework for NRDL updates, with the goal of creating a more dynamic process, allowing for more frequent updates, as well as defining clear criteria to differentiate truly innovative medicines from others. These initiatives are necessary and welcome, but more value-based assessment approaches should be applied in upcoming NRDL updates.

Novartis suggestions

Cell and gene therapies may offer transformative benefits to patients and reduce the total cost and burden of disease, ultimately enabling patients and caregivers to resume healthy and productive lives. Reimbursement and healthcare system policies may have to be modernized to appropriately recognize, integrate, and reward these transformative therapies. Focusing on the value they deliver and allocating resources to the interventions that bring the highest value to the healthcare systems can reduce inefficiencies and set sustainable incentives for

innovative high-value solutions. Other factors to consider include that most cell and gene therapies are one-time treatments with the potential of a complete cure and relatively few patients require these advanced therapies.

Novartis recognizes that for potentially curative cell and gene therapies affordability can be challenging even when prices are considered cost-effective. To address this, we are piloting payment models using real-world evidence, with payers only reimbursing for real-world outcomes. For instance, Novartis has implemented a novel collaboration with the U.S. Centers for Medicare & Medicaid Services for our CAR-T therapy, Kymriah, that will allow for payment only when pediatric and young adult patients with acute lymphoblastic leukaemia respond to the therapy by the end of the first month.

Other flexible payment models that Novartis is exploring with various governments include outcome-based guarantees and annuity payments.

b. Consideration of alternative funding models

Situational analysis in China

Apart from further increasing the coverage of public reimbursement, China has begun looking into alternative funding models, including:

- *Commercial insurance*: Facing difficulties like increasing health burden and health inequity, China government began promoting commercial health insurances in recent decades and published a number of policies designed to create a favourable environment for their development.[8] However, the

[8] www.hindawi.com/journals/bmri/2018/3163746/

development of commercial health insurance remains in the early stages, particularly since awareness and understanding of the concept and benefits of insurance are low among the population.

- *Pooled funds*: One example is the Critical Illness Insurance (CII) that emerged from the Guidance on implementation of residents' critical illness insurance system, issued in 2012 by the National Development and Reform Commission, the Ministry of Health, and four other ministries and commissions. This model is meant to relieve the economic burden of disease faced by patients and their families and to reduce catastrophic health expenditure. The implementation of this type of insurance is different and fragmented among provinces. However, in 2016 the CII covered more than 1 billion urban and rural residents, and according to provincial policies, the actual reimbursement ratio was raised by 10 to 15 percent.

Many cell and gene therapies can potentially replace costly, intensive, and long-term care with a one-time treatment that could result in a complete cure. However, these unprecedented high-value therapies have higher upfront costs than conventional therapies, bringing new challenges surrounding funding models for the industry and payers.

Novartis suggestions

Coverage of highly innovative advanced therapies like cell and gene therapies by China's basic medical insurance is not the only option available. The Chinese government may also consider commercial insurances or pooled funds, among other models. Each of the funding options requires a framework with detailed

guidance on criteria and procedural steps, as well as clearly defined roles and responsibilities.

To reshape patient funding models a discussion is needed that brings in all relevant stakeholders, including China's new National Healthcare Security Administration, payers, healthcare professionals, and the pharmaceutical industry. Pertinent questions include:

- Shall payments be covered by the basic medical insurance or by commercial insurance schemes?
- What would a suitable payment model look like that covers high upfront payments for a one-time treatment that provides potentially complete cure?
- Since these therapies may be administered in a very limited number of specialized hospitals, could contracts with individual hospitals be considered?

In tandem with this discussion, efforts are needed to raise awareness and education among the general population on the concepts behind health insurance in general and of particular insurance options. Such an educational initiative would increase the general acceptability of insurance and, as a result, health insurance coverage of diseases.

Summary

Funding is a clear obstacle to improved patient access to cell and gene therapies. Efforts to overcome this should include:

- Establish flexible payment mechanisms that consider the value of cell and gene therapies for patients and caregivers.

- Develop alternative funding models to ensure the significant benefits of cell and gene therapies are accessible to patients, who may have no other treatment option. Funding models could include commercial health insurance and pooled funds, such as critical illness insurance.

III. Conclusion

Cell and gene therapies may offer effective innovative solutions for a broad range of disease areas, including immunodeficiency diseases and cancers, as well as neurological, haematological and eye disorders. These therapies may have long-lasting effects and may be curative by addressing the genetic root-cause of disease. To enable patient access to those advanced therapies, innovative policy solutions and close collaboration among companies, authorities, and specialist healthcare providers are required.

The development and application of cell and gene therapies is a fast moving area in medical science. Experiences are made and regulatory standards are being defined. Engagement in this new field offers great opportunities for China to shape the policy environment and be a thought leader for the international community. Novartis is committed to working with the Chinese government, regulatory agencies, and healthcare providers, as well as payers, to establish an optimal regulatory framework and payment models that enable timely and affordable access for patients. Implementation and enforcement of this framework will support China’s goals in its ongoing healthcare reform effort, and will benefit patients.