FROM THE ANALYST'S COUCH

Innovative drug R&D in China

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With a population of 1.3 billion people and a rapidly expanding economy, China has recently risen to become the third largest pharmaceutical market globally, and it has been predicted that this market will grow by 25–27% to a value of more than US$50 billion in 2011 (REF. 1). Although many of the drugs in the current market are either generic versions or developed outside China, several multinational pharmaceutical companies have now located research and development (R&D) centres in China, and Chinese pharmaceutical companies are increasingly focusing on innovative drug R&D. Furthermore, the Chinese government implemented a special drug R&D funding programme in which $2.7 billion was invested from 2008 to 2010, with another $6 billion to follow in the next 5 years.

However, information on the output of innovative drug R&D in China is limited. With the aim of addressing this issue, we have collected and analysed information from the Chinese State Food and Drug Administration (SFDA) and the Center for Drug Evaluation of the SFDA (CDE) for all novel pharmaceuticals for which new drug applications (NDAs) and investigational new drug applications (INDs) were approved in China between 2003 and 2010. The novel pharmaceuticals discussed in this article only include chemical drugs in classes 1.1 and 1.2 and biological drugs in class 1, which are defined by the SFDA as not being previously approved for marketing as a drug anywhere else in the world. Thus, the scope of novel drugs in this article is narrower than that of the new chemical entities (NCEs) used by the US Food and Drug Administration (FDA). For example, if a drug was first approved by the FDA or the European Medicines Agency, it would not be qualified as a class 1 new drug by the SFDA when its approval is later sought in China. Multinational pharmaceutical companies usually market their drugs in developed countries first, and in our survey, all the innovative drugs approved as class 1 by the SFDA are from domestic Chinese pharmaceutical companies. Consequently, the class 1 approvals by the SFDA reflect the status of innovative drug development solely in domestic Chinese pharmaceutical companies. Additionally, traditional Chinese medicine and vaccines are not discussed here.

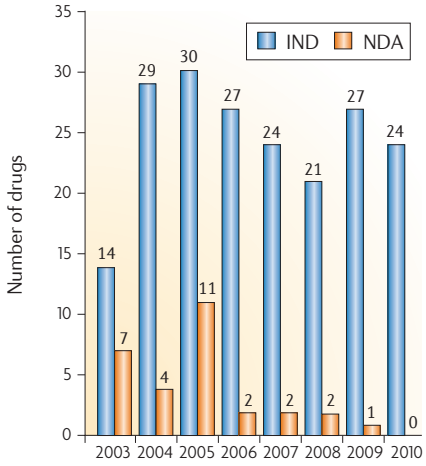


Figure 1 | **Annual number of approved INDs and NDAs for innovative drugs from Chinese companies.** Data were collected from the website of the Chinese State Food and Drug Administration (SFDA) and the Center for Drug Evaluation of the SFDA. IND, investigational new drug application; NDA, new drug application.

Analysis

In the period analysed, ~25 drug candidates were approved for entry into clinical trials (that is, an IND was granted) and an average of four drugs were approved for marketing per year (FIG. 1). However, there was a significant reduction in the number of drugs approved for marketing since 2006, with less than two approvals per year in comparison with the preceding years that ended with 11 approvals in 2005. This is primarily due to the introduction by the SFDA in 2007 of much more stringent rules and regulations regarding new drug approval and registration.

A total of 187 novel therapeutics are currently in clinical trials. Nearly two-thirds of the therapeutics are in Phase I trials, with those in Phase II and III trials accounting for 19% and 22%, respectively (FIG. 2a). As shown in FIG. 2b, oncology is the most common therapeutic area (32% of therapeutics analysed), followed by infectious diseases (17%) and cardiovascular diseases (10%).

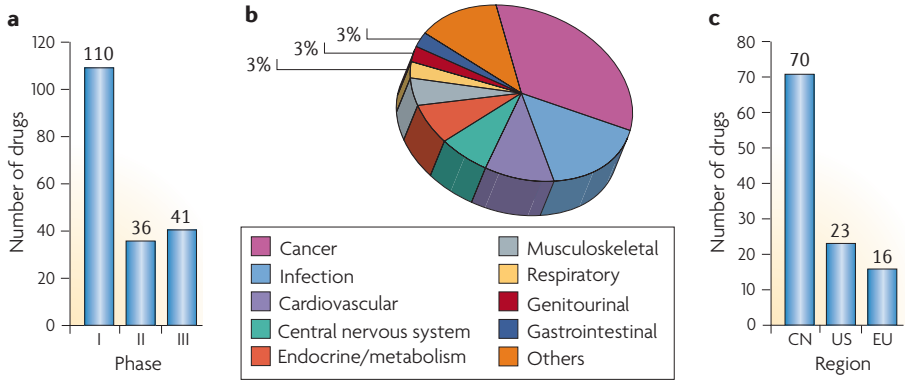
Bearing in mind the importance of patent protection in drug R&D as well as the evolution of Chinese patent law in recent years, we also analysed the patenting of the investigational therapeutics in China. Patents for pharmaceuticals are divided into two categories: compound patents and secondary patents, which include preparation, detection, pharmaceutical composition and usage. Out of 187 investigational drugs, 70 have compound patent protection in China, whereas 23 have compound patent protection in the United States and 16 in Europe (FIG. 2c). We also investigated the characteristics of those novel therapeutics that had patent protection in either the United States or Europe, which are presented in TABLE 1.

Outlook

The increased investment by the Chinese government and multinational pharmaceutical companies, as well as other improvements (discussed below), are creating a stronger environment for innovative drug R&D in China. First, in the past two decades, the Chinese regulatory system has undergone a systematic transformation to adapt to the emergence of more INDs. The first drug administration law in China was enacted in 1985, and there have been four major amendments since, with the latest one enacted in 2007. As mentioned above, the SFDA (which itself was founded in 2003) has introduced more robust regulations regarding new drug approval and registration, and to improve transparency and efficiency, which could pave the way for the emergence of more innovative drugs in the long term. For example, the registration status of an IND or NDA is publicly available, and applicants have easy access to all information regarding the approval process for their drugs. Local agencies of the SFDA are authorized to conduct preliminary approval procedures to increase efficiency. Companies that provide false information or samples will be penalized and barred from submitting NDAs for up to 3 years.

Patent protection is a second factor that is essential in innovative drug development. The current Chinese patent law was enacted ▸

R&D IN CHINA | MARKET INDICATORS



▸ Figure 2 | **Characteristics of novel investigational drugs in China. a** | Number of drugs in each phase of clinical trials. **b** | Indications of these drugs. **c** | Patent protection of these drugs. Some drugs have patent protection not only in China (CN), but also in the United States (US) or the European Union (EU). Data were collected by the end of 2010 from websites of the Chinese State Food and Drug Administration (SFDA) and the Center for Drug Evaluation of the SFDA, the Chinese State Intellectual Property Office, the US Patent and Trademark Office, the European Patent Office and company press releases.

in 1984, but until it was amended in 1992, pharmaceutical compositions were not patentable. Now, the patent system has evolved to provide greater protection for innovative drugs. The final judgment from the Beijing High People's Court in 2007 on the patent dispute over sildenafil (Viagra; Pfizer) is one example. The judgment rejected the patent challenge from 12 domestic generics companies, effectively providing patent protection for sildenafil until 2014. Interestingly, the patent that was under dispute is a method-of-use patent, which is more vulnerable to challenges from generics companies than compound patents.

Table 1 | **Novel drugs in clinical trials with issued compound patents in the US or EU**

Compound	Developer	Therapeutic area	Patent	Stage
Iptakalim	Nhwa	Cardiovascular	EU	III
Aildenafil	Wannianchun	Genitourinal	US	III
Cymipristone	Xianju	Genitourinal	US/EU	III
Icotinib	Beida	Cancer	US	III
rSIFN	Huiyang	Cancer	US/EU	III
Sulcardine	SIMM	Cardiovascular	US/EU	II
Trichosanthin	Xiangtianmu	Infection	US	II
Sifuvirtide	FusoGen	Infection	US/EU	II
Chiglitazar	Chipscreen	Endocrine/metabolism	US	II
Tyroservatide	Yitai	Cancer	US	II
Trantinterol	Jiutai	Respiratory	US/EU	II
Chidamide	Chipscreen	Cancer	US	II
Buagafuran	SIMM	Central nervous system	US	I
Ethaselen	Qizheng	Cancer	US	I
Nemonoxacin	Huayu	Infection	US/EU	I
Albuvirtide	Frontier	Infection	US	I
Thienorphine	IPT	Central nervous system	US/EU	I
Triptolide	SIMM	Musculoskeletal	US	I
Novaferon	Genova	Cancer	US	I
PEG-rhArginase	BCT	Cancer	EU	I
yPEG–rhGCSF	Amoytop	Cancer	EU	I
yPEG–rhGH	Amoytop	Endocrine/metabolism	EU	I
Citricplatin	Sansiweier	Cancer	US/EU	I
yPEG–rhIFNα2a	Amoytop	Infection	EU	I

EU, European Union; GCSF, granulocyte colony-stimulating factor; GH, growth hormone; IPT, Institute of Pharmacology and Toxicology; PEG, polyethylene glycol; rh, recombinant human; rSIFN, recombinant super compound interferon (IFN); SIMM, Shanghai Institute of Materia Medica; SIPI, Shanghai Institute of Pharmaceutical Industry; US, United States of America; yPEG, Y-shape branched PEG.

Third, to improve investment, ChiNext, China's 'NASDAQ', was launched in 2009, focusing on innovative enterprises and other fledgling venture enterprises. ChiNext provides an important exit for investment, such as venture capital in the field of innovative R&D. Fourth, China initiated a health-care reform plan in 2009, which will create a demand for innovative pharmaceutical products in the years to come. Finally, with regard to talent, the current wave of returnees to China includes many experienced professionals from pharmaceutical and biotechnology companies elsewhere in the world.

In conclusion, although the innovative pharmaceutical industry in China is still in the early stages of development, it has progressed rapidly in the past decade. Moreover, China has made considerable improvements and continues to improve the key factors — regulatory systems, patent protection, basic research, investment, talent and market incentives — for the creation of a first-class environment for innovative drug R&D.

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Competing financial interests
The authors declare no competing financial interests.