New Zealand’s drug development industry—strengths and opportunities

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Abstract

Aim Globally the traditional model of drug development is changing and the large pharmaceutical companies are looking externally for innovative compounds, new technologies and cost-effective drug development services. New Zealand (NZ) can capitalise on its expertise in innovative drug discovery and development but needs to be able to define and promote its capabilities to the global drug development industry. An approach that will enable a ready assessment of NZ’s expertise is presented.

Method Interviews will be carried out with key senior personnel from NZ drug discovery groups, drug development companies and organisations that provide a wide range of research and development services. The resulting data will be collated to document current capabilities and expertise, as well as limitations, in NZ’s industry and assess their potential for the future. Participants will be asked to identify factors that support and factors that limit their organisation’s progress in drug development and to suggest policies that could be implemented to positively influence future performance.

Conclusion A formal assessment of New Zealand’s capabilities, strengths and limitations in drug development will aid in the promotion of its expertise to overseas organisations and enhance the economic benefits that could accrue to New Zealand.

Background

The changing model of drug development—The model of drug development is changing. Whereas the traditional approach was that of large pharmaceutical companies developing their own pipeline compounds and focussing on a few blockbuster products, we have now entered an era of partnerships and alliances between big PHARMA and smaller companies and universities the latter being sources of innovative compounds and specialised drug development services. This has resulted in a trend towards personalised therapeutic approaches with niche products that may not provide a high volume of sales but which can, nevertheless, be highly profitable.¹

This change in the traditional approach to drug development has occurred as the industry adapts to an evolving environment caused by:¹⁻³

- The failure of the large pharmaceutical companies to identify sufficient promising new compounds, leading to waning investor confidence;
- The disease categories that require therapeutic innovation (e.g. cancers, neurodegenerative diseases) are less well understood and hence more difficult
to research than disorders that already have a wide range of treatment options (e.g. in cardiovascular and infectious fields);

- Escalating research and development (R&D) costs;
- The wide range of new scientific and technological improvements which make it impossible for one firm to keep up-to-date with all opportunities that they create;
- Current blockbuster drugs coming off-patent and increasing generic competition;
- An increasingly risk-averse regulatory environment which has been exacerbated by safety issues associated with some high profile drugs (e.g. Cox-2 inhibitors); and
- More demanding users who have extremely high expectations of the efficacy, safety and value of their medicines.

The costs and risks of drug development—The average capitalised cost to develop a pharmaceutical agent, taking into account costs of discovery, lead generation and failed candidates, has risen with time reaching $US1.24 billion in 2005 dollars. The 3 phases of clinical drug development (Phase 1—first pharmacokinetic and safety studies; Phase 2—larger safety and efficacy studies in patients; Phase 3—safety and efficacy studies in large numbers of patients, usually required for drug registration) carry different risks and costs. The largest variation being in the costs of phase 3 as they are most dependent on the therapeutic indication being sought.

Table 1. Clinical development: average (range) cost and chance of success for each phase in a drug’s development

<table>
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<tr>
<th>Clinical development phase</th>
<th>Average (range) cost ($US)</th>
<th>Chance of success</th>
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<tbody>
<tr>
<td>1</td>
<td>15.2 million (9–23 million)</td>
<td>70–80%</td>
</tr>
<tr>
<td>2</td>
<td>24.0 million (20–31 million)</td>
<td>30%</td>
</tr>
<tr>
<td>3</td>
<td>86.8 million (65–137 million)</td>
<td>80%</td>
</tr>
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Phase 2 (i.e. showing clinical proof of principle) is more expensive and has a much higher risk of failure than phase 1. The Phase 3 programme is the most expensive due to the numbers of patients required to establish both efficacy and safety in the long-term and to obtain data in special populations. In addition to these costs of running the clinical programme there are the costs arising from pre-clinical studies, manufacturing and formulation.

From every 10,000 molecules that are screened, approximately 5 will enter clinical trials and only 20% of these will succeed to the end of phase 3. Even then, regulatory approval is not guaranteed and some compounds are discontinued for reasons including commercial viability and long-term animal toxicity issues.

**The opportunity for New Zealand**—The uncertainties and changes in the global drug development industry noted above create opportunities for countries with recognised capabilities. New Zealand (NZ) can capitalise on the advantages of a
strong biomedical research basis for drug discovery, a resourceful and entrepreneurial society that encourages innovation, a reputation for conducting world-class medical and clinical research, an acknowledged ability to produce research results “on time”, and a comparatively weak dollar which leads to competitively priced drug R&D services.

Potential opportunities available in this new world of drug development include the discovery and development of innovative compounds, production of generic medicines, reformulation and new presentations of existing medicines, and provision of drug development support services.

NZ has the potential to add value and effectively compete on a global basis in at least three of these areas:

- The discovery of innovative compounds targeted to treat diseases that currently have insufficient treatment options.
- The development of novel compounds.
- The provision of R&D services to the global drug development industry.

Each of these could bring substantial economic benefits to NZ and the research proposal outlined in brief here is aimed at assessing the viability of these three opportunities.

Though a high-risk enterprise requiring significant financial investment, the discovery and development of a NZ novel compound has the potential to provide significant financial returns to its investors as well as economic and knowledge benefits to all NZers.

NZ’s most recent success in this regard is the anti-cancer agent, DMXAA, identified in 1989 at the Auckland Cancer Society Research Centre (ACSRC) and developed under the direction of Professors Bruce Baguley and Bill Denny. The development was complicated and protracted due to lack of funds and expertise in NZ at the time. However, DMXAA, now named Vadimezan, was licensed by Novartis in 2007 and phase 3 trials are underway.

The case of DMXAA highlights some problems and potential benefits to NZ of identifying and developing novel compounds. Much of the clinical development of DMXAA involved NZ clinical sites and the out-license agreement with Novartis included upfront and milestone payments, and royalties on eventual sales. However, in reality, some of these financial returns may be quite limited as the NZ investment has been diluted by larger overseas investment partners and, because of the protracted development process, Vadimezan may well be off-patent by the time it reaches the market.

At $US1.24 billion the cost of drug development is too high for the NZ government and NZ private investor funding even if the costs in NZ are much lower than elsewhere (e.g. by using NZ’s Centres of Research Excellence and less expensive local drug development service organisations).

In order for NZ to maximise the returns from its innovative drug discovery and development industry it needs to have access to sufficient capital and to assess the best point in the development process at which to share the risks and costs.
The provision of R&D services (e.g. chemistry, formulation and manufacturing, clinical research and project management) to the global pharmaceutical industry is less profitable than the potential returns from sales of a novel pharmaceutical. However it carries a much lower risk, does not require a large financial investment and can still contribute significant economic returns on a regular basis.

There are already a number of successful but R&D centres in NZ working under contract with large pharmaceutical companies and there seems every reason to build upon the success of these endeavours.

In order to capitalise on its opportunities NZ needs to be able to compete against countries such as Australia, the UK, India and Singapore which are also seeking to attract overseas partners and investors to assist in the discovery and development of novel compounds and to obtain drug development contracts from large pharmaceutical companies. NZ needs to be able to define and promote its drug discovery and development capabilities to the global pharmaceutical industry. This paper outlines research already underway which aims to define those capabilities.

The research approach

Questionnaires based on developed theoretical frameworks will be administered during semi-structured interviews with individuals who have a key role in NZ drug discovery, drug development or R&D organisations. The questionnaires will be used to collect data on drug discovery and development capabilities, industry enablers and barriers, and the potential economic benefit to NZ.

Assessment of capabilities, knowledge management and innovation—Data will be collected to assess the expertise and capabilities of both the participant and the organisation they represent. All eligible drug development companies and R&D support services organisations will be approached to participate. A representative sample of the drug discovery groups will also be taken into account.

For the purposes of this research, a drug development company must be registered in NZ and have conducted at least one clinical trial on a novel compound in the last 5 years. The R&D organisations will include those that provide any of the following services: chemistry, pharmaceutical formulation, analytical methods, toxicology, data management and statistics, clinical research and project management. The drug discovery groups will be those with the potential to carry a compound into human clinical trials in the next 5 years.

The participant information collected to assess the expertise in drug discovery and development will include qualifications, relevant career experience and outputs (such as publications, especially in peer-reviewed journals, and conference presentations), personal competencies, membership of appropriate organisations and any formal recognition of their expertise. Similarly the information collected on the organisations will include their range of drug discovery and development capabilities, qualifications and experience of staff and, where applicable, data on previous and current compounds in discovery and development.

Participants will be asked to compare their organisation’s knowledge sharing and knowledge management behaviours both within their organisation and externally with that of their facet of the industry. Based on a knowledge management questionnaire...
developed by Lui and Lui,\textsuperscript{11} participants will also be asked to rate the importance of different sources of knowledge (e.g. codified and non-codified information, external and internal sources). Since the process involved in the discovery and development of a new medicine requires extensive knowledge in different specialities distributed across many individuals, knowledge acquisition and sharing is essential.\textsuperscript{11,12}

Measuring innovative performance objectively is very difficult because measures such as the number of patents registered or scientific papers published can be affected by the type of organisation. Thompson and Heron\textsuperscript{13} adapted seven ‘innovator’ questions from a broader scope instrument and used this sub-scale as a measure of innovative behaviour in organisations. This sub-scale will be used by participants to rate their organisation’s ability to produce new ideas, develop contacts with external experts, make time to work on ideas and projects, solve problems that caused others difficulty, project planning, innovative output, teamwork and communication.

The inter-relationships between NZ drug discovery groups, the NZ drug development companies and the R&D support services organisations used both locally and by overseas companies will be explored. NZ’s interconnecting network of expertise will be compiled and assessed in terms of the quality and quantity of expertise, and ability to adhere to timelines and budgets.

**Enablers and barriers to NZ’s drug development industry**—Participants representing the three facets of NZ’s industry will be asked to identify the enablers and barriers that have affected their organisation’s efforts in drug discovery and development. In addition they, plus government agencies and other industry stakeholders, will be asked for their opinion on which factors have encouraged and threatened NZ’s industry as a whole and policies that NZ could implement in order to further support growth of its drug development industry.

**Economic benefit to New Zealand**—An assessment of the economic benefits that NZ’s drug discovery and development industry could provide will be made based on the estimated sales potential of a novel compound discovered and developed in NZ, and on NZ’s R&D capability being used by overseas firms.

NZ needs to carefully consider its options for compounds entering clinical development or that have positive data from phase 1 studies. The outcome of the NZ compounds that have entered clinical development in the last 5 years will be considered in order to assess the best time to look for a partner to share risks and costs. Different funding and risk-sharing scenarios will be used to obtain a range of potential economic returns if a NZ-discovered and developed compound reaches the market.

Estimates of the economic benefits that would accrue to NZ through the provision of drug development services to overseas companies will be made. NZ’s competitiveness in the provision of these drug development services will be assessed by comparing quotes from NZ companies for standardised services (e.g. investigator fees, hourly rates of personnel associated with clinical research, laboratory tests, ECG costs) with those from equivalent companies in competitor countries such as Australia, the US and India. In addition the cost and time required to obtain the regulatory and ethical approvals to initiate clinical studies will be compared.
Conclusions

The NZ Government invests in science, research and technology with a goal to maximise NZ’s potential to conduct excellent and relevant health research and ensure that the economic benefits of health research are captured for NZ. With the current major change in the landscape of new drug development, it is important to assess the potential of NZ to play a much greater role in this evolving industry.

The major aim of this project is to calculate the potential economic value of the NZ drug development industry and the feasibility of supporting those facets that could be internationally competitive:

- Drug discovery
- Development of NZ novel compounds
- Provision of R&D services to overseas drug development companies

This formal assessment of NZ’s capabilities in drug discovery and development will aid in the promotion of NZ’s expertise to overseas organisations and may assist in attracting investors to fund the discovery and development of NZ’s novel compounds, thereby reducing the risk to local investors. Both these outcomes will enhance the economic benefits that accrue to NZ from investing in and promoting its industry.

Competing interests: None known.

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