



Intellectual Property Report 2005

Intellectual Property Report

March 30, 2005
AnGes MG, Inc.

1 Introduction

Welcome to the first Intellectual Property Report to be issued by AnGes MG, Inc. (hereafter, AnGes MG).

A company is a member of society. As such, our company is committed to actively responding to the government policy of strengthening the intellectual property nation. Further, as part of our broad corporate responsibility to society, we are committed also to responding to the demand for greater information disclosure.



Ei Yamada, Ph.D.
President & CEO

This demand for information disclosure is not directed only at large corporations. It is desirable for venture business also, as their activities become more widely recognized throughout society, to concentrate their efforts on gaining understanding of the significance of their existence. In particular, it is essential for bio-ventures, which require substantial investment for early-stage research and development, and are by nature high-risk/high-return businesses, to publicly disclose and provide to investors and analysts a variety of corporate information so that their goals and present status can be accurately conveyed and evaluated. For AnGes MG, as a pioneer university-launched venture that went public, this is one important mission of our company.

In particular, the disclosure of information concerning intellectual property plays an important role. In response to the increasing recognition in this country of the significance of intellectual property to corporate strategy, last year 16 companies released intellectual property reports. However, most of these were major corporations. Considering the significance of intellectual property to corporate strategy, it could be said that it ought to be venture business that take the lead and actively strive for greater information disclosure. This constitutes the background for the release of this Intellectual Property Report.

This Intellectual Property Report is the first for a venture business, and its contents differ from the intellectual property reports previously published by major corporations. We have produced this report from our own unique standpoint.

While the number of intellectual property cases held by our company, AnGes MG is of a small scale when compared to major corporations, the relative importance and weight of each individual intellectual property to our corporate strategy and corporate value is very high, so in this respect we differ greatly from major corporations. It is our hope that by this Intellectual Property Report, we will be able to gain your understanding of our company's fundamental stance and recognition of intellectual property as well as of our corporate activities based on AnGes MG's unique policies and intellectual property strategies.

2 Intellectual Property for Drug Manufacturing Venture Businesses

It is typical for large drug manufacturers to initiate research projects based on promising candidates obtained at their own laboratories. Consequently, the substance patents and medical use patents that support their research projects are most often based on their own inventions. Further, to obtain comprehensive protection of their rights, it is typical for such manufacturers to construct a web of patents based on their own technologies and inventions by obtaining patents on drug preparations, drug substance manufacturing methods, and second medical uses (supplementary indications). Further, to support and develop their giant organizations, they should avoid the pressure on or reduction of profits resulting from use of the patent rights of others.

However, in the gene/nucleic acid medicine field which we target:

- (1) There is a history of research and development at universities and venture business being ahead of major drug manufacturers;**
- (2) Unlike low molecular medicines, since this is a new field, accurate assessment of development risk is difficult, so major drug manufacturers have been slow to participate; and**
- (3) Since this is a cutting edge field, the development of examination standards at the Patent Offices of various countries is still in catch-up mode, so various competing rights conflict and overlap.**

Consequently, the circumstances surrounding intellectual property in this field differ completely from the case of conventional medicines.

Under such circumstances, even a major drug manufacturer, for example, would find it difficult to completely secure all the intellectual property rights necessary for development by themselves, and could only begin development and commercialization after extensive efforts expended in obtaining assignment of or licenses over the rights of other companies.

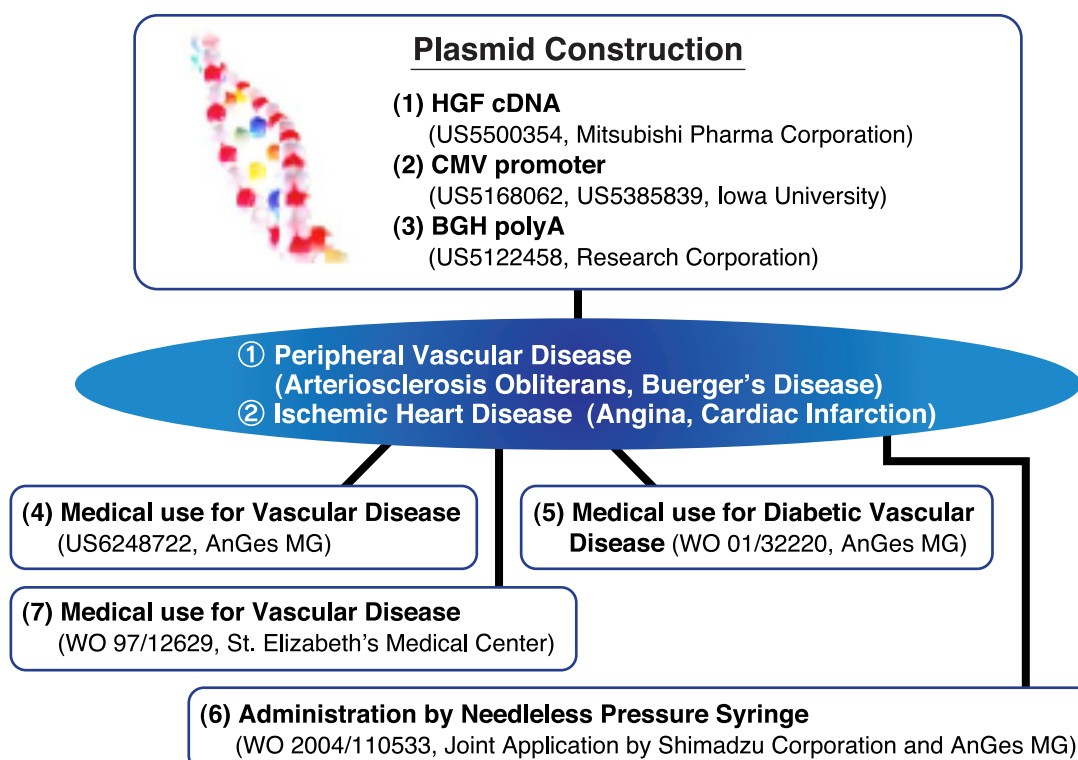
In contrast, it is no overstatement to say that venture businesses have an advantage in terms of competitive strategy in that they need not adhere to the idea of in-house technologies/rights but rely on an intellectual property strategy of not holding many technologies/rights themselves, but obtaining assignments or license rights. Taking advantage of the particular characteristics of a venture business specializing in the development of medicines in a particular field, and focusing on the detailed expansion of indications (medical uses) as well as improving manufacturing and drug delivery methods, enables the construction of an intricate web of patents inclusive of partnerships and alliances.

The business style and approach of such drug-creation venture businesses provides hope to patients who eagerly await new therapeutic agents with high efficacy and safety, contributing in various ways to the improvement of their quality of life (QOL). This is true also all those patients who suffer from rare diseases for which there is little incentive for development of treatments.

3 HGF Project and Intellectual Property

Firstly, we explain the intellectual property covering our HGF project under the following headings: (1) Use for vascular conditions, and (2) Other conditions and administration forms.

(1) Vascular Conditions



The HGF gene therapy currently under clinical development is applicable to the following vascular conditions:

- i) Peripheral Vascular Disease (Arteriosclerosis Obliterans, Buerger's Disease)
- ii) Ischemic Heart Disease (Angina, Cardiac Infarction)

These projects are covered by the following group of patents: (Only published applications are indicated both here and throughout.)

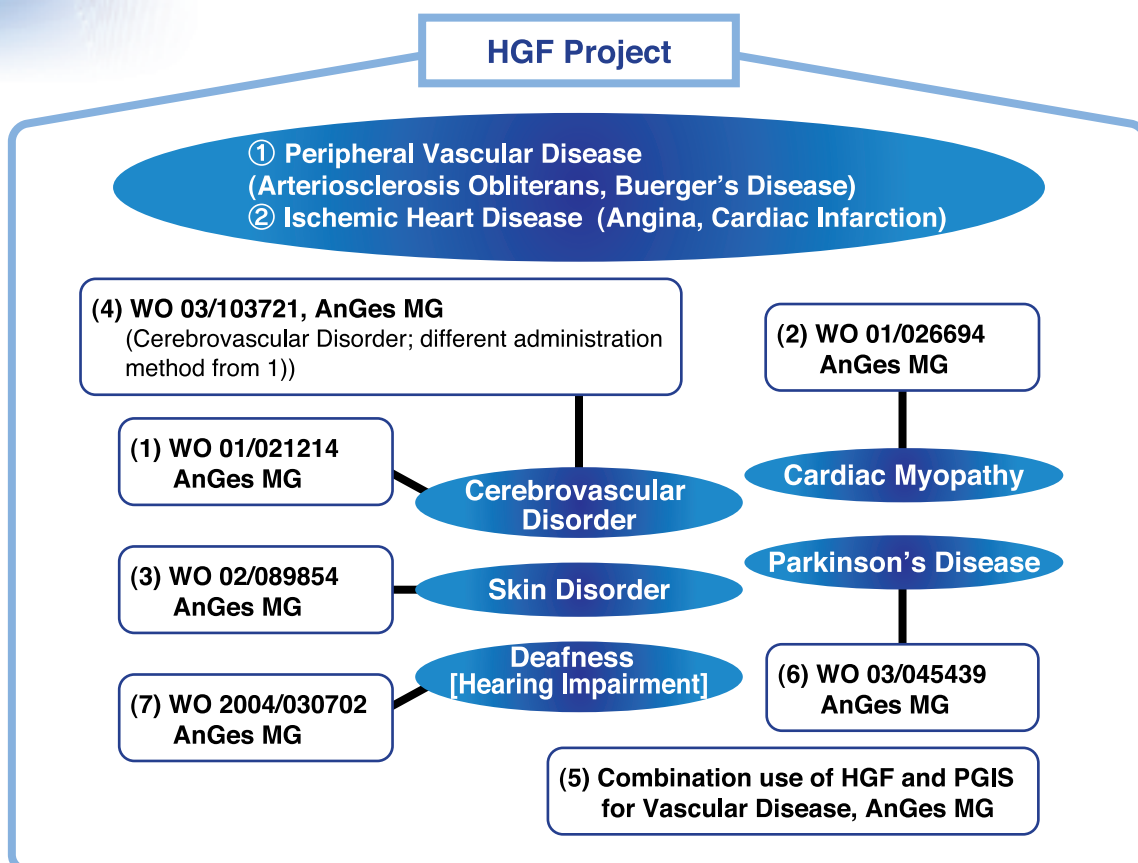
- 1) US5500354 (HGF cDNA, Mitsubishi Pharma. Corporation)
- 2) US5168062, US5385839 (Plasmid construction, Iowa University)
- 3) US5122458 (Plasmid construction, Research Corporation Technologies)
- 4) US6248722 (Medical use for Vascular Disease, AnGes MG)
- 5) WO 01/32220 (Medical use for Diabetic Vascular Disease, AnGes MG)
- 6) WO 2004/110533 (Administration by Needleless Pressure Syringe, Joint Application by Shimadzu Corporation and AnGes MG)
- 7) WO 97/12629 (Medical use for Vascular Disease, St. Elizabeth's medical center)

As is clear from the above, this project cannot be realized relying only on the intellectual property held by one corporation. Development has only become possible through the establishment of broad alliances.

Further, since we respect the intellectual property of others, and from the standpoint of preemptively avoiding unnecessary conflict, we regularly monitor the patents and patent applications of other companies relating to HGF gene therapy on a global basis.

In addition, we are pursuing a basic company policy of providing greater benefits to patients. We seek to develop bio-medicines which are safer and more effective, non-invasive, and which realize improve quality of life (QOL). To this end, we are examining and pursuing as one option broader alliances and partnerships in relation to intellectual property.

(2) Other Conditions and Forms of Administration



■ HGF Project and The Intellectual Property (2) Other Diseases, Administration Methods ■

HGF possesses a diverse range of physiological activities apart from those described above. Thus, there is the possibility that it can contribute to the improvement of the quality of life (QOL) of patients suffering from conditions for which no effective therapeutic agents yet exist.

From such a standpoint, we have been concentrating our efforts on expanding the applicable indications (medical uses) of the HGF gene. As a result, we have the following patent applications covering these indications:

- 1) WO 01/021214 (Cerebrovascular Disorder, AnGes MG)
- 2) WO 01/026694 (Cardiac Myopathy, AnGes MG)
- 3) WO 02/089854 (Skin Disorder, AnGes MG)
- 4) WO 03/103721 (Cerebrovascular Disorder; different administration method from 1), AnGes MG)
- 5) WO 01/089581 (Combination use of HGF and PGIS for Vascular Disease, AnGes MG)
- 6) WO 03/045439 (Parkinson's Disease, AnGes MG)
- 7) WO 2004/030702 (Deafness [Hearing Impairment], AnGes MG)

We will continue actively to conduct pre-clinical/clinical research aimed at expanding the applicable applications of the HGF gene, and at the same time seek to establish further intellectual property rights pertaining thereto.

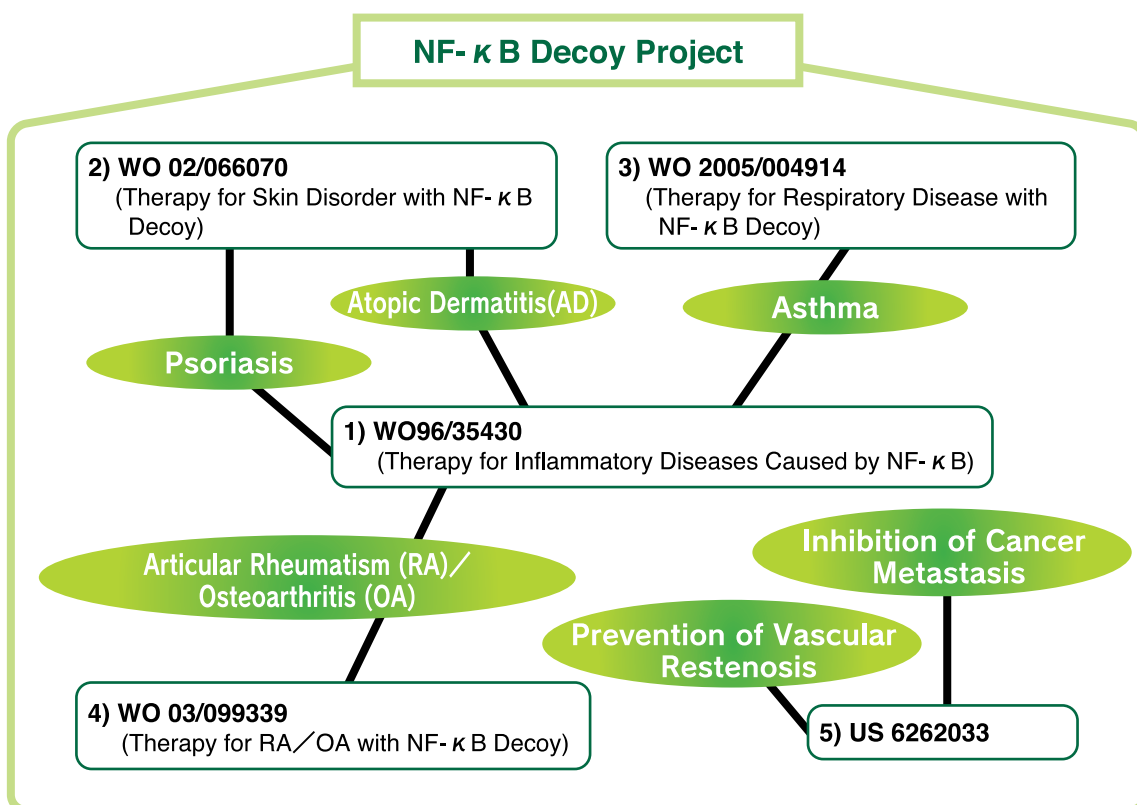
Since there exists a substantial amount of neighboring prior art when it comes to novel medical uses of known genes, it is common for there to be difficult hurdles to establishment of such rights when compared to patents for substances. However, our intellectual property division through their ingenuity and determination continue to strongly support our development projects, and consequently we are committed to achieving our targets.

Avoiding the situation where failure to establish intellectual property rights would result in termination of development - this is what we regard, as the intellectual property division of a venture business, as our duty, entrusted to us by the many patients eagerly awaiting new medicines.

4 NF- κ B Decoy Project and Intellectual Property

Next, we explain the intellectual property covering the NF- κ B Decoy Project, in the following order: (1) Indications currently under clinical development, (2) Other indications and Modified-form decoy.

(1) NF- κ B Decoy Project Currently Undertaking Clinical Development



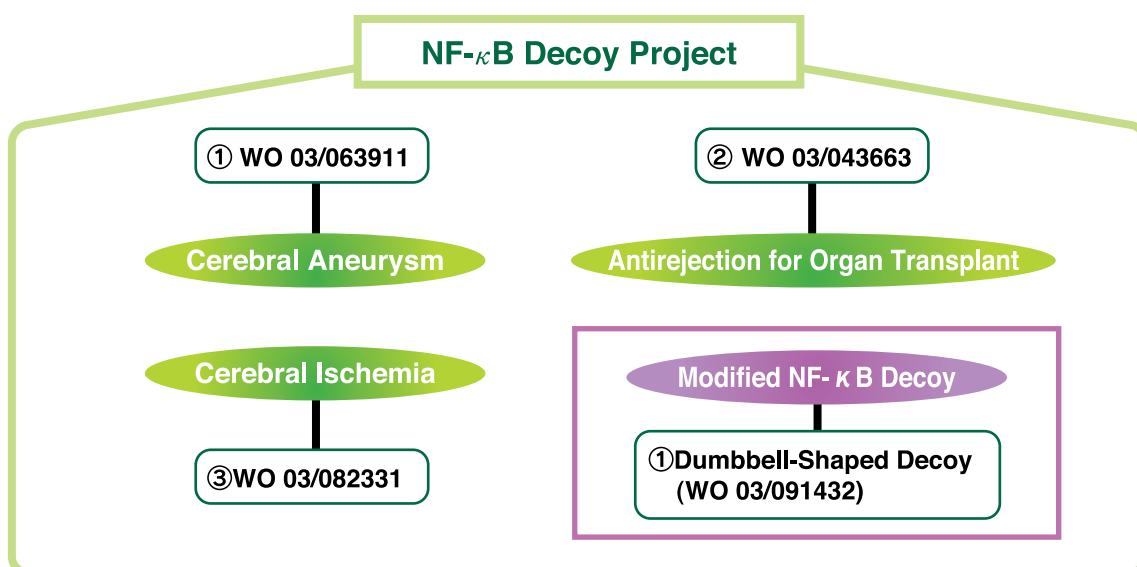
We are currently undertaking clinical development of the NF- κ B decoy project in respect of the following indications:

- (1) Atopic dermatitis (AD)
- (2) Asthma
- (3) Psoriasis
- (4) Rheumatic arthritis (RA)/osteoarthritis (OA)
- (5) Prevention of restenosis
- (6) Inhibition of cancer metastasis

The development projects are covered by the following patent groups in relation to each indication:

- (1) Atopic dermatitis (AD) and Psoriasis
 - 1) WO 96/35430 (Covering inflammatory conditions attributable to NF- κ B)
 - 2) WO 02/066070 (Treatment of skin conditions by NF- κ B decoy)
- (2) Asthma
 - 1) WO 96/35430 (Covering inflammatory conditions attributable to NF- κ B)
 - 2) WO 2005/004914 (Treatment of respiratory conditions by NF- κ B decoy)
- (3) Rheumatic arthritis (RA)/osteoarthritis (OA)
 - 1) WO 96/35430 (Covering inflammatory conditions attributable to NF- κ B)
 - 2) WO 03/099339 (Treatment of RA/OA by NF- κ B decoy)
- (4) Prevention of restenosis and Inhibition of cancer metastasis
 - 1) US 6262033

(2) Other Indications and Modified (Improved) NF- κ B Decoy



1) Other Indications

The following patent applications cover indications other than those of the development projects described in (1) above:

- (1) Cerebral Aneurysm (WO 03/063911)
- (2) Inhibition of rejection of organ transplants (WO 03/043663)
- (3) Cerebral ischemia (WO 03/082331)

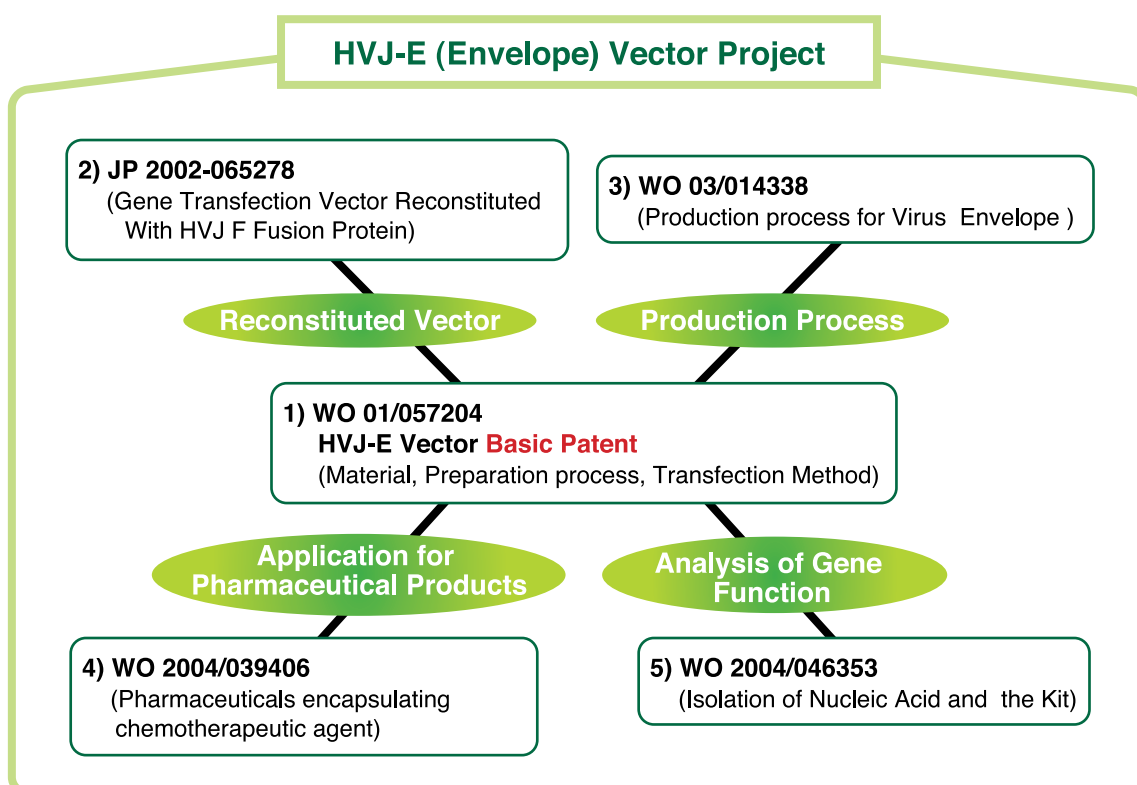
2) Modified (Improved) NF- κ B Decoy

Because NF- κ B decoy has a tendency to breakdown easily in the bloodstream, we have the following patent covering a next-generation NF- κ B decoy with improved stability:

- (1) Dumbbell-type decoy (WO 03/091432)

5 HVJ-E (Envelope) Vector Project and Intellectual Property

Next, we explain our intellectual property covering the HVJ-E Vector Project.



■ HVJ-E(Envelope) Vector Project and The Intellectual Property ■

The HVJ-E Vector project incorporates the following group of patents relating to the virus envelope vector per se, a reconstituted vector, Preparation process, and use such as medical applications and gene function analysis:

①HVJ-E Vector Basic Patent (Product, Preparation process, Transfection method)

WO 01/057204

②Reconstituted vector

JP 2002-065278

③Preparation process

WO 03/014338

④Medical Use (Pharmaceuticals encapsulating chemotherapeutic agent)

WO 2004/039406

⑤Analysis of Gene Function

WO 2004/046353

6 Active Overseas Patenting

It is well known that development of medicines involves substantial costs. With domestic development alone it would be difficult to recover development costs let alone provide funding to support future development projects.

Further, there are imbalances in terms of the numbers of patients in each country for which gene therapy or nucleic acid medicine therapy would be appropriate. So, from the point of view of promptly supplying new therapeutic medicines to patients who need them, early development and commercialization is needed in foreign markets/countries also.

Given this background, we are filing foreign applications quite aggressively for a venture company. Specifically, we have been pursuing a strategy of filing international applications (PCT) based on US provisional applications or domestic applications, and then actively effecting national/regional phase entry in Japan, the United States, Europe, Australia, Canada, China, and other states where necessary.

7 Intellectual Property Management

Based on the fundamental policies 1 to 6 above, our company is constructing a more elaborate web of patents covering our three main projects: (1) HGF Gene Therapy, (2) NF- κ B Decoy Nucleic Acid Medicine, and (3) HVJ-E Vector. Moreover, for the purpose of securing a platform for our company's future development we are pursuing a policy of actively filing applications and obtaining rights for improvement patents also. As a result, we have secured, on an application basis, 60 patent assets, and we are

increasing this number year by year. If foreign applications are included, this number is more than several times greater.

However, accompanying the expansion of our patent assets, there is an increase in our cost burden. If costs of maintenance and prosecution of these assets is included, the amount is substantial. As a venture business, having fewer resources to draw on compared to major drug manufacturers, the proper management of our intellectual property portfolio becomes a significant business issue. From the standpoint of business management, we are at a stage where measures need to be adopted.

For this reason, we conduct a regular evaluation of our intellectual property assets, with a focus on patents, and review our budget distribution on a stage-by-stage basis depending on relative importance, so that we manage and maintain our intellectual property at an appropriate level corresponding to our corporate strength.

8 Collaboration with External Research Organizations

When considering intellectual property in the biotechnology field, the existence of outside entities such as university and regional TLOs (Technology Licensing Organizations) that possess the promising candidates of high technologies is very important.

However, there is a limit to which such external entities are capable of performing pre-clinical and clinical trials. Further, there are cases where precious technologies have gone unexploited due to a lack of intellectual property specialists. Previously in most cases, such external entities have simply handed over their technologies to drug manufacturers for commercialization by way of simple assignment or license.

However, working with such external entities, we have redesigned this conventional relationship, and through a novel business style taking advantage of the particular characteristics of both parties, we are working towards the fostering and commercialization of the novel promising candidate which might otherwise remain buried.

For example, we are able to provide our intellectual property know-how and experience to external entities when they seek to establish strong, broad intellectual property rights. By establishing a cooperative relationship at an early stage soon after the original patent application (the first application), we can contribute to the establishment of a stronger more substantial patent right. Further, the external entity, by seeking new collaborators and partners beyond the demarcation lines of the university or region, is now able to inject resources and energy into the their own specialized fields.

By promoting a collaborative relationship with the division of labor described above, even though we obtain assignment of or a license over the relevant rights, it becomes possible to establish intellectual property rights with high enforceability and based thereon, to commercialize the rights. Thus, it is possible to obtain a result that is good for both the external entity and our company, as well as provide substantial profit.

We are committed to contributing to society by the practical application of superior cutting-edge technologies through collaboration with external entities.

9 Proposal for An Intellectual Property Nation

The importance of intellectual property to business activity cannot be overstated. We indicated the importance to intellectual property to the venture business at the start of this report. Venture businesses in particular are mostly businesses seeking to commercialize cutting-edge technologies brimming with novelty and ingenuity that go beyond and break away from established concepts, and the establishment of new forms of intellectual property will greatly influence the growth and development of such businesses.

However, there is a substantial lack of uniformity in terms of the intellectual property protection afforded to cutting-edge technology under the patent systems of various jurisdictions. In particular, when compared to the United States, the scope of protection available in this country is quite narrow. For example, methods of treatment using gene or nucleic acid medicines, or regenerative medicine employing cells taken from a patient, are not patentable subject matter at present in Japan.

As a result, the commercialization of ingenious inventions employing such advanced technologies is not progressing and technological innovation is stalling. Forceful lobbying on the part of the business community toward an intellectual property nation is required in order to lead us out of this present circumstance.

Bearing in mind international competition and international standards, we will continue our efforts via various channels, including activities in the business and academic worlds to promote the strengthening of intellectual property protection for cutting-edge technologies in the field of biotechnology and medicine.



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