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To those concerned

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Notification related to R&D items

R-Tech Ueno, Ltd. (Chiyoda-ku, Tokyo, Representative Director & President Yukihiro Mashima) discussed the R&D policy at the meeting of board of directors held today and determined the R&D items as follows.

R-Tech Ueno, Ltd. intends to actively strengthen the R&D entities in the ophthalmologic & dermatological fields that are its priority and exclusive areas, and promote relevant affiliation, etc. with external entities.

Note

1. Development code UF-021 (eye diseases)

The item in question is isopropyl unoproston, the effective ingredient of “Rescula® eyedrop 0.12%”) that is marketed as a therapeutic drug for glaucoma and ocular hypertension. This drug is now being developed by R-Tech Ueno for the indication of retinitis pigmentosa. The drug is introduced to Sucampo Pharma Americas Ltd. in the USA to be developed for the indication of atrophic age-related macular degeneration.

2. Development code RTU-007 (eye diseases)

The license is obtained for the substance to inhibit the enzyme that increases in the patients with diabetes mellitus from Astellas Pharmaceutical. We intend to proceed with the development of this substance to be indicated for diabetic cataract, diabetic retinopathy and age-related macular degeneration.

3. Development code RU-10 (eye diseases)

Dry eye is targeted for development of the drug that contains gene recombination human serum albumin as the effective ingredient. Though the clinical study is currently interrupted, we intend to look for overseas affiliation soon because the need for treatment of dry eye is globally unmet (that is, there are currently few therapeutic drugs).

4. Development code RK-023 (dermatological diseases)

This item is a physiologically active fatty acid derivative that is a new compound developed by R-Tech Ueno and is being developed as a drug indicated for male pattern alopecia. We intend to proceed with negotiations for affiliation in Japan and abroad in the future. We also plan to newly develop this drug indicated for eyelash hypotrichosis.

5. Development code RTU-1096 (dermatological and neurological diseases)

This compound newly developed by R-Tech Ueno demonstrates an unconventional action, VAP-1 inhibition. We intend to develop this compound as a drug indicated for atopic dermatitis, contact dermatitis and psoriasis vulgaris in the dermatological field, and diabetic neuropathy in the neurological field.

We plan to report on the development status of each item in the home page of R-Tech Ueno.

- VAP-1 inhibitor

Vascular adhesion protein-1 (VAP-1) is also called semicarbazide-sensitive amine oxidase (SSAO). There are two types of VAP-1/SSAO, that is, the membrane binding type present in the vascular endothelium and free type present in the serum. The former serves as a molecule adherent to white blood cell and lymphocyte and is involved in inflammation while the latter detoxifies amine in the living body by its amine oxidase activity. In other words, VAP-1 is a protein that demonstrates two different functions. The increase in VAP-1/SSAO activity is observed in the serum and various tissues of the patients with diabetes mellitus, atopic dermatitis, obesity, arteriosclerosis, heart disease, etc. In this regard, VAP-1 inhibitor inhibits the excessive function of VAP-1/SSAO.

- Glaucoma

Glaucoma ranks the first among the causes of vision disorder. Among those in their forties or older, one in about 20 has glaucoma (epidemiological survey: TAJIMI Study). It is a chronic and progressive disease featured by a characteristic change in optic nerve (glaucomatous optic nerve cupping) and associated visual field abnormality (glaucomatous visual field defect). If left untreated, the defect in visual field progresses and this may result in loss of eyesight in the severe symptom cases. Glaucoma is a multiple factor disease in which intraocular pressure, fragile optic nerve head and circulation disorder, etc. are involved. However, the utmost risk factor in the progress of glaucoma is intraocular pressure. The basis of glaucoma treatment is to reduce the intraocular pressure, thereby suppressing or inhibiting the progress of visual field disorder. At present, various intraocular pressure-decreasing drugs including Rescula® eyedrop 0.12% are marketed.

- Retinitis pigmentosa

Retinitis pigmentosa is a genetic chorioretinal degenerative disease. Major symptoms of this disease are progressive night blindness and constriction of visual field which may result in loss of vision in severe symptom cases. Up to present, no effective treatment against this disease has been established. Retinitis pigmentosa is ranked the third (ranked the first among those under 60 years old) in the causes of vision disorder in Japan.

- Atrophic age-related macular degeneration

This is one of the major primary diseases for acquired blindness in Western countries and Japan, and about 1/100 people over 50 years of age have age-related macular degeneration in Japan (epidemiologic survey: Hisayamacho Study). Currently about 2 million patients have severe visual disorder in the US, and this number is expected to increase to 3 million by 2020. Atrophic type without neovascularization, where atrophy in the macula area leads to severe visual loss, is common in Western countries. Treatment with oral supplements is actually conducted, but no effective drug has been developed.

- Cataract

Cataract refers to opacity in the lens. It seems to be caused by possible complex factors, and the major cause seems to be age-related change in the lens proteins. Ultraviolet and diabetes are also included in the risk factors. Blurring and photophobia are perceived as symptoms. If these symptoms begin to disturb daily life, surgical therapy may be conducted. Currently about 2.5 million patients with diabetes are under treatment (Ministry of Health, Labor and Welfare: Summary of Patient Research in 2005), and about 7.4 million people are strongly suspected to have diabetes in Japan. Combined with potential population who cannot rule out the possibility, one in 6 adults is considered to be potential diabetic individual.

- Diabetic retinopathy

This is one of the three major complications of diabetes, and prevalence of retinopathy is 80% in cases with disease period of 20 years or longer. It is the second common cause of visual disorder in Japan. It consists of proliferative retinopathy that may lead to blindness, and nonproliferative retinopathy that can be improved by blood sugar control. Proliferative retinopathy is treated by photocoagulation therapy and/or vitrectomy surgery.

- Dry eye

Dry eye is a chronic and multifactorial condition characterized by disorders in the tear layer and/or the ocular surface (keratoconjunctive epithelium) due to various factors. It is associated with ocular discomfort and/or abnormal visual function. In modern society, the eyes are severely used in various occasion and the number of patients with dry eye is increasing year by year, with up to 22 million patients estimated in Japan.

- Male pattern alopecia

Male pattern alopecia is a gradually progressive hair-thinning and alopecic disease with replacement of thick long hair by thin, short and soft hair without hair regeneration localized in the parietal to the frontal region under effect of androgenic hormone after puberty, finally leading to atrophy in the hair follicles and reduction in the number of hair. About 12 million males are affected in Japan. Propecia® tablet (ethical drug) and RiUP® (Class-1 nonprescription drug) have been commercialized as therapeutic agents with effect proved by scientific clinical trials, but there is actually individual difference in the therapeutic effect of these drugs.

- Hypotrichosis of eyelashes

Hypotrichosis of eyelashes is a disease with the thin, short, sporadic and/or pale eyelashes that inhibit its intrinsic functions, namely, preventing foreign materials like dust or abnormal light from entering into the eye. No treatment agent for hypotrichosis of eyelashes has been marketed in Japan, but an ethical drug Latisse®, which was approved last year by FDA (Food and Drug Administration), has been marketed in the US. The distributor Allergan has announced its target annual sales as 500 million dollars.

- Atopic dermatitis

Chronic eczema and dermatitis with itching due to reduced skin barrier function associated with allergic constitution, as well as various additional stimuli, has repeated exacerbations and improvements of symptoms. Previously, it was believed to spontaneously resolve in later

childhood, but there have been increasing number of remaining cases even in adulthood and cases with onset/relapse in adulthood. Symptomatic therapies with medicines are used, with topical steroids and immunosuppressant, oral antihistaminic drugs and application of humectant.

- Contact dermatitis

Dermatitis (rash) caused by allergic reaction against a substance or stimulus, localized in the contact site. Redness and/or bulla are found in consistent with the contact site. Basic treatment is blocking from the contact source, mainly in combination with topical steroid.

- Psoriasis vulgaris

Inflammatory skin keratinization with red eruption and papule are found in any body site, frequently in the sites receiving strong external stimuli like the scalp, the knees and the elbows. Symptomatic therapies are used with topical active vitamin D ointment, topical steroids, ultraviolet therapy (PUVA therapy), and oral immunosuppressants.

- Diabetic neuropathy

This is one of the three major diabetic complications, which is peripheral nerve disorder in the hand and the feet causing symptoms like strange feeling, numbness and pain in prolonged hyperglycemic condition. Foot ulcer or gangrene may develop if perception is reduced in advanced condition. Furthermore, the autonomic nerve (the nerve controlling organ function) may be damaged in addition to the peripheral nerve, leading to symptoms like orthostatic dizziness, poor urination, impotency, constipation and diarrhea. It is said that these neuropathies tend to occur in individuals who have been on poor blood sugar control for a long period.

- About R-Tech Ueno, Ltd.

R-Tech Ueno was established in September 1989 for the purpose of marketing and R&D of drugs. Under leadership of the CEO, also a medical doctor, the company is developing new drugs on the theme “Physician-Oriented New Drug Innovation”, targeting ophthalmologic and dermatologic diseases that previously had no effective therapeutic agent.

The company’s main product Rescula® eyedrop 0.12% is a therapeutic drug for glaucoma and ocular hypertension and has been marketed in Japan since 1994. R-Tech Ueno was the first in the world to take advantage of the substance “prostone” in the development of Rescula®. Prostone was discovered in 1980 by Dr. Ryuji Ueno, the founder of the company.

Rescula® eyedrop 0.12% that causes less topical and systemic adverse reactions, demonstrates steady ocular pressure decreasing action by twice a day instillation. Such excellent therapeutic effects are realized through its optic nerve protection and ocular blood flow increasing mechanism.

Concerning Rescula® (isopropyl unoprostone) for the treatment of glaucoma and ocular hypertension, R-Tech Ueno concluded a contract with Sucampo Pharma Americas, Inc. in April 2009 for the approval and assignment of distributorship, as well as for licensing the relevant patents and granting exclusive right to manufacture and supply in USA and Canada.

Product Pipeline

Ophthalmology

Product Name/ Code No.	Generic Name	Target Indication	Origin	Pre-clinical	Phase I	Phase II	Phase III	NDA	Approval	Launch
Rescula [®] /UF-021	Isopropyl Unoprostone	Glaucoma • Ocular hypertension	In-house	Launch at October 1994						
	Isopropyl Unoprostone	Retinitis pigmentosa	In-house							
	Isopropyl Unoprostone	Glaucoma • Ocular hypertension	License-out(SPA)*1	Approval at August 2000 (USA)						
	Isopropyl Unoprostone	Dry type Age-related macula degeneration	License-out(SPA)*1							
RTU-007		Diabetic cataract	Astellas Pharma							
		Diabetic retinopathy	Astellas Pharma							
		Age-related macula degeneration	Astellas Pharma							
RU-10	Recombinant Human Serum Albumin	Dry eye	In-house*2							

*1 SPA : Sucampo Pharma Americas, Inc.
License for development, commercialization and supply in USA and Canada at April 2009

*2 See our announcement on July 29, 2009.

Dermatology

Code No.	Generic Name	Target Indication	Origin	Pre-clinical	Phase I	Phase II	Phase III	NDA	Approval	Launch
RK-023		Alopecia	In-house							
		hypotrichosis of the eyelashes	In-house							
RTU-1096		Atopic dermatitis	In-house							
		Contact dermatitis	In-house							
		Psoriasis vulgaris	In-house							

Neuropathy

Code No.	Generic Name	Target Indication	Origin	Pre-clinical	Phase I	Phase II	Phase III	NDA	Approval	Launch
RTU-1096		Diabetic neuropathy	In-house							