KYORIN Pharmaceutical Group New
Mid-Term Business Plan

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Your health is KYORIN's mission.

HOPE 100 －Stage 1－
(Fiscal 2010～2015)

R&D Strategy: Pipeline Status

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Director, KYORIN Co., Ltd.
KYORIN Pharmaceutical Co., Ltd.
Representative Director,
President and Chief Executive Officer　Keiji Hirai

R&D Initiatives Focused on Time Frames

Initiatives to be taken under the medium-term business plan (stage 1) are labeled T1, T2, or T3 according to the stage at which results will materialize.

T1：Today–For Results in Stage 1
T2：Tomorrow–For Results in Stage 2
T3：The day after tomorrow–For Results in Stage 3

Ethical Drug Business

T1

＜New drugs group＞
■Maximize Popularity of Core Products　(Kipres, Uritos)
■Early launch of the products under development ：KRP-108
■Out-licensing of product under development：KRP-104
■LCM (Uritos OD tablets)

＜Original products group＞
■LCM (Mucodyne DS 50%, new application/ dosage for Pentasa)

T2

＜New drugs group＞
■Aim for early application and approval of newly developed products and enhance and strengthen the pipeline
・Develop and promote KRP-209, KRP-203, AS-3201, KRP-110, and antibacterial agents
・Secure licensed-in drugs (FC domain： respiratory medicine, otolaryngology and urology)

T3

＜New drugs group＞
■Strengthen drug discovery capabilities： Create new global pharmaceuticals
・Actions for fundamental reform of drug discovery system

LCM： Life Cycle Management

Provide Products to Market Quickly and Enhance and Strengthen Product Pipeline

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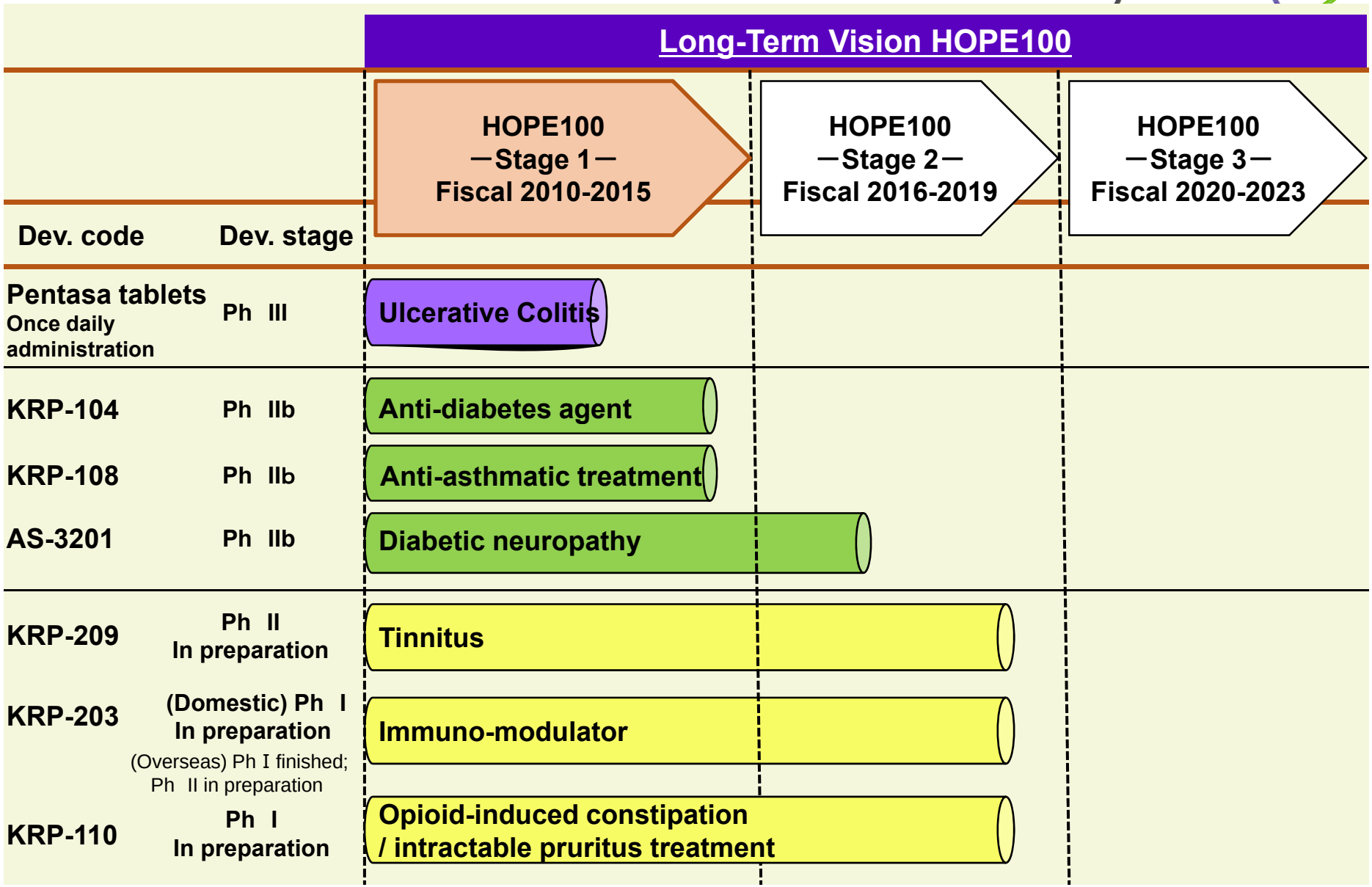
	HOPE100－Stage 1－ Fiscal 2010-2015	HOPE100－Stage－ 2 Fiscal 2016-2019	HOPE100－Stage 3－ Fiscal 2020-2023
	・**Focus efforts on LCM** ・**Aim to launch KRP-108 to market in fiscal 2014** ・**Aim to license KRP-104**	Application and approval for products under development Strengthen and enhance pipeline	Global, original new drug discovery
	Aim to secure licensed-in drugs		
LCM	Mucodyne DS 50 Uritos OD tablets Pentasa New application/dosage (Once daily administration)		LCM: Life Cycle Management
Products Under Development **＊Including in-licensed products**	KRP-108 (Asthma treatment) KRP-104 (Anti-diabetes agent) Candidate compounds for in-licensing (respiratory, urological, etc.)	AS-3201 (Diabetic neuropathy treatment) KRP-209 (Tinnitus treatment) KRP-203 (Immunosuppressant) KRP-110 (Constipation, intractable pruritus treatment) Antibacterial agents	
In-House Drug Discovery	■Work to reform the R&D process based on the "market-in" concept ・Promotion of partnering, in-licensing, LCM, research topic selection, review evaluation and decision-making related to products under development. ■Restructure the drug discovery network: ・Review the functions of ActivX and KSRL (actively utilize as drug discovery bases in key domains) ・Proactive external collaboration		
	In-House Drug Discovery Focus Domains **Respiratory, urological, infectious diseases, etc.**		

Key Products Under Development



Development Status of KRP-108

Ph II completed

Ph III clinical trial in preparation

- ❑ Target indication
  - ・Asthma
- ❑ New ethical combination product
  - ・Best combination of ICS and LABA
  - ・Optimal device
    - ・ICS: Fluticasone propionate
    - ・LABA: Formoterol fumarate
    - ・Device: Pressurised Metered Dose Inhaler (pMDI)

ICS: Inhaled steroid
LABA: Long-acting β2 stimulant

Development Status

❖Domestic:
- Ph II clinical trials completed
- In preparation for Ph-III clinical trial
- Japanese NDA targeted for fiscal 2012

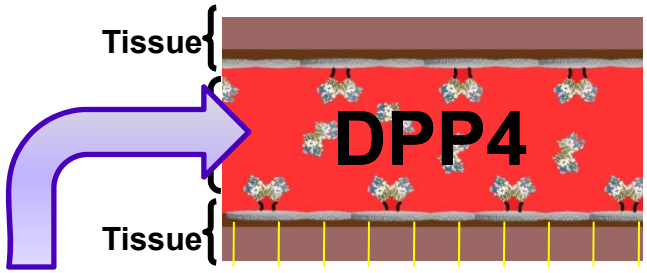
❖Overseas:

US ＜Abbott/SkyePharma＞
- ・NDA filed in March 2009

Europe＜Mundipharma＞
- ・MAA submitted in March 2010

Development Status of KRP-104

Oversea Ph IIb ongoing
Domestic Ph IIb completed



High safety expected

- Target indication: Type Ⅱ diabetes
- Extremely low tissue penetration and intracellular permeability; works by staying in the bloodstream, which is target organ of DPP4i
- Does not act on other DPP subtypes (ex, DPP8/9), less chance of side effects
- In late-stage development (Overseas and domestic)

Development Status

- Domestic: Ph IIb clinical trial completed
  - Results confirmed in February 2010
- Overseas: Multinational Ph IIb trial on going
  - Started in November 2009
  - Expected to confirm results in 2011

Overview of Clinical Trials

- Domestic
  - Explored recommended clinical dose in Type II diabetes
  - Twice daily dose for 12 weeks

⇒ Confirmed safety as expected and confirmed robust effect at all doses (highly significant in all dose groups). Dose-dependent effects observed

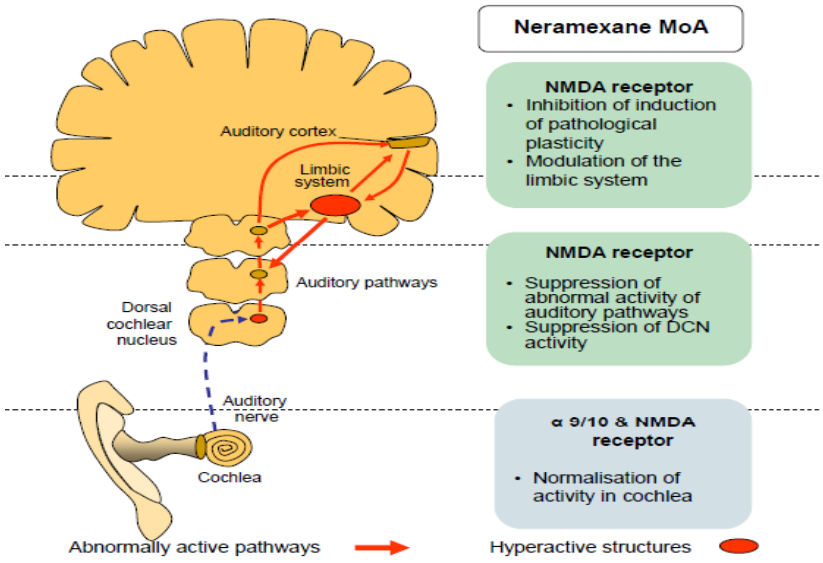
- Overseas
  - Exploring recommended clinical dose in Type II diabetes uncontrolled with Metformin
  - Once daily dose for 24 weeks

Development Status of KRP-209

Ph I study (Japanese single PK) completed in the US

Ph II domestic clinical trial in preparation

- **Target indication**:
  - Subjective tinnitus
- **First-in-class agent**
  - Medical field with high unmet needs with no frontrunner in Japan
  - A novel oral drug for tinnitus suppressing abnormal spontaneous activity and nerve action potential in the inner ear, nerves, and cerebral cortex



Development Status

❖ **Domestic**:
- **In preparation for Ph II clinical trial (Planned to start in 2011)**

❖ **Overseas**: **Europe/US ＜Merz Pharma＞**
- **Ph III clinical trials ongoing**
- **EU MAA targeted for 2011**
- **US NDA targeted for 2012**

Development Status of KRP-110

Ph I clinical trials in preparation

Development Status

Overseas: In preparation for Ph I clinical trials

・Planned to start in 2010

❑ Characteristics of KRP-110

・Highly selective μ opioid receptor antagonist

・ Good oral absorption and high safety profile expected

❑ Target indications

・Opioid-induced constipation*

(* Serious constipation induced by opioid analgesics)

・Ideal mode of action to directly block the adverse effect of opioid analgesics

・No inhibitory effect on analgesic effect of opioids

・Contributes to pain treatment by alleviating constipation and associated abdominal symptoms

・Intractable pruritus**

(** Systemic and chronic itching associated with end stage renal disease and cholestatic disease, and atopic dermatitis)

・Blocks the pruritus signal transmitted by the opiod peptide

・Effective even for pruritus ineffective with existing therapy

・Improves QOL impaired by chronic pruritus

Main R&D Activities①（ May 11 , 2010 Release)

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Ph II～Application

＊：Describe the latest changes

Stage		Compound/ Code	Therapy area/ Action	Origin	Features	Comments
Domestic	Overseas					
Ph III (12/2009)		PENTASA Tablets	Ulcerative colitis	Ferring Pharma-ceuticals	New dosage regimen for ulcerative colitis in the remission phase (once a day)	
Ph II （3/2005）	(Eisai: PhⅢ)	AS-3201 （Tablets ）	Diabetic neuropathy	Dainippon Sumitomo	Aldose reductase inhibitor to reduce the sorbitol accumulation in the cell, and improve diabetic neuropathy	Co-development with Dainippon Sumitomo ・PhⅡb（9/2007）
Ph II （2/2008）	PhⅡ （9/2007）	KRP-104	Anti-diabetes agent	In-house	A DPPIV inhibitor to reduce blood glucose through suppression of the degradation of insulin-releasing hormone. Diabetic therapy with fewer side effects is expected than existing treatments.	・PhⅡb in overseas (11/2009) ＊PhⅡb in domestic completed（3/2010）
Ph II （8/2008）	US: Abbott NDA filed (3/2009) Europe: Mundipharma MAA submitted (3/2010)	KRP-108	anti-asthmatic	Skye Pharma PLC	An ICS/LABA combination product, which offers better compliance and convenience to the patients.	License Agreement with SkyePharma (4/2008) ＊Ph II completed in domestic (4/2010)

Other Comments

※Orally Disintegrating Tablet of Immidafenasin（INN), a Drug for Overactive Bladder : Application(12/2009)

※Mucoregulating drug “Mucodyne DS50% : Approval (1/2010)

Main R&D Activities②（May 11 , 2010 Release)

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POC Project（Pre-clinical～Ph I）

＊：Describe the latest changes

Stage		Compound/ Code	Therapy area/ Action	Origin	Features	Comments
Domestic	Overseas					
＊Ph I in preparation	Ph I (7/2007)	KRP-203	Transplantation and autoimmune diseases treatment	In-house	An immunosuppressant with novel mechanism called S1P-agonist. It may have a better safety profile than previous ones as well as an excellent effect under concomitant use with other types of immunomodulator	License agreement with Novartis (2/2006)
	Ph I in preparation	KRP-110	Opioid-induced constipation and intractable pruritus	In-house	A highly selective μ-opioid receptor antagonist. It is expected to block constipation induced by opioid analgesics without interrupting the analgesic effect of opioids. It is orally effective in various itching models, indicating potential of a novel anti-itch drug for intractable pruritus.	

※Amorolfine HCl Nail lacquer and KRP-105 have been deleted from the list of development pipeline since both product were discontinued from the standpoint of our R&D strategy

※The standard on the information disclosure has been changed and the products, which has been decided to enter the clinical stage, will be disclosed. Therefore, KRP-107 and KRP-109 have been deleted from this list while the developments of KRP-107 and KRP-109 will be continued.

In licensing

Stage		Compound/ Code	Therapy area/ Action	Origin	Features	Comments
Domestic	Overseas					
*Ph-II in preparation	Ph-III (Merz)	KRP-209	Tinnitus	Merz	KRP-209 (Neramexane) is expected to improve the patients' annoyance and difficulties in their life caused by tinnitus through mainly its two pharmacological properties: 1)NMDA antagonistic activity and 2)Nicotinic acetylcholine antagonistic activity	License Agreement with Merz (11/2009) Ph I clinical trial in Japanese (single dose PK) in US completed by Merz (03/2010)

Main R&D Activities③（ May 13 , 2009 Release)

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Licensing development

＊：Describe the latest changes

Product name・Code	Stage	Licensee・ Collaborative research	Therapy area/ Action	Origin	Comments
Alphagan/ Alphagan P	Domestic Ph III（7/2007）	Senju Seiyaku	Glaucoma	Allergan (US)	・Licensed from Allergan （Cross license of gatifloxacin ophthalmic solution ） ・License-out to Senju（5/2004）
Ketas	Overseas Ph II（8/2005）	MediciNova (US)	Cerebrovascular disorders	In-house	・KYORIN grants MediciNova an exclusive license in all countries worldwide except for Japan,China, South Korea and Taiwan to develop, manufacture and sell the compound and products for the multiple sclerosis indication.(10/2004) Result of Ph Ⅱ was reported in April 2008.
KCA-757	Overseas Ph III (Anti-bronchial Asthma:11/2006) Ph II/III (Interstitial cystitis: 5/2005)	MediciNova (US)	Anti-bronchial asthma and Interstitial cystitis agent	In-house	・KYORIN grants MediciNova an exclusive license in all countries worldwide except for Japan,China, South Korea and Taiwan to develop, manufacture and sell the compound and products ・Interstitial cystitis:Results of Ph Ⅱ/Ⅲ was reported in January 2007 and ceased development ・Bronchial asthma: Clinical trial oversea was discontinued.
KRP-203	Overseas Ph I（7/2007）	Novartis (Switzerland)	Transplantation and autoimmune diseases treatment	In-house	An immunosuppressant with novel mechanism called S1P-agonist. It may have a better safety profile than previous ones as well as an excellent effect under concomitant use with other types of immunosuppressants.

The End