Status of Clinical Development

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- Increase R&D capabilities and development speed
  - ◆ Successfully shortened period and improved efficiency of clinical and non-clinical studies

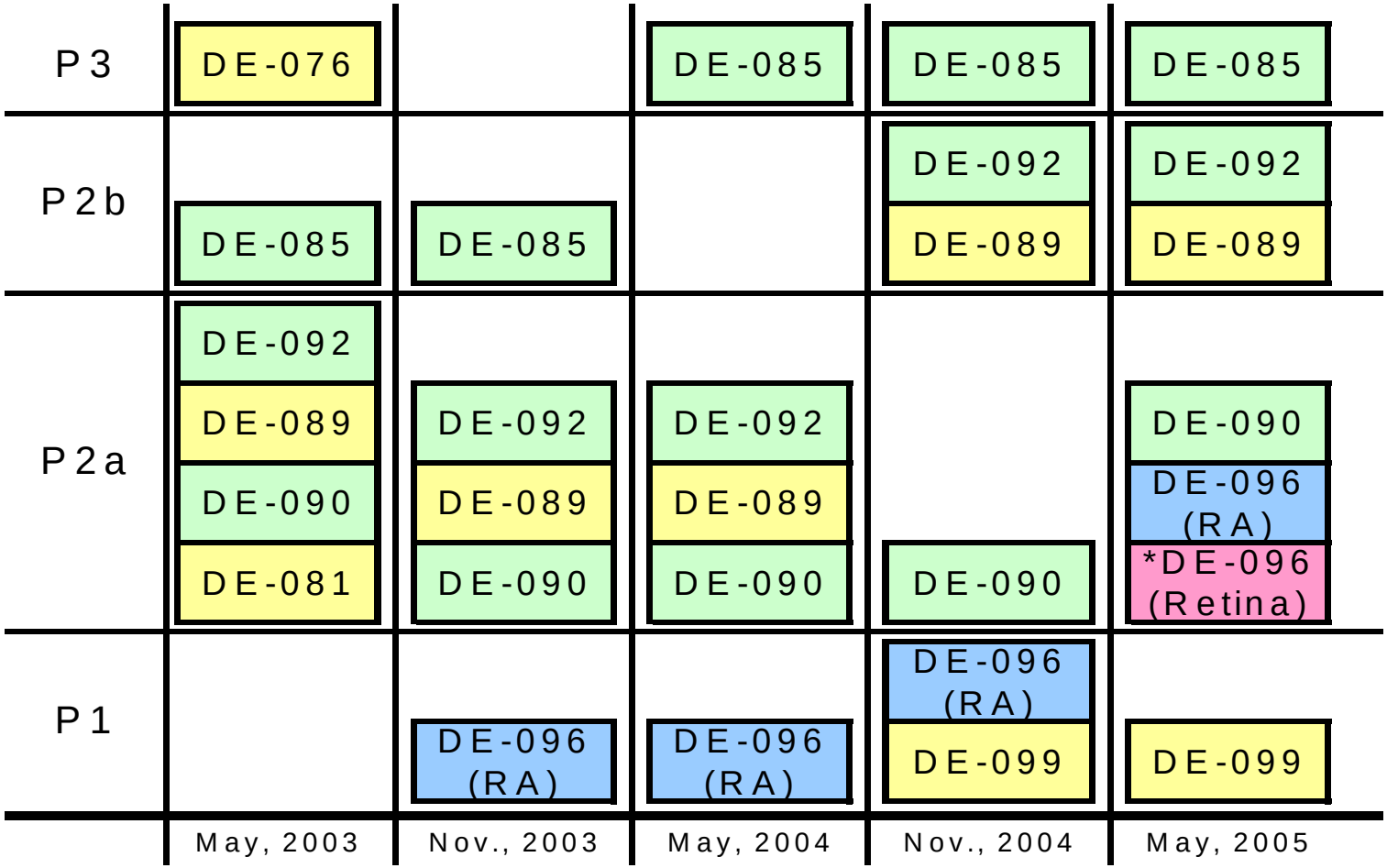
1. From P1 to NDA submission: 5 Yrs.
   e.g. DE-085: P2b submission of clinical trials to P3 LPO
   → Achieve in less than 3 Yrs.
   DE-092: P2a submission of clinical trials to P2b LPO
   DE-089: P2a submission of clinical trials to P2b LPO
   → Both DE-092 and DE-089: Achieve in 2.5 Yrs.
   → At present it takes 5 to 5.5 Yrs. from P1 to NDA submission
2. Non-clinical development: 1.5 Yrs.
   e.g. Two projects in progress in Glaucoma and Cornea treatments
   → Aiming to start clinical trial in one year
3. Utilize the clinical data from overseas
   → Implemented in DE-085, DE-092 projects

- Focused resource allocation

  - ◆Focus resources on promising research themes
    - Concentrate resources in high priority therapeutic areas
      → Discovery of candidate compounds

  - ◆Integrate our know-how of rheumatic and osteoarthritic research and a part of ophthalmic research
    - Implemented in two projects (FY03, 04)
      → Set up several projects mainly in treatment for ophthalmic disorder from FY05
  - ◆Expand opportunities through alliances
    - Entered into agreement with Argenes Inc. on R&D of anti-APO-1 antibody in Japan

Progress of the 2003-2005 Medium-term Management Plan
-Progress in domestic clinical trials -



DE-096: Preparation for P2a (Retina)
DE-076: NDA filed in August, 2003
DE-081: Discontinued study in November, 2003

: Glaucoma
: **Retina**
: **Inflammatory, Cornea**
: **RA**

Product Pipeline: Glaucoma, Retina

●Glaucoma

Generic name (Development code)	Indication	Category/Mechanism	Original/Licensor	Stage
Tafluprost (DE-085)	Glaucoma and ocular hyper-tension	Prostanoid FP-receptor agonist. Promotes uveoscleral outflow	Original (co-development with Asahi Glass)	Japan: P3 US/Europe: P3
Olmesartan (DE-092)	Glaucoma and ocular hyper-tension	Angiotensin II AT1 receptor antagonist. Promotes uvescleral outflow	In-licensed (Sankyo)	Japan: P2b US/Europe: P2
Lomerizine hydrochloride (DE-090)	Glaucoma	Calcium channel blocker. Improves ocular blood-flow circulation	In-licensed (Nippon Organon)	Japan: P2a

●Retina

Generic name (Development code)	Indication	Category/Mechanism	Original/Licensor	Stage
Undetermined (DE-096)	Diabetes Mellitus Edema	An oral TNF-alpha inhibitor Inhibits production of TNF-alpha	Original	In preparation for P2a

Underlined part in red shows changes from announcement of 2004/11/05

Product Pipeline: Anti-inflammatory, Cornea and Anti-infective

Generic name (Development code/ brand name)	Indication	Category/Mechanism	Original/ Licensor	Stage
Levofloxacin 1.5% (IQUIX)	Bacterial corneal ulcer	DNA gyrase inhibitor. Anti-intefcive action	In-licensed (Daiichi)	US: approved
Ciclosporin (DE-076)	Vernal kerato-conjunctivitis	Calicyneurin inhibitor. Immunosuppressant	In-licensed (Novartis)	Japan: NDA
Diquafosol tetrasodium (DE-089)	Corneal & conjunctival epithelial disorder associated with dry eye, etc.	$P2Y_2$ receptor agonist. Stimulates tear secretion	In-licensed (Inspire)	Japan: P2b
Levofloxacin + Prednisolone (DE-094)	Infectious keratitis	Fluoroquinolone + steroid. Anti-infective + anti-inflammatory action	In-licensed (Daiichi)	US: P2
Gefarnate (DE-099)	Corneal & conjunctival epithelial disorder associated with dry eye, etc.	Muco-membranous protective agent. Stimulates mucin secretion	Original	Japan: P1

Product Pipeline: Bones and Joints

Generic name (Development code/brand name)	Indication	Category/Mechanism	Original/ Licensor	Stage
Undetermined (DE-096)	Rheumatoid Arthritis (RA)	TNF-alpha inhibitor. Inhibits production of TNF-alpha	Original	Japan: P1→P2a
Bucillamine (Rimatil)	Osteoarthritis	DMOAD. Protects cartilage and modifies edema	Original	Japan: preparing for clinical trials

- License out

Generic name (Development code/ brand name)	Indication	Category/Mechanism	Licensee	Stage
Undetermined (DE-098)	Rheumatoid Arthritis (RA)	Anti-APO-1 antibody. Induces apoptosis in synovial cells	Argenes	Japan: preparing for clinical trials

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