# Status of Clinical Development

November 5, 2004

Toshiaki Nishihata, Ph.D.
Senior Corporate Officer
Head of Research and Development Division

# Progress of the Medium-term Management Plan (1)

- Increase R&D capabilities and development speed
  - ◆ Successfully shortened period and improved efficiency of clinical and non-clinical studies
    [Medium-term Plan target:
    5 years from Phase 1 to NDA, 1.5 years in non-clinical]

1. Leverage overseas bases
   - Mutual use of clinical data
     → Implementing measures including discussion with governments
   - New policy for non-clinical up to Phase 2a
     → Policy formulated and implementation underway
2. Expand number of clinical trial sites
   → Japan: 80% of plan implemented for ophthalmic area
3. Shorten period between clinical development Phases
   → Implemented in two projects that proceeded from Phase 2a to Phase 2b during six months ended September 2004
4. Bolster clinical development staff
   → Japan, Europe and US: 70% of plan implemented

# Progress of the Medium-term Management Plan (2)

- Focused resource allocation

  - ◆ Focus resources on promising research themes
    - Concentrate resources in specific therapeutic areas
      → Candidate compound for near-future clinical development emerged

  - ◆ Expand opportunities through alliances
    - Entered into agreement with Argenes Inc. on R&D of anti-APO-1 antibody in Japan

  - ◆ Integrate know-how of rheumatic and osteoarthritic research and a part of ophthalmic research
    - Planning to implement in two projects

# Product Pipeline: Glaucoma Treatment

| 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<br>US/Europe: P3 |
| Olmesartan (DE-092) | Glaucoma and ocular hyper-tension | Angiotensin II AT1 receptor antagonist. Promotes uvescleral outflow | In-licensed (Sankyo) | Japan: P2<br>US/Europe: preparing for P2 → P2 |
| Lomerizine hydrochloride (DE-090) | Glaucoma | Calcium channel blocker. Improves ocular blood-flow circulation | In-licensed (Nippon Organon) | Japan: P2 |

Underlined part in red shows changes from announcement of 2004/5/10

# 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 uler | 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 |
| levofloxacin + prednisolone (DE-094) | Infectious keratitis | Fluoroquinolone + steroid. Anti-infective + anti-inflammatory action | In-licensed (Daiichi) | US: P2 |
| diquafosol tetrasodium (DE-089) | Dry eye | $P2Y_2$ receptor agonist. Stimulates tear secretion | In-licensed (Inspire) | Japan: P2 |
| gefarnate (DE-099) | Corneal & conjunctival epithelial disorder associated with dry eye, etc. | Muco-membranous protective agent. Stimulates mucin secretion | Original | Japan: preparing for P1 → P1 |
| sodium hyaluronate (HYALEIN) | Dry eye | Biopolymer cytoprotective agent. Retains water and promotes corneal wound healing | Original | US: preparing for P2 → discontinued (Japan: on sale) |

Underlined parts in red show changes from announcement of 2004/5/10

# 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 |
| 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 |