

## Reference information

# Research & development

### Pipeline of prescription pharmaceuticals (Clinical studies)

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Levofloxacin (0.5%)	Cravit Quixin Ofaquix	Bacterial conjunctivitis	Daiichi Pharmaceutical	Japan						Apr-00
				USA						Nov-00
				Europe						May-02
Levofloxacin (1.5%)	Iquix	Bacterial corneal ulcer	Daiichi Pharmaceutical	USA					Mar-04	
Levofloxacin + prednisolone A	DE-094	Infectious keratitis	Daiichi Pharmaceutical	USA						

Characteristics: Fluoroquinolone antibacterial agent. In Europe, Ofaquix has obtained marketing authorization in 11 countries and was launched in five countries including Germany. Iquix is a higher-concentration fluoroquinolone with potent antibacterial action. Levofloxacin + prednisolone A is a combination treatment with steroids.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Pemirolast potassium	Alegysal Alamast Alamast	Allergic conjunctivitis	Mitsubishi Pharma	Japan						Apr-95
				USA						Jul-00
				Europe					Dec-99	

Characteristics: A mast cell stabilizer with superior efficacy on allergic conjunctivitis and vernal keratoconjunctivitis.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Ciclosporin	DE-076	Vernal keratoconjunctivitis	Novartis Pharma	Japan					Aug-03	

Characteristics: An orphan drug. Ophthalmic application of immuno-suppressant ciclosporin. Expected to treat advanced vernal keratoconjunctivitis for which existing anti-allergic agents are not effective. Because it is an ophthalmic solution, virtually no generalized side effects are noted.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Tafloprost	DE-085	Glaucoma/ ocular hypertension	Co-development with Asahi Glass	Japan USA/Europe						

Characteristics: Prostaglandin glaucoma treatment that reduces intraocular pressure. Clinical trials are being conducted in parallel in Japan, the U.S. and Europe. Expected to have greater efficacy in reducing intraocular pressure than other prostaglandin products. Can be stored at room temperature.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Olmesartan	DE-092	Glaucoma/ ocular hypertension	Sankyo	Japan USA/Europe						

Characteristics: The only angiotensin II receptor antagonist in full-fledged development as a glaucoma treatment. Comparable to prostaglandin products in reducing intraocular pressure. Very few side effects, including conjunctival hyperemia, are expected. Great potential for the U.S. and European markets where patients with ocular hypertension account for the majority of the glaucoma population.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Lomerizine HCL	DE-090	Glaucoma	Nippon Organon	Japan						

Characteristics: A new type of oral glaucoma treatment studied for inhibiting the progression of visual field defects. The only calcium antagonist in full-fledged development as a glaucoma treatment. Compared with NMDA receptor antagonists, fewer generalized side effects are expected, thus having excellent safety. Marketed by Nippon Organon as a migraine drug.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Diquafosol tetrasodium	DE-089	Dry eye	Inspire Pharm.	Japan						

Characteristics: A treatment for dry eye that stimulates the ocular surface to secrete tear fluid and moisture. Expected to be used in combination with existing dry eye treatments, and be effective for patients for whom existing treatments are insufficient.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
(Undetermined)	DE-096	Rheumatoid arthritis	Original	Japan						

Characteristics: An oral TNF inhibitor. Anti-rheumatic effect comparable to injectable biological agents has been observed in basic research.

Generic name	Brand name/dev. code	Indication	Original/licensor	Region	Ph I	Ph II	Ph III	NDA Filed	Approved	Launched
Gefarnate	DE-099	Corneal and conjunctival epithelial disorder associated with dry eye, etc.	Original	Japan						

Characteristics: Treats corneal and conjunctival epithelial disorder mostly associated with dry eye, by stimulating the secretion of mucin and promoting the corneal epithelial migration. Preservative-free eye ointment that can be used in combination with existing drugs.

### Pipeline of prescription pharmaceuticals (In preparation for clinical trials)

Generic name	Brand name/dev. code	Indication	Original/in-licensor
Bucillamine	Rimatil	Osteoarthritis (additional indication)	Original

Characteristics: Shown to be effective on joint inflammation caused by osteoarthritis.

### Pipeline of medical devices

Product under development	Product name	Region
Intraocular lens	MD-14	Japan and USA

Characteristics: Foldable intraocular lens using new material with high refractive index. Developed by U.S. subsidiary Advanced Vision Science, Inc.

### License out

Brand name/dev. code	Indication	Region	Licensee	Status	in-licensor
DE-098 (Anti-APO-1 antibody)	Rheumatoid arthritis	Japan	Argenes	preparing for clinical trials	Centocor

Characteristics: Joint injection that induces apoptosis in diseased joints of rheumatoid arthritis patients. Bulk pharmaceutical manufacturing process for actual production scale has been established, and drug development is being studied. Santen granted the domestic development rights to Argenes, Inc. The compound had been in-licensed from Centocor. Santen continues to hold the marketing rights in Japan and the overseas marketing and development rights.

### Changes from May 7, 2004

#### [Progress]

Brand name/dev. code	Indication	Region	Status change
Olmesartan/DE-092	Glaucoma/ocular hypertension	USA/Europe	In preparation for phase II to phase II
Gefarnate/ DE-099	Corneal and conjunctival epithelial disorder associated with dry eye, etc.	Japan	In preparation for clinical trials to phase I

#### [Discontinued study]

Product name	Indication	Region	Status before cancellation
Hyalein	dry eye	USA	In preparation for phase II

Discontinued development plan due to requirement of additional large-scale clinical trials and higher prospect of other dry eye candidate.

#### [Discontinued launch plan]

Product name	Product under development	Region
MD-13	Intraocular lens	Japan

Discontinued launch plan in consideration of marketability.

### Number of employees in R&D

	2000.3	2001.3	2002.3	2003.3	2004.3
R&D personnel (consolidated)	370	404	482	485	455

# Pharmaceutical market in Japan

Revision of National Health Insurance (NHI) drug prices													(%)
	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Industry average	-8.1	-	-6.6	-	-6.8	-4.4	-9.7	-	-7.0	-	-6.3	-	-4.2
Ophthalmic drugs	-0.6	-	-1.6	-	-3.5	-1.8	-7.5	-	-6.2	-	-6.0	-	-2.7
Santen	0.9	-	-0.4	-	-2.6	-1.3	-7.2	-	-5.7	-	-6.0	-	-3.2

(Compiled by Santen)

Revision of NHI drug prices: In Japan, drug prices are generally revised every two years to reflect their market price. The drugs marketed at lower market prices will bear larger reduction margins at the revision.

## Major healthcare reforms

	1997	Enforcement of the Revised Health Insurance System Law. Increased contribution for insured employees (10% to 20%) Revision of the Insurance Law for Seniors Contribution: 500 yen/day for out-patients (up to four times a month) and 1,000 yen/day for in-patients
	2001	Revision of the Insurance Law for Seniors Contribution: fixed rate of 10% for out-patients and in-patients
April	2002	Reimbursed consulting fee for physicians were reduced by 2.7% on average Revision of prescription fee (two points are added for every prescription of generic drugs)
October	2002	Increased contribution for seniors (fixed amount system was abolished for a uniform fixed rate system of 10% contribution)
April	2003	Increased contribution for insured employees (20% to 30%)

### Market shares

(Billions of yen)

Half year/year to	9/2002	3/2003	9/2003	3/2004	9/2004
Prescription ophthalmics	40.3% 97.1	38.9% 195.8	39.6% 97.3	39.0% 194.7	39.4% 100.3
Anti-rheumatic drugs	41.9% 10.7	42.1% 21.1	42.8% 11.1	42.5% 22.2	42.4% 11.7

Notes: - On an NHI drug price basis.

- Lower figures indicate market size.

- Anti-rheumatic drugs exclude immunosuppressants and biologic agents.

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Source: Santen analysis based on IMS data

Period: 2002-2004; Unauthorized copy prohibited

### Market shares by therapeutic area - prescription ophthalmics

(Billions of yen)

Half year/year to	9/2002	3/2003	9/2003	3/2004	9/2004
Anti-glaucoma	17.5% 35.0	17.3% 69.0	16.9% 35.5	16.7% 71.7	16.3% 37.6
Anti-infective	81.0% 14.9	80.9% 27.6	80.8% 14.1	81.0% 26.9	81.2% 14.1
Anti-allergy	16.9% 9.3	17.5% 25.0	21.2% 9.7	20.7% 20.8	23.4% 9.7
Agents for surgeries	40.1% 7.7	39.6% 14.8	39.4% 7.4	39.1% 14.5	39.9% 6.8
Corneal disease treatments	86.9% 9.3	85.4% 18.8	82.9% 10.1	82.4% 21.0	81.2% 11.4
Anti-cataract	52.7% 4.0	53.3% 7.7	54.7% 3.7	55.4% 7.1	56.7% 3.6
Corticosteroids	53.3% 5.8	53.1% 11.4	51.8% 5.6	51.6% 10.9	52.1% 5.6

Notes: - On an NHI drug price basis.

- Lower figures indicate market size.

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Source: Santen analysis based on IMS data

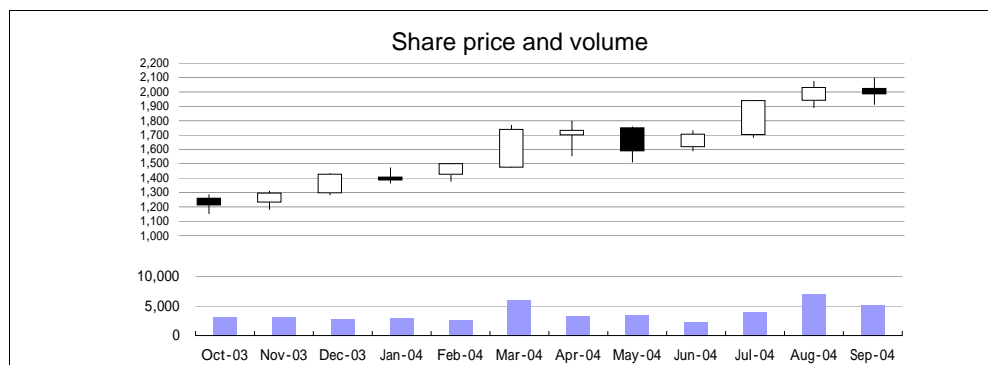
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# Stock information

Stock price (Osaka Securities Exchange 1st market)

(Yen and thousand shares)

	Oct-03	Nov-03	Dec-03	Jan-04	Feb-04	Mar-04	Apr-04	May-04	Jun-04	Jul-04	Aug-04	Sep-04
Share price:												
Open	1,260	1,231	1,295	1,408	1,426	1,475	1,700	1,750	1,617	1,701	1,940	2,025
High	1,288	1,312	1,435	1,475	1,501	1,770	1,799	1,760	1,733	1,943	2,075	2,100
Low	1,152	1,180	1,280	1,362	1,376	1,475	1,552	1,510	1,588	1,681	1,888	1,910
End of month	1,211	1,295	1,427	1,386	1,500	1,740	1,733	1,587	1,706	1,940	2,030	1,985
Volume	3,182	3,154	2,886	3,026	2,675	5,930	3,344	3,438	2,286	3,930	7,047	5,123



## Major shareholders

As of September 30, 2004

Name	Number of	Percentage of
	shares Held	voting rights
	Thousand shares	%
Northern Trust CO.(AVFC) Sub-account American Clients	7,596	8.7
Japan master Trust and Banking Co., Ltd.	5,233	5.9
Mita Sangyo Co., Ltd.	4,756	5.4
Japan Trustee Service Bank, Ltd.	4,620	5.3
Nippon Life Insurance Company	3,108	3.5
Northern Trust CO. AVFC Re U.S. tax exempted Pension Funds	2,971	3.4
The Tokio Marine and Fire Insurance Co., Ltd.	2,668	3.0
UFJ Bank Limited	2,358	2.7
The Bank of Tokyo-Mitsubishi, Ltd.	2,358	2.7
Trust and Custody Services Bank, Ltd.	2,188	2.5

## Shares, convertible bonds and stock option

At half-year/year end	3/2000	3/2001	3/2002	3/2003	3/2004	9/2004
Number of shares outstanding (thousand shares)	95,074	92,720	90,704	90,704	87,963	87,982
Third Unsecured Convertible Bonds -balance (millions of yen)	19,945	19,945	19,945	19,945	-	-
Stock option balance (thousand shares)	172	199	243	335	473	513.8
Granted in June 1998 - 106 thousand shares at 1,540 yen/share	106	73	62	62	62	53
Granted in June 1999 - 66 thousand shares at 2,480 yen/share	66	66	66	66	66	66
Granted in June 2000 - 60 thousand shares at 2,705 yen/share	-	60	60	60	60	60
Granted in June 2001 - 55 thousand shares at 2,299 yen/share	-	-	55	55	55	55
Granted in June 2002 - 92 thousand shares at 1,326 yen/share	-	-	-	92	92	82
Granted in June 2003 - 137.6 thousand shares at 1,176 yen/share	-	-	-	-	137.6	137.6
Granted in June 2004 - 78.2 thousand shares at 1,743 yen/share	-	-	-	-	-	78.2

Note: 1 The company repurchased and retired 2,378 thousand shares in March 2001 and 2,027 thousand shares in March 2002.

2 The convertible bonds were redeemed on September 30, 2003.

3 The company has a stock-based compensation plans under which stock options are granted to directors and corporate officers. The grants are fully exercisable after two years.

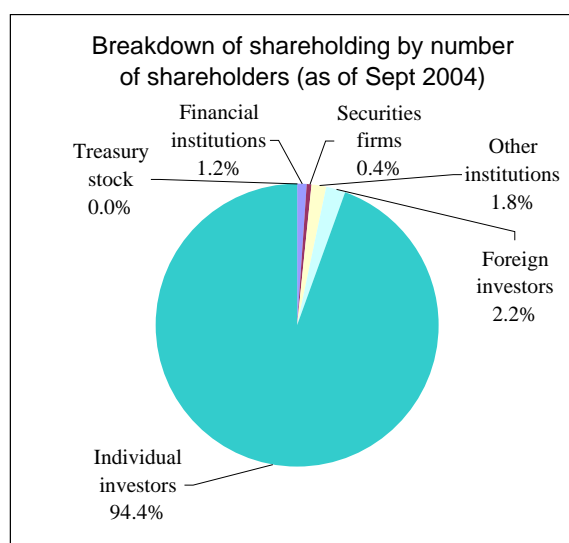
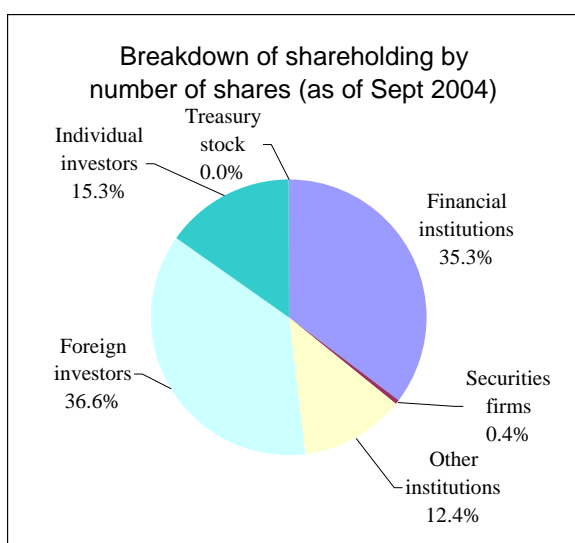
### Breakdown of shareholding by number of shares

At half-year/year end	9/2002		3/2003		9/2003		3/2004		9/2004	
	Thousand shares	Proportion (%)	Thousand shares	Proportion (%)	Thousand shares	Proportion (%)	Thousand shares	Proportion (%)	Thousand shares	Proportion (%)
Financial institutions	38,284	42.2	36,302	40.0	32,568	35.9	30,740	34.9	31,089	35.3
City & regional banks	8,846	9.8	6,660	7.3	6,592	7.3	5,428	6.2	5,429	6.2
Trust banks	18,339	20.2	19,018	21.0	15,535	17.1	16,201	18.4	16,072	18.2
(concerned in trust works)	15,609		15,743	0	12,371		13,422		13,515	
Life and non-life insurance	10,527	11.6	10,414	11.5	10,012	11.0	9,007	10.2	9,542	10.8
Other financial institutions	571	0.6	208	0.2	428	0.5	103	0.1	46	0.1
Securities firms	343	0.4	293	0.3	661	0.7	368	0.4	330	0.4
Other institutions	10,277	11.3	10,555	11.6	10,585	11.7	10,512	12.0	10,944	12.4
Foreign investors	24,288	26.8	24,580	27.1	27,593	30.4	31,306	35.6	32,154	36.6
Individual investors	17,492	19.3	16,200	17.9	16,523	18.2	15,001	17.1	13,430	15.3
Treasury stock	18	0.0	2,771	3.1	2,773	3.1	33	0.0	36	0.0
Total	90,704	100.0	90,704	100.0	90,704	100.0	87,963	100.0	87,982	100.0

Note: Trading unit for Santen shares were reduced to 100 shares from 1,000 shares effective August 1, 2002

### Breakdown of shareholding by number of shareholders

At half-year/year end	9/2002		3/2003		9/2003		3/2004		9/2004	
	Number of shareholders	Proportion (%)	Number of shareholders	Proportion (%)	Number of shareholders	Proportion (%)	Number of shareholders	Proportion (%)	Number of shareholders	Proportion (%)
Financial institutions	97	1.2	98	1.2	88	1.0	83	1.0	86	1.2
City & regional banks	10	0.1	8	0.1	7	0.1	7	0.1	7	0.1
Trust banks	53	0.7	55	0.7	46	0.5	46	0.6	48	0.7
Life and non-life insurance	26	0.3	29	0.4	28	0.3	27	0.3	30	0.4
Other financial institutions	8	0.1	6	0.1	7	0.1	3	0.0	1	0.0
Securities firms	40	0.5	28	0.4	37	0.4	28	0.4	27	0.4
Other institutions	139	1.7	134	1.7	134	1.6	130	1.7	124	1.8
Foreign investors	110	1.3	119	1.5	127	1.5	122	1.5	153	2.2
Individual investors	7,883	95.3	7,493	95.2	8,134	95.5	7,498	95.4	6,608	94.4
Treasury stock	1	0.0	1	0.0	1	0.0	1	0.0	1	0.0
Total	8,270	100.0	7,873	100.0	8,521	100.0	7,862	100.0	6,999	100.0



# News releases

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## News releases during April 2004-September 2004

For details, please refer to our Investor Relations Web site (<http://www.santen.co.jp/ir/en/news>).

- | (Date)        | (Summary)   |
|---------------|---|
| <b>7-May</b>  | <b>Santen to Issue Stock Acquisition Rights for the Purpose of Granting Stock Options</b><br>Santen's Board of Directors adopted a resolution to issue stock acquisition rights for the purpose of granting stock options to Santen's directors, corporate officers and directors of major overseas subsidiaries. The resolution was approved at the 92nd Annual General Meeting of Shareholders held on June 25.   |
| <b>12-Jul</b> | <b>Agreement Concerning Glaucoma and Ocular Hypertension Treatment RESCULA Eye Drops</b><br>Santen acquired the exclusive marketing rights in Japan for RESCULA Eye Drops (generic name: unoprostone isopropyl) from R-Tech Ueno, Ltd. On October 1, Santen started the sales of RESCULA Eye Drops for the treatment of glaucoma and ocular hypertension. R-Tech Ueno holds the manufacturing approval and will develop plans for marketing and promotion of the product. |
| <b>20-Jul</b> | <b>Santen Launches Anti- rheumatic METOLATE Tablets 2mg</b><br>Santen launched the anti-rheumatic METOLATE Tablets 2mg (generic name: methotrexate) in Japan. METOLATE Tablets 2mg has shown efficacy in low-dose weekly administrations. This new product launch enhances Santen's anti-rheumatic product portfolio and will allow us to offer more detailed therapeutic options tailored to each patient's condition.   |

