

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549



02025326

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16 OF
THE SECURITIES EXCHANGE ACT OF 1934

P.F.
3-1-02

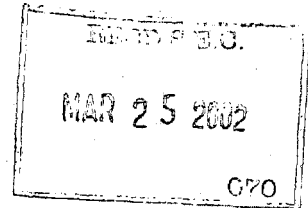
For the month of March, 2002.

Serono S.A.
(Registrant's Name)

15 bis, Chemin des Mines
Case Postale 54
CH-1211 Geneva 20
Switzerland

(Address of Principal Executive Offices)

1-15096
(Commission File No.)



PROCESSED

APR 01 2002

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FINANCIAL P

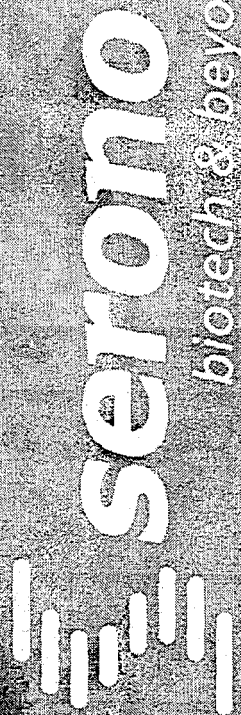
(Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.)

Form 20-F ☒ Form 40-F ☐

(Indicate by check mark whether the registrant by furnishing the information contained in this form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.)

Yes ☐ No ☒

(If "Yes" is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b): 82-_____)



Annual Management Roadshow

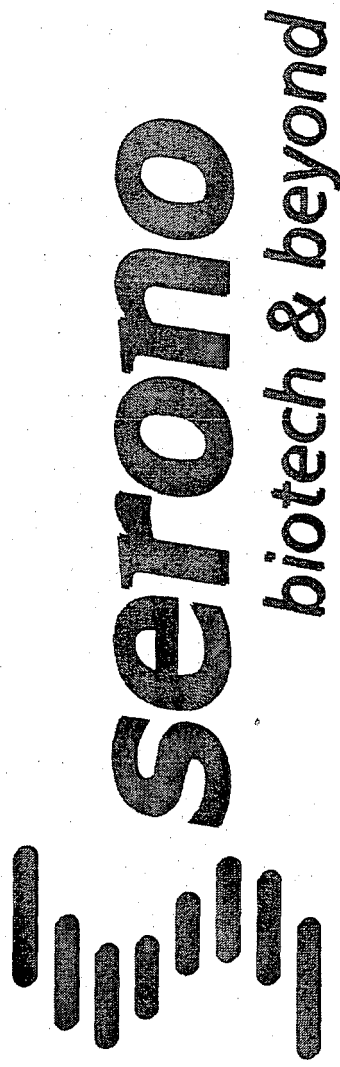
London, New York, San Francisco, Geneva, Zurich

March 25 – April 3, 2002

Ernesto Bertarelli
Chief Executive Officer

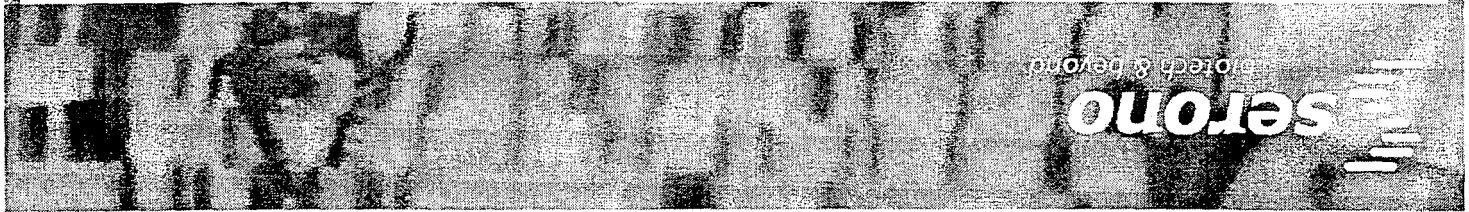
Jacques Theurillat
Chief Financial Officer

Andrew Galazka M.D.
Senior VP Scientific Affairs



This presentation may contain forward-looking statements that reflect management's current views as to the company's collaborative arrangements, clinical trials, product developments, regulatory approvals, manufacturing scale-up, and other future events and operations. These forward-looking statements involve uncertainties and other risks that are detailed in Serono's filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" and "Operating and Financial Review and Prospects" sections of Serono's Annual Report on Form 20-F filed on April 23, 2001. Actual results could differ materially from these forward-looking statements.

This presentation is intended only for the purpose of providing information relevant to the investment community and should not be used for any other purposes.



2001 - Delivering Expectations

- Sales: \$1,249m up 15.0%
(like-for-like, in local currencies)
- Royalty and license income: \$127m up 37.2%
(in local currencies)
- Gross margin: increases further to 82.9%
- Net income: up 5.2% to \$316.7m, following investment in US for early Rebif launch
- R&D delivered its commitments

Rebif US Approval

MARCH 7 2002

APPROVED

MARCH 11 2002

LAUNCH IN THE US

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Immunology

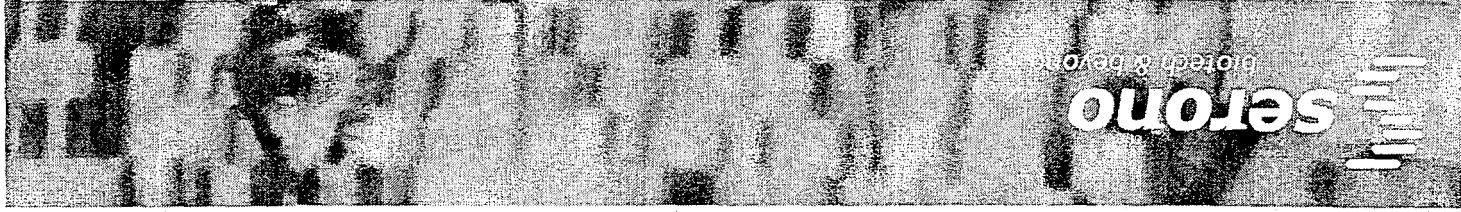
The Vision

We will be the world's leader in
Biotechnology...

by growing each of our businesses to the
1 position in sales,
and by building the richest R&D pipeline in
our chosen Therapeutic Areas.

Our innovative products will
fight debilitating diseases and improve the
lives of our patients

**Rebif launch in the US is a major step
forward in making our Vision real**



Our Vision is Alive

- Biotechnology is a global industry
- First time in history that Orphan Drug Exclusivity overcome on clinical superiority
- We have a clinically superior product to treat MS
- Rebif is now available to patients in the US
- Our Vision is alive! Our Vision is to bring biotechnology to people
- Rebif is a tangible expression of our vision!

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We are Going to Become Market Leader in the US

- **We are entering the market in a very strong position**
- **We intend to become market leader in the US...**
- **the same way we have become market leader in the rest of the world**

Now Time to Change the US MS Paradigm

- All interferon therapies are not equal
- FDA has found Rebif to be clinically superior to Avonex
- Now patients can choose efficacy without making any trade-off!
- Rebif is convenient – liquid prefilled syringe with Rebiject

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Serono's Depth of Understanding of MS

- **ETOMS:** Early treatment of MS *Lancet*, May 2001
 - Reinforces the paradigm of early treatment
- **SPECTRIMS:** Rebif in treatment of early secondary progressive MS *Neurology*, June 2001
 - Rebif label to include relapsing forms of MS
- **PRISMS 4:** Long term data on Relapsing Remitting MS *Neurology*, June 2001
 - 4 year data show superiority of 44 mcg three times per week (EU recommended dose)
- **EVIDENCE:** Rebif versus Avonex comparative data *World Congress of Neurology*, June 2001
 - Overcome Orphan Drug on clinical superiority
- **American Academy of Neurology review** regards all the above Serono studies as Class I *Neurology*, Jan 2002

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Rebif is Clinically Superior to Avonex

- "... the comparative clinical study demonstrates that Rebif is more effective than Avonex such that it provides a significant therapeutic advantage over Avonex: 74.9% of study subjects taking Rebif were exacerbation-free versus 63.3% of Avonex subjects. This is a meaningful difference, because it means, among other things, that a patient on Rebif is 32% less likely to experience an MS exacerbation, which can substantially lower his or her quality of life for weeks or months."

Dr C. Rask, Medical reviewer CBER, FDA, March 7, 2002

www.fda.gov/cber/products/ifnbser030702.htm

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Rebif is Clinically Superior to Avonex

- “FDA has considered a number of other issues concerning the adequacy of the comparative study and the safety and effectiveness of Rebif. As described below in the body of this memorandum, FDA has fully evaluated these issues and has determined that Rebif is clinically superior to Avonex.”

Dr C. Rask, Medical reviewer CBER, FDA, March 7, 2002

www.fda.gov/cber/products/ifnbser030702.htm

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Rebif Treatment Effect Maintained at 1 year

- [Exacerbations]: “Thus, the treatment effect observed during the initial 24 weeks on study was maintained during the succeeding 6 months.”
- [MRI]: “During the second 24 weeks, the development of similar numbers of lesions in the 2 groups would have been consistent with maintenance of the treatment effect. Instead, these data show additional differences favoring Rebif in new or enlarging lesions during the second 24 weeks. As with exacerbations, there is no suggestion of any reversal in the treatment effect.”

Dr C. Rask, Medical reviewer CBER, FDA, March 7, 2002

www.fda.gov/cber/products/ifnbser030702.htm

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The Proof of the Pudding...

- Largest clinical experience in the field (all studies Class I)
- Rebif BLA reviewed in 6 months
- Rebif found to be clinically superior to Avonex
- Product launched within 2 working days of approval
- Rebif is market leader outside of the US
- **We are ready for market leadership in the USA!**

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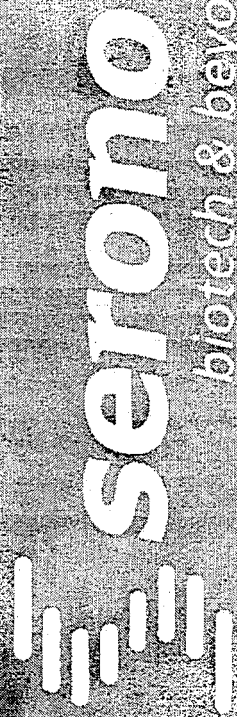
Imaging

Our Business is in Great Shape

- **Neurology**
 - Rebif is a blockbuster
- **Reproductive Health**
 - Launch of Gonal-F Multidose, Ovidrel and Luveris
 - Gonal-F grew by 14.7% to \$411m in 2001
- **Growth and Metabolism**
 - Launch of Saizen in adult GH deficiency
 - Rollout of new GH delivery devices
 - Strong growth of Saizen (up 23% to \$107m)
- **Research and development**
 - 7 new molecules entered pre-clinical development

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Financial & Business Overview

Jacques Theurillat
Chief Financial Officer

2001 Financial Highlights

- **Sales:** \$1,249m up 15.0%
(like-for-like, in local currencies)
- **Royalty and license income:** \$127m up 37.2%
(in local currencies)
- **Gross margin:** increases further to 82.9%
- **Net income:** up 5.2% to \$316.7m, following
investment in US for early Rebif launch

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2001 Revenues

- **Q401 Product sales \$338m (+17.1% like-for-like^{**})**
- **2001 Product sales \$1,249m (+15.0% like-for-like^{**})**
 - **Neurology: \$379.6m (+54.1%^{*})**
 - **Reproductive Health: \$574.3m (+3.7%^{**})**
 - **Growth & Metabolism: \$232.6m (+3.9%^{*})**
- **2001 Royalty and license income: \$127m (+37.2%^{*})**
- **2001 Total revenues: \$1,376m (+13.5%^{*})**

* in local currencies

** in local currencies and excluding sales of Crinone (temporarily withdrawn, relaunched in the US in March 2002) and Curosurf (sold to Chiesi)

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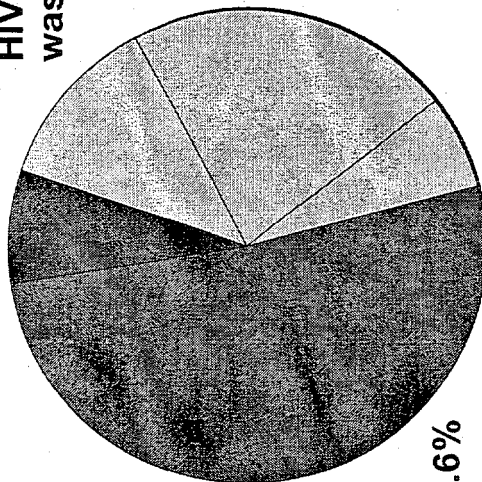
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Diversified Portfolio with a Potential Blockbuster

2000

Growth 7.8%

HIV-associated
wasting 12.0%



MS 22.2%

RH 51.6%

Other 6.4%

\$1,147m

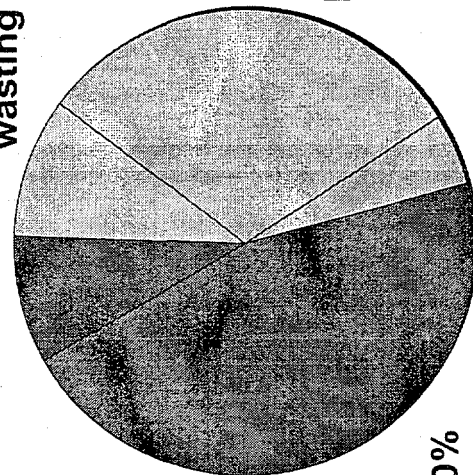
+15.0% *

\$1,249m

2001

Growth 8.6%

HIV-associated
wasting 10.0%



MS 30.4%

RH 46.0%

Other 5.0%

* in local currencies and excluding sales of Crinone (temporarily withdrawn) and Curosurf (sold to Chiesi)

Gonal-F Leads Recombinant Segment

- In line with our strategy, 72% of RH product sales are now derived from recombinant products (2000: 62%)
- Worldwide market leader with 58% of recombinant segment
- Gonal-F growth in Q4: up 16.4%* to \$109.7m
- Gonal-F growth in 2001: up 14.7%* \$410.5m

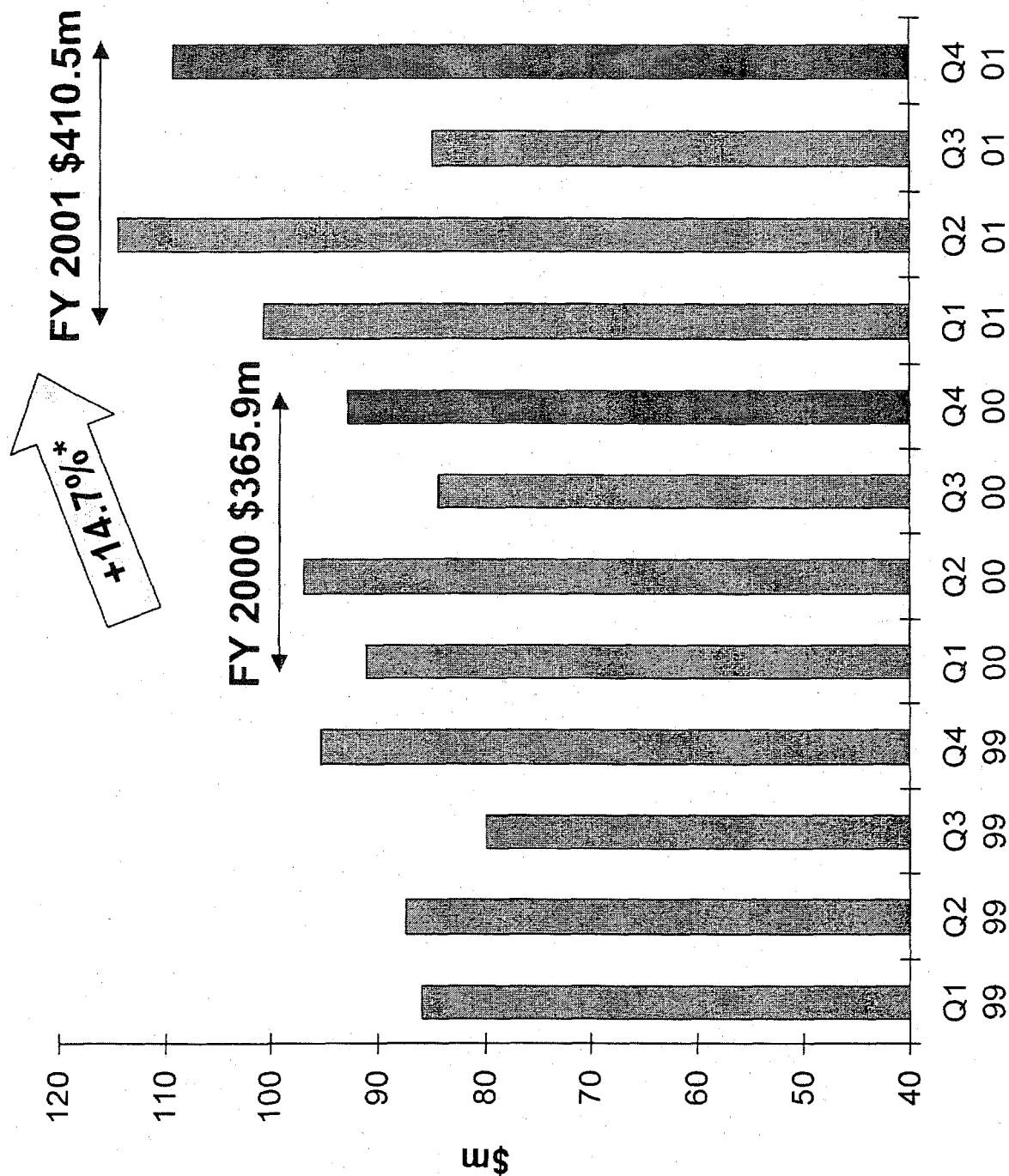
* In local currencies

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Gonal-F Continues Double-digit Growth



* in local currencies (+12.2% in actual \$ terms)

Reproductive Health: **New Investments to Maintain Leadership**

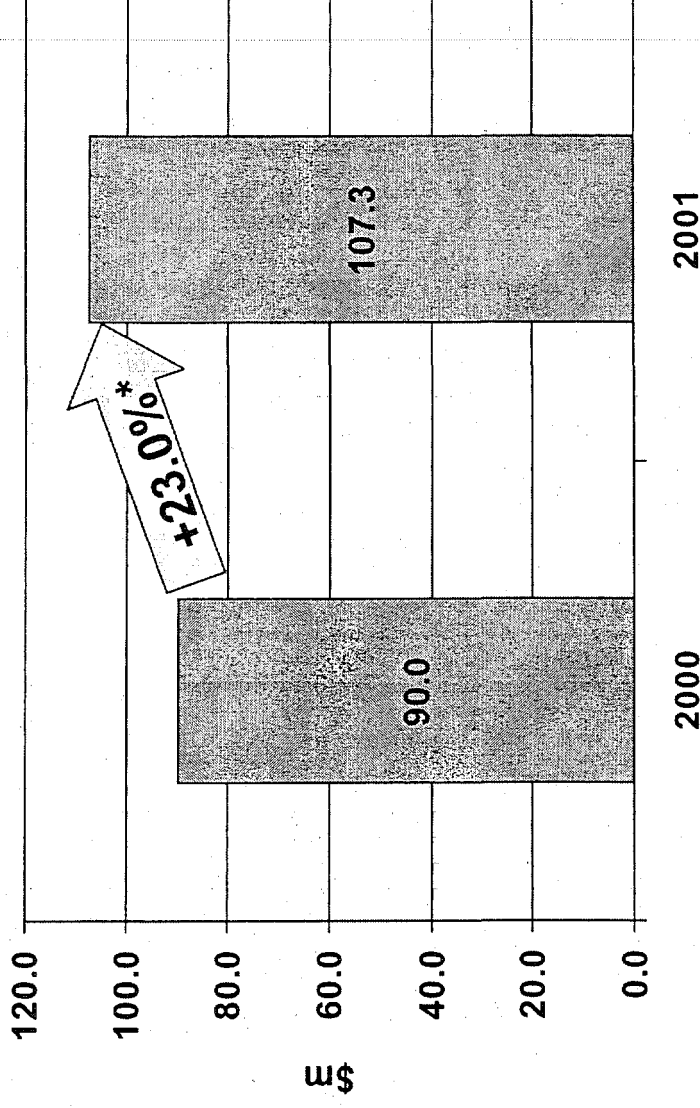
- Launch of Gonal-F multi-dose by mid-2001
 - 10% of 2001 Gonal-F sales
 - 20% of December sales
- Initial launch of Ovidrel (r-hCG) and Luveris (r-LH) late 2001
- Serono is the only company with 3 infertility hormones derived from recombinant technology (r-FSH, r-LH, r-hCG) on the market
- Crinone relaunched in the US in March 2002

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Saizen an Excellent Year 2001

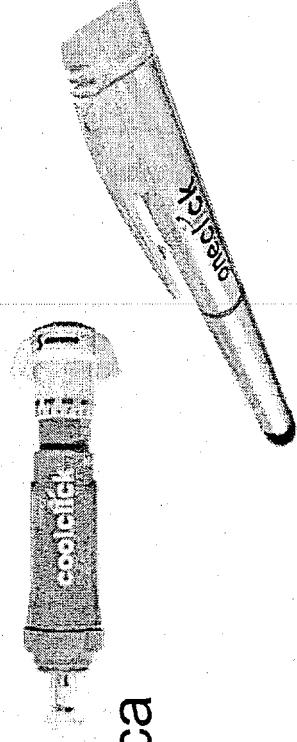


■ Saizen very strong growth based on introduction of delivery devices

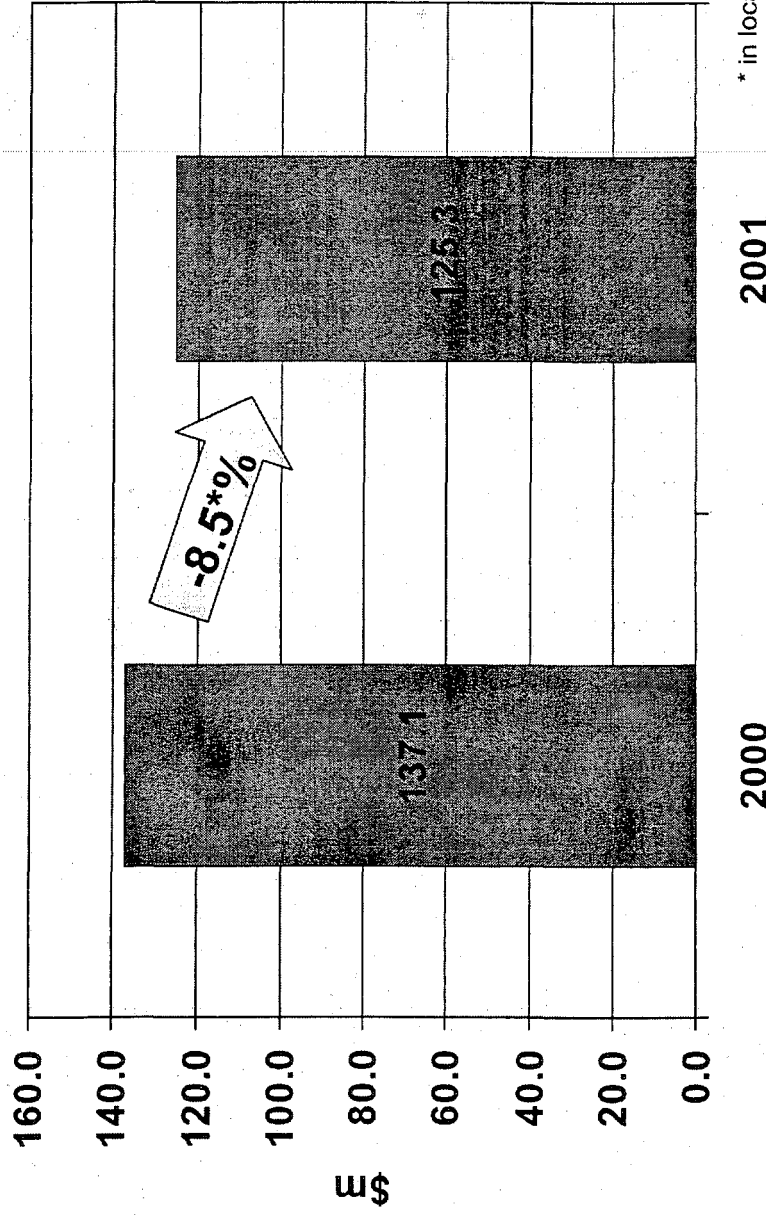
■ cool.click in North America

■ one.click in Europe

* in local currencies

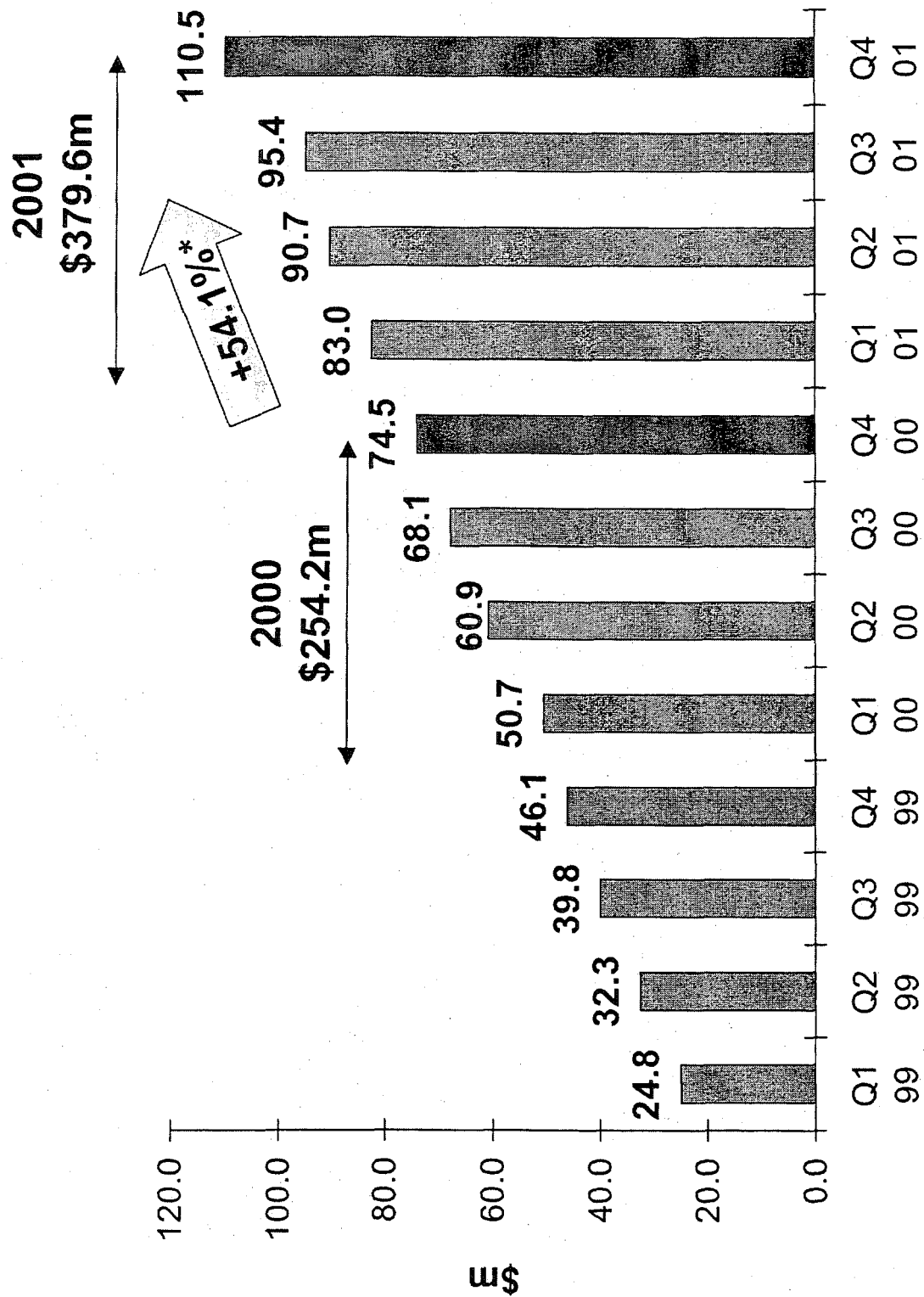


Serostim – Difficult Environment



- Gap between demand and ex-factory sales: currently being investigated
- On-going investigations and prior authorization procedures are slowing down prescriptions
- Reimbursement issues largely overcome
- Serojet needle free injection device launched February 2002
- Outcome of phase 2/3 study in lipodystrophy expected Q3, 2002

Rebif - Quarterly Sales



* in local currencies (+49.3% in actual \$ terms)

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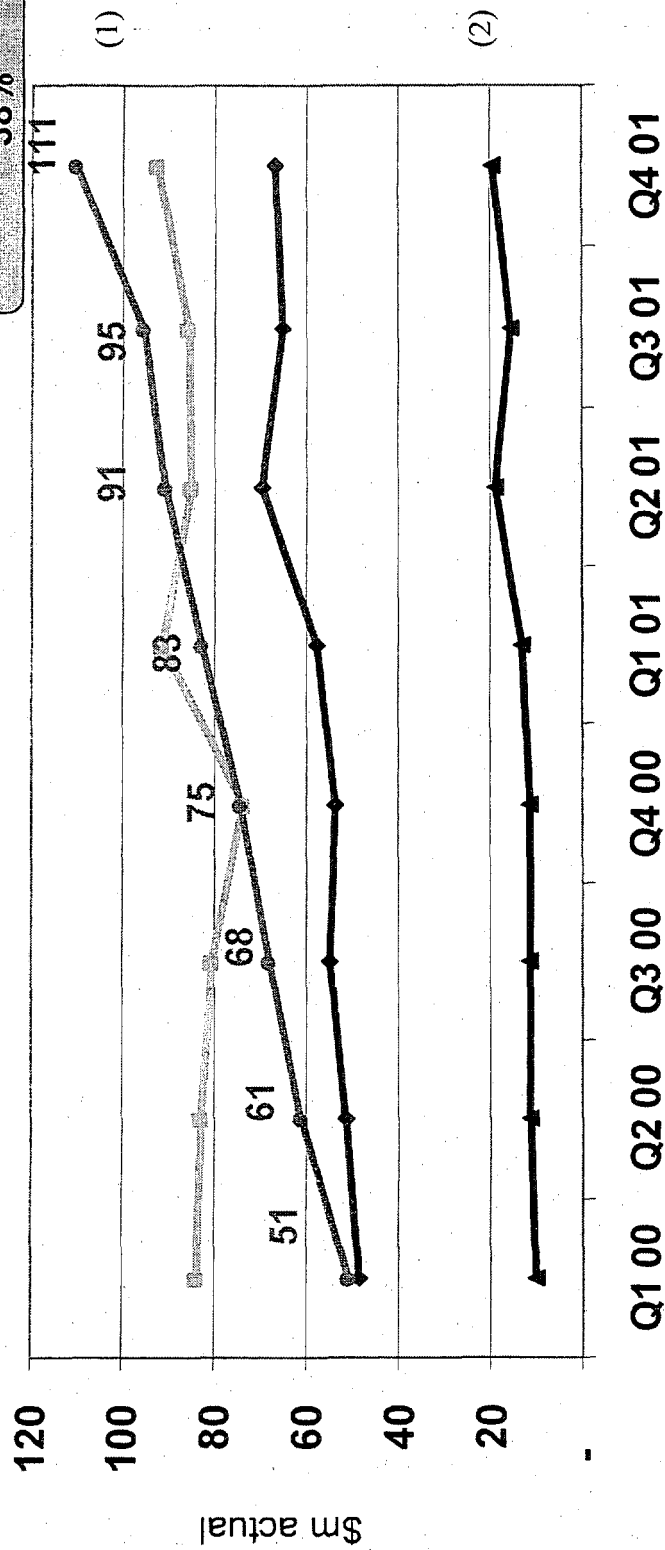


Market Leadership - Foundation: Efficacy

MS Sales Ex-USA

Q1 00	Q2 00	Q3 00	Q4 00	Q1 01	Q2 01	Q3 01	Q4 01
193	207	215	214	245	265	261	290

Q4, 01 mkt. share
38%



(1) Betaferon sales are reported by Schering AG in €, conversion to US\$ is done internally.

(2) Copaxone USA sales are based on internal estimate. Teva reports total North America region.

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Strongest Label in US, **Based on PRISMS and EVIDENCE**

- Indication: decreases the frequency of relapses and delays the accumulation of physical disability
- Relapsing MS
- Based on **two** pivotal studies (PRISMS & EVIDENCE)
- Label shows positive results of Rebif versus Avonex. Comparative claims can be made in promotional material. As usual they will be compatible with the label, and will be based on any of the scientific data which has been reviewed and approved by the FDA.

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Strongest Label in US, **Based on PRISMS and EVIDENCE**

Additionally...

- Unique liquid pre-filled syringe with Rebiject autoinjector
- Storage at room temperature
- The recommended dose is 44 mcg 3x per week
- Adverse events generally similar between Rebif and Avonex. Exception of injection site reactions, hepatic disorders, leucopenia

2001 Results

In actual US\$ m.	2001	% of sales	2000	% of sales	Change (%) actual currencies
Sales (1)	1,249		1,147		8.9%
Royalty & License Income	127		93		37.1%
Revenues	1,376		1,240		11.0%
Cost of good sold	213	17.1%	230	20.0%	
Product Gross Margin					
		82.9%		80.0%	
S G & A Expenses	447	35.8%	394	34.3%	13.5%
R&D Expenses	309	24.7%	263	22.9%	17.3%
Other Operating Expense	70		31		
Operating Income (EBIT)	338	27.0%	322	28.0%	4.9%
Financial Income	51		52		
Taxes	70		70		
Net Income	317	25.3%	301	26.2%	5.2%

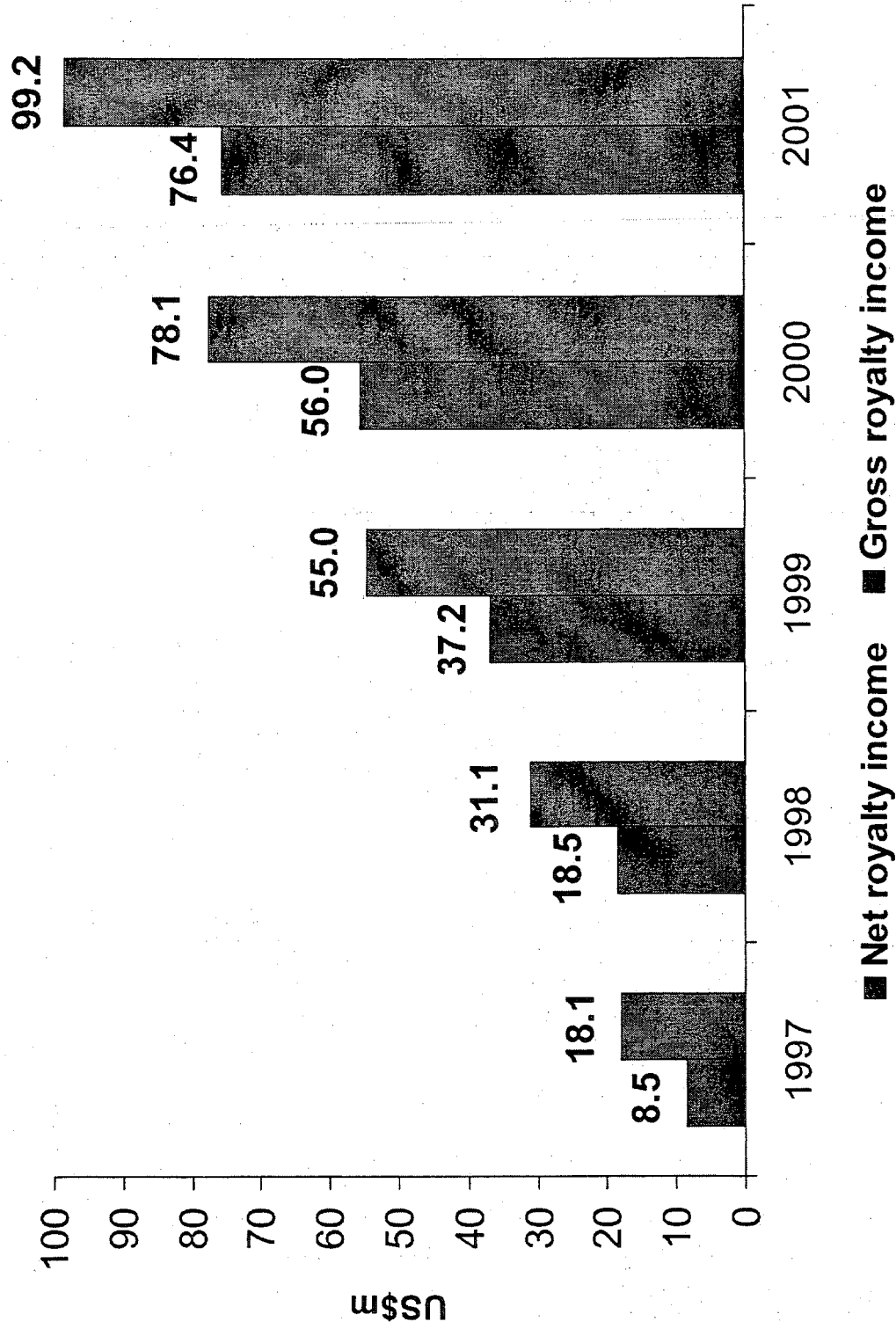
(1) Like-for-like sales (i.e. excluding Crinone and Curosurf) in local currency increased 15%

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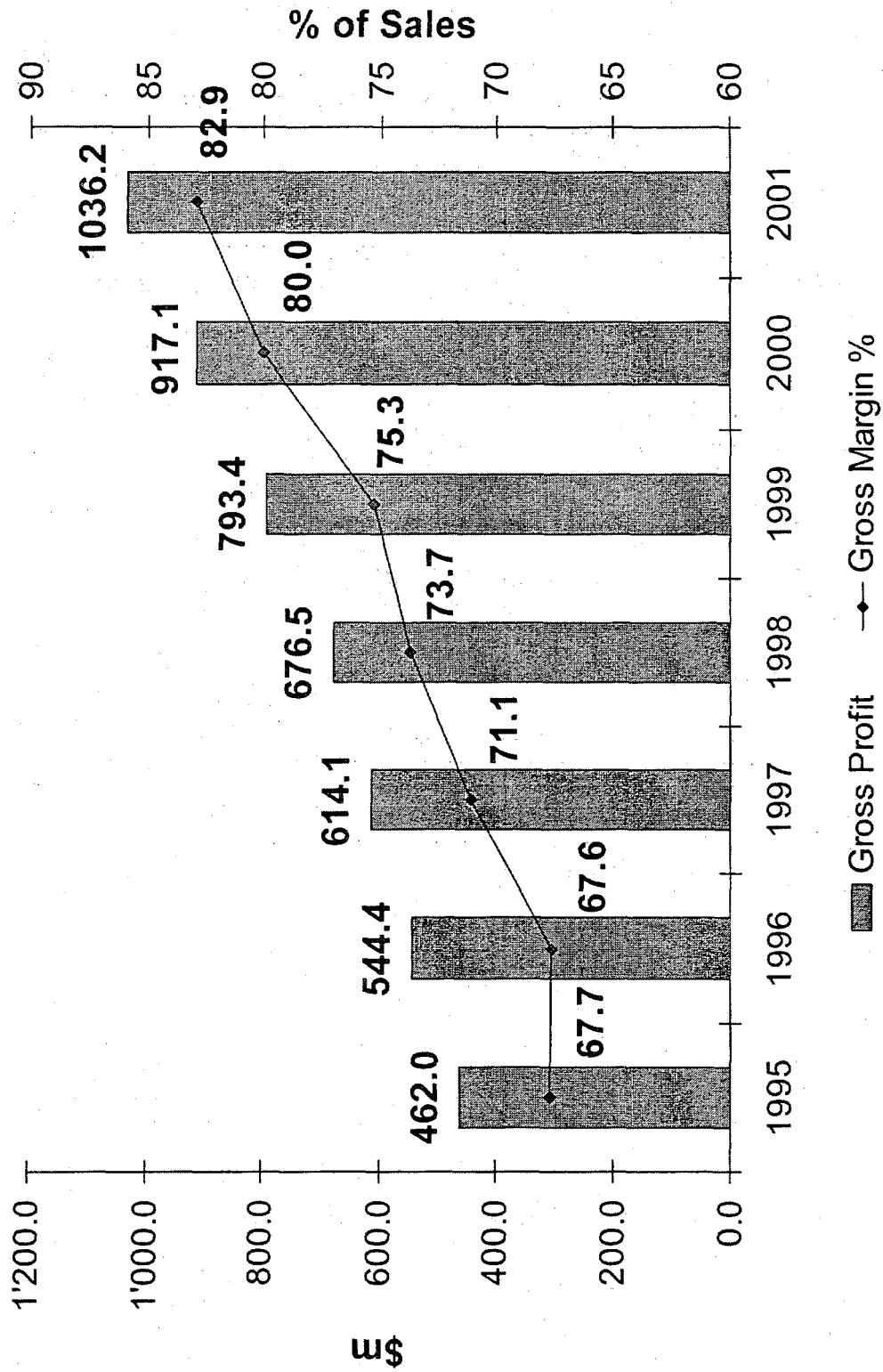
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Strong Royalty Income from Biotech IP rights*

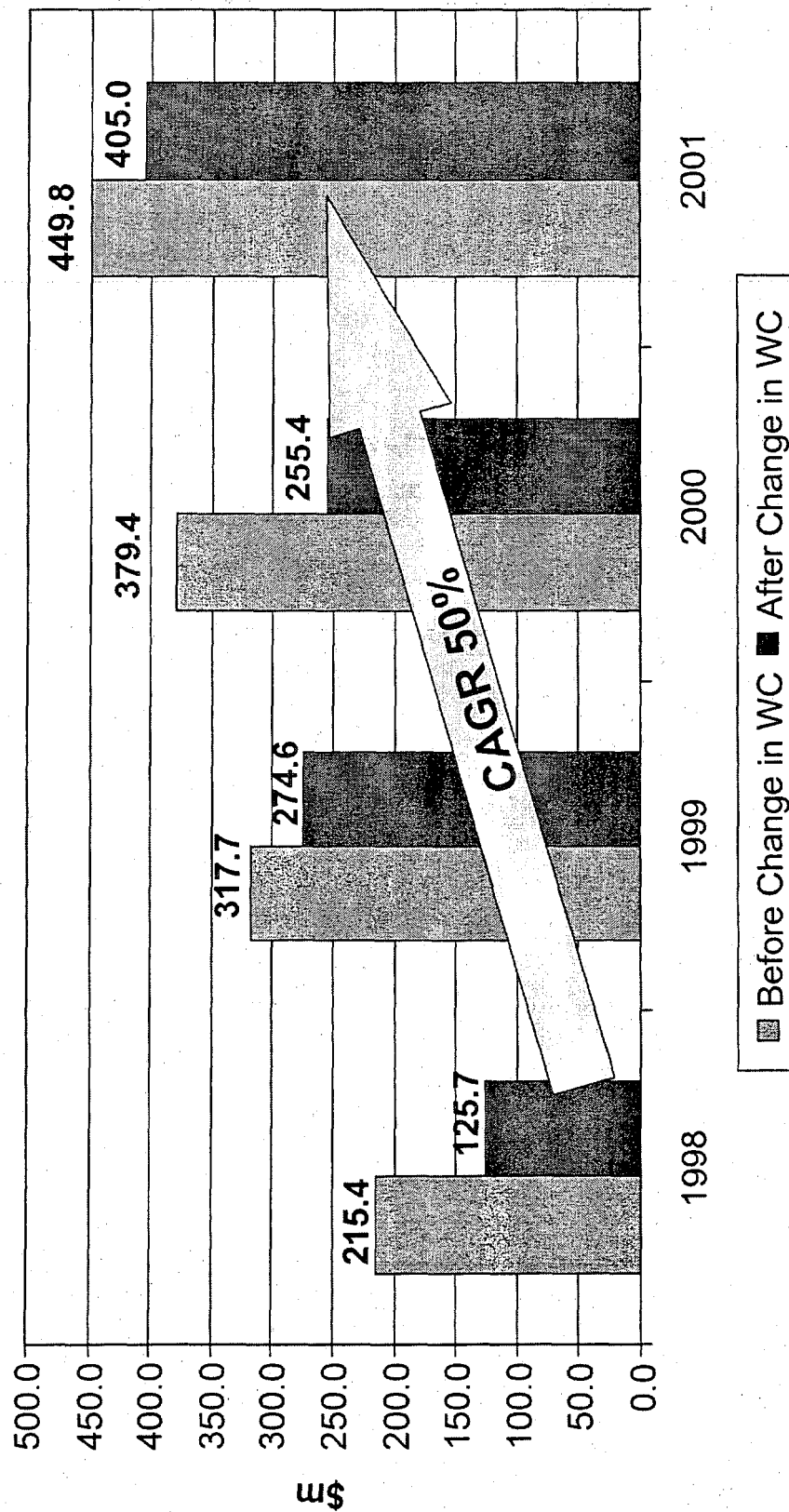


* On sales of Avonex (Biogen), Puregon (Organon NV), Enbrel (Immunex)

Consistent Improvement in Gross Margin



Cash Flow from Operations



2002 Objectives

- Approval and successful launch of Rebif in the US
- Maintain Rebif rollout momentum worldwide
- Maintain strong leadership in Reproductive Health
- Achieve major clinical milestones
- Strong financial growth

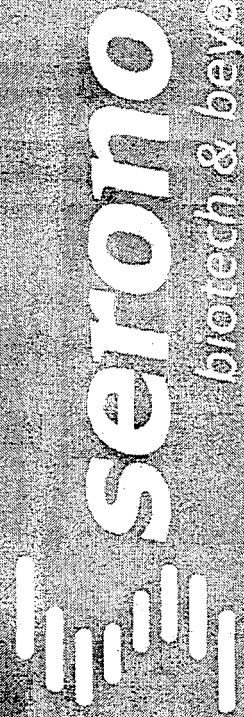
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Guidance for 2002

- Rebif sales: 43-48%* growth
- Gonal-F sales: 10-15%* growth
- GH sales
 - Saizen: 10-15%* growth
 - Serostim: \$90-100m
- Total product sales: 15%* growth
- Gross margin: 84-85% of product sales
- SG&A: 33-35% of product sales
- R&D: 23-25% of product sales
- Net income: 15-17% growth

* In local currencies

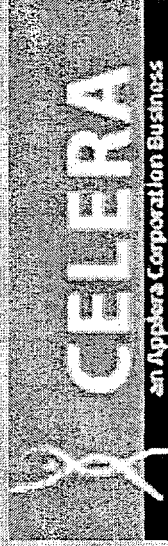


R&D Overview

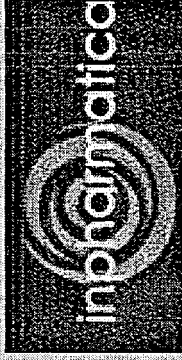
Andrew Galazka MD
Senior VP Scientific Affairs

Serono Drug Discovery

- 1300 people in R&D
- Discovery organization reshaped over the last 4 years
- Two major sites (SPRI, Geneva; SRBI, Rockland, Mass.)
- Significant number of biotech collaborations. In 2001:



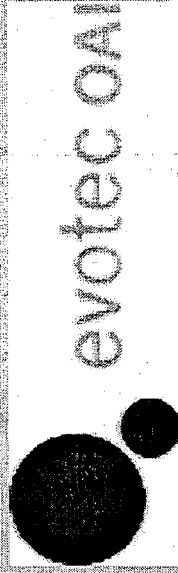
Genomics



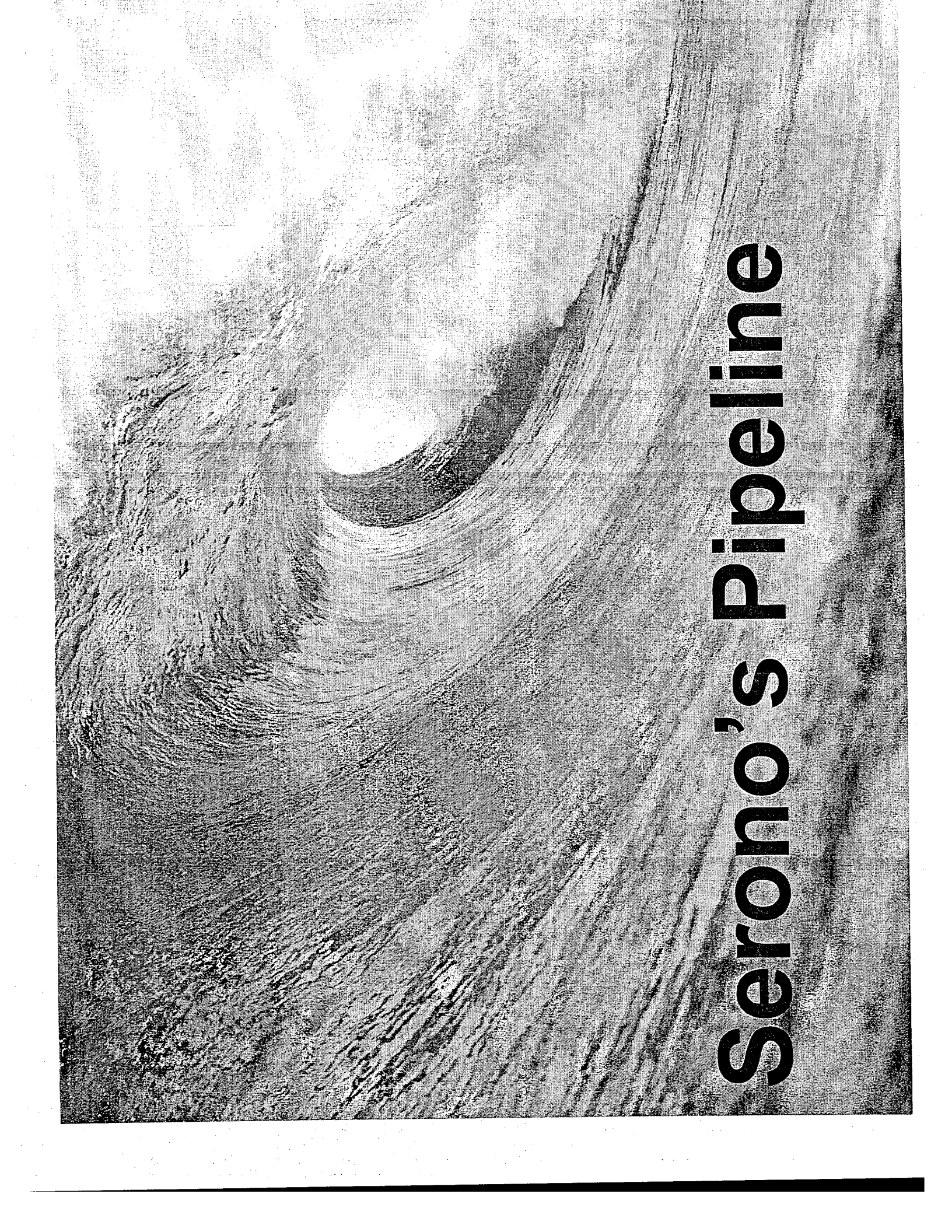
Novel genes using structural
bioinformatics

ZYMOGENETICS

Autoimmune diseases
(TACI, BCMA)



Combinatorial chemistry and
chemical libraries



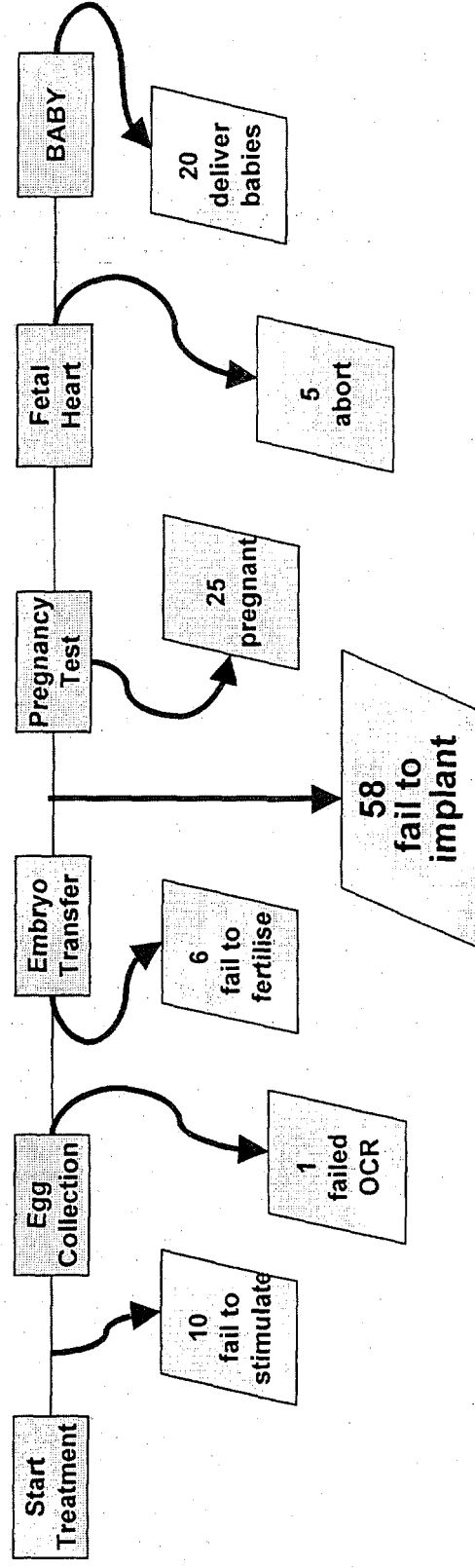
Serono's Pipeline

Therapeutic area	Preclinical phase	Phase 1	Phase 2	Phase 3
Reproductive health	oxytocin receptor antagonist • pre-term labour	microencapsulated r-FSH • to reduce the frequency of administration of r-FSH r-LIF • embryo implantation failure type 1 5-alpha reductase inhibitor • hirsutism associated with polycystic ovarian syndrome	r-LH (high dose) • ovulation trigger in female infertility (OI) r-TBP-1 • endometriosis (planned)	r-LH (high dose) • ovulation trigger in female infertility (ART)
Neurology	breaker peptide • Alzheimer's disease chemokine inhibitor • multiple sclerosis IKK-2 inhibitor • multiple sclerosis JNK inhibitor • central nervous system disorders	IFNAR-2 • to increase the half life of IFNβ-1a PEG r-IFNβ-1a • to increase the half life of IFNβ-1a	r-IFNβ-1a • Guillain-Barré syndrome	
Growth and metabolism	PEG GHRF • growth retardation		r-GH • HARS/Lipodystrophy	
Gastroenterology		r-IL-18 bp • Crohn's disease	r-IFNβ-1a • Crohn's disease r-IFNβ-1a • ulcerative colitis r-TBP-1 • Crohn's disease r-IFNβ-1a • chronic hepatitis C – a genotypic subgroup of patients	r-GH • short bowel syndrome
Inflammatory and autoimmune diseases	IKK-2 inhibitor • rheumatoid arthritis JNK inhibitor • ischemic and inflammatory conditions TACI • autoimmune conditions BCMA • autoimmune conditions	r-IL-18 bp • rheumatoid arthritis	r-IFNβ-1a • rheumatoid arthritis r-TBP-1 • rheumatoid arthritis r-TBP-1 • psoriasis and psoriatic arthritis	
Oncology	itirelix nanospheres (GnRH antagonist) • prostate cancer	type 1 5-alpha reductase inhibitor • prostate disease	r-hCG • breast cancer	
Cardiology			r-TBP-1 • cardiac reperfusion injury	

Therapeutic area	Preclinical phase	Phase 1	Phase 2	Phase 3
Reproductive health	oxytocin receptor antagonist • pre-term labour	microencapsulated r-FSH • to reduce the frequency of administration of r-FSH r-LIF • embryo implantation failure inhibitor • hirsutism associated with polycystic ovarian syndrome	r-LH (high dose) • ovulation trigger in female infertility (OI) r-TBP-1 • endometriosis (planned)	r-LH (high dose) • ovulation trigger in female infertility (ART)
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Growth and metabolism	PEG GHRF			r-GH
Gastroenterology		r-IL-18 bp • Crohn's disease	r-IFNβ-1a • Crohn's disease r-IFNβ-1a • ulcerative colitis r-TBP-1 • Crohn's disease r-IFNβ-1a • chronic hepatitis C – a genotypic subgroup of patients	r-GH • short bowel syndrome
Inflammatory and autoimmune diseases	IKK-2 inhibitor • rheumatoid arthritis JNK inhibitor • ischemic and inflammatory conditions TACI • autoimmune conditions BCMA • autoimmune conditions	r-IL-18 bp • rheumatoid arthritis	r-IFNβ-1a • rheumatoid arthritis r-TBP-1 • rheumatoid arthritis r-TBP-1 • psoriasis and psoriatic arthritis	
Oncology	itirelix nanospheres (GnRH antagonist)	type 1 5-alpha reductase inhibitor • prostate disease	r-hCG • breast cancer	
Cardiology			r-TBP-1 • cardiac reperfusion injury	

LIF in Embryo Implantation

■ What happens to 100 IVF patients?

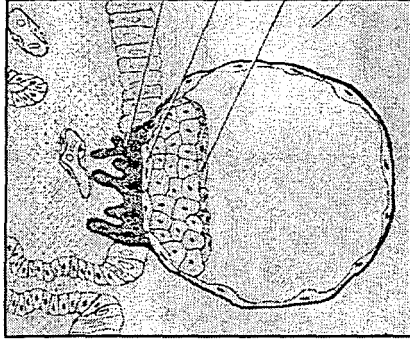


■ LIF is believed to prepare uterine lining for blastocyst attachment and to therefore be essential for embryo implantation.

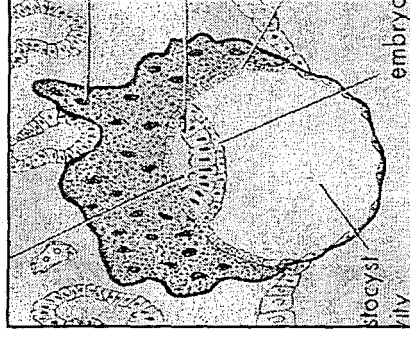
■ Uterine levels of LIF concentrations are low in women who suffer from recurrent miscarriage or unexplained infertility

■ In knockout mice (LIF -/-) normal blastocysts are formed but these fail to implant. However normal implantation occurs if they are treated with murine LIF.

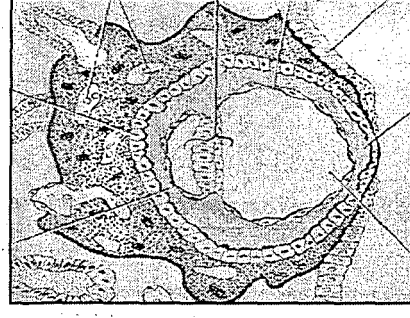
LIF in Embryo Implantation



Day 5/6



Day 7/8

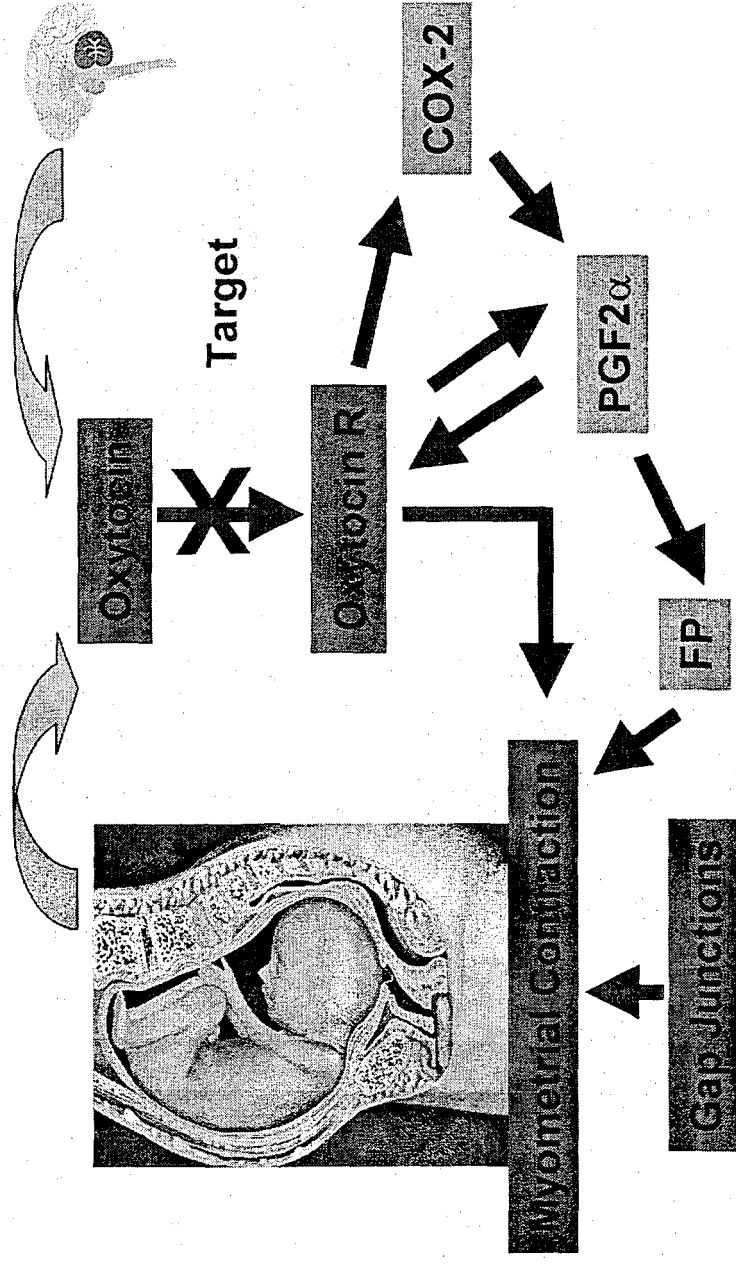


Day 9/10

- LIF is a pleiotropic, glycosylated cytokine; 180 amino acids, 4 main alpha helices, 6 cysteine residues
- Proof of concept study in patients nearing completion - to investigate the potential of LIF administration to overcome embryo implantation failure following IVF
- Formulation development on-going to ensure high uterine levels
- Outcome: mid-2002. If positive Phase 2 (IVF) planned for H2, 02

Pre-Term Labor – Oxytocin receptor antagonist

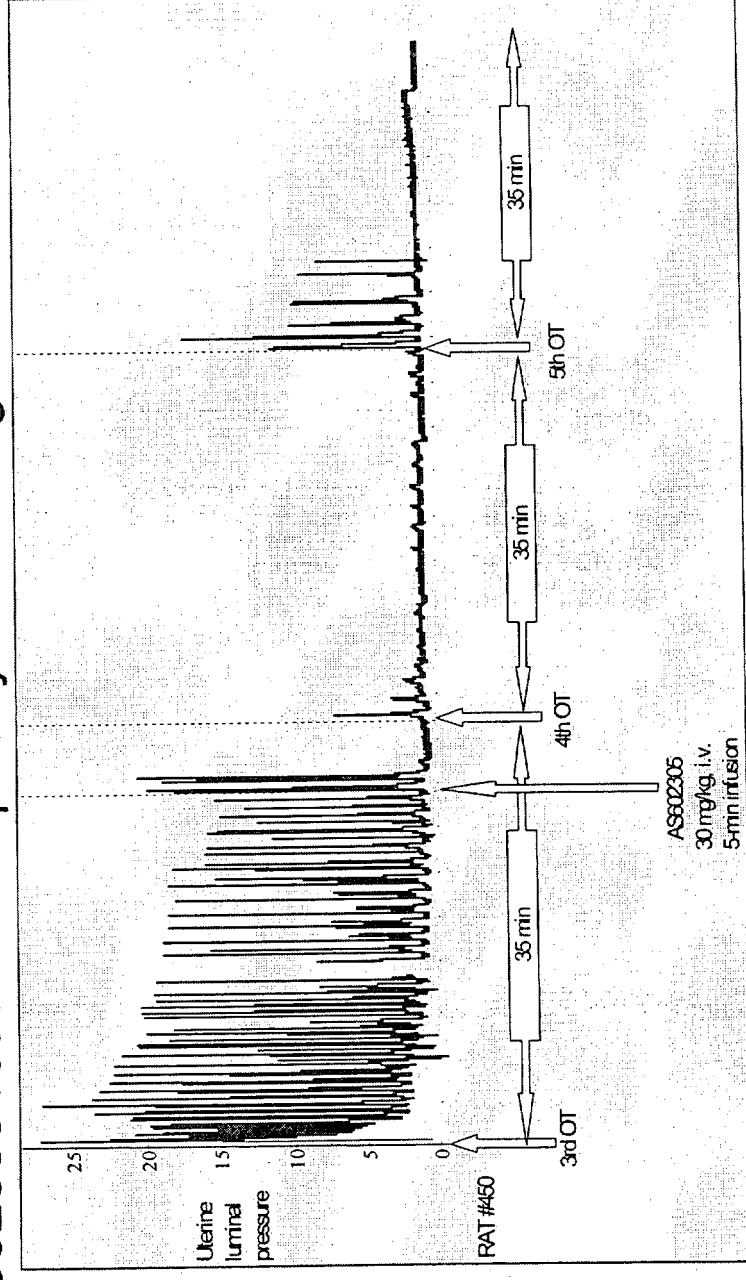
- A potentially novel approach to the treatment of premature labor, currently a largely unmet medical need (5000 deaths/year and costs of \$>6bln/year in US alone)



- In labor, uterine contractions are mediated by the pituitary hormone, oxytocin. A compound which interferes with oxytocin receptor binding should inhibit uterine contractions

Oxytocin receptor antagonist

- Using high throughput screening, we have discovered a small molecule, AS602305, a potent and specific oxytocin receptor antagonist. Pharmacologically characterized (Chollet et al, Annual Meeting Society Gynecologic Investig. 23 March 2002)
- AS602305 reduces frequency and strength of uterine contractions

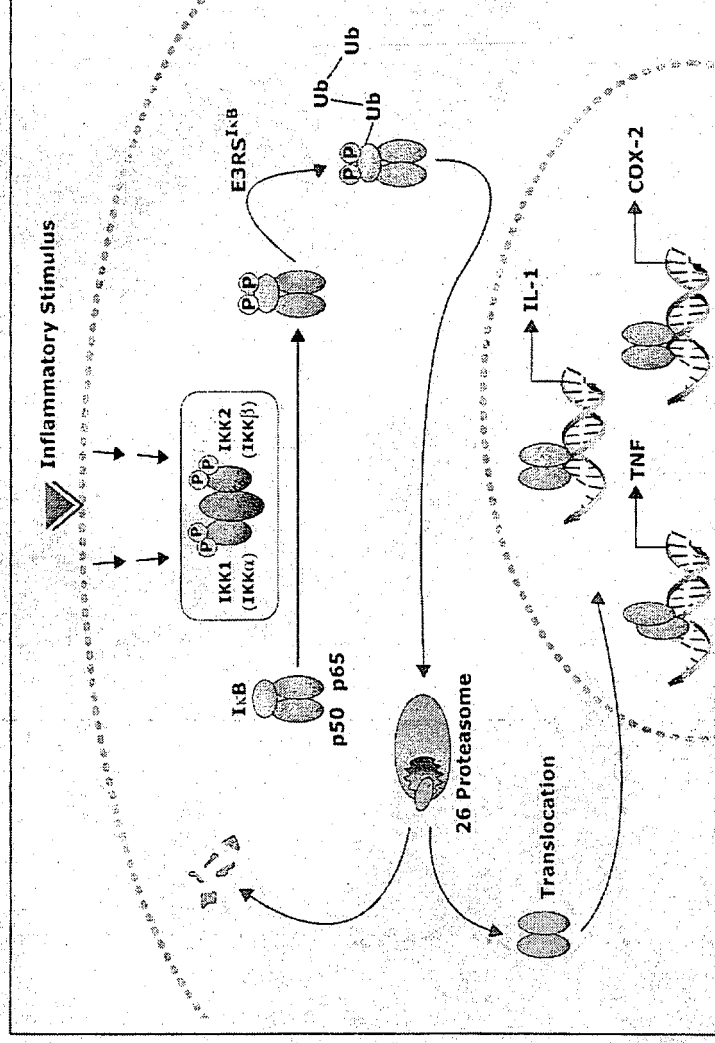


- Pre-clinical development started Q2, 2001. Phase 1: H1 2003

Therapeutic area	Preclinical phase	Phase 1	Phase 2	Phase 3
Reproductive health	oxytocin receptor antagonist • pre-term labour	microencapsulated r-FSH • to reduce the frequency of administration of r-FSH r-LIF • embryo implantation failure type 1 5-alpha reductase inhibitor • hirsutism associated with polycystic ovarian syndrome	r-LH (high dose) • ovulation trigger in female infertility (OI) r-TBP-1 • endometriosis (planned)	r-LH (high dose) • ovulation trigger in female infertility (ART)
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Inflammatory and autoimmune diseases	IKK-2 inhibitor • rheumatoid arthritis JNK inhibitor • ischemic and inflammatory conditions TACI • autoimmune conditions BCMA • autoimmune conditions	r-IL-18 bp • rheumatoid arthritis	r-IFNβ-1a • rheumatoid arthritis r-TBP-1 • rheumatoid arthritis r-TBP-1 • psoriasis and psoriatic arthritis	
Oncology	itirelix nanospheres (GnRH antagonist) • prostate cancer	type 1 5-alpha reductase inhibitor • prostate disease	r-hCG • breast cancer	
Cardiology			r-TBP-1 • cardiac reperfusion injury	

IKK-2 Inhibitor Project

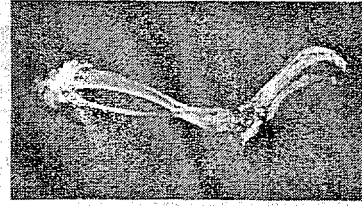
- IKK-2 (I-Kappa B Kinase 2 or IKK-b) demonstrated to be the key player in the activation of the NF- κ B pathway and the subsequent induction of pro-inflammatory mediators



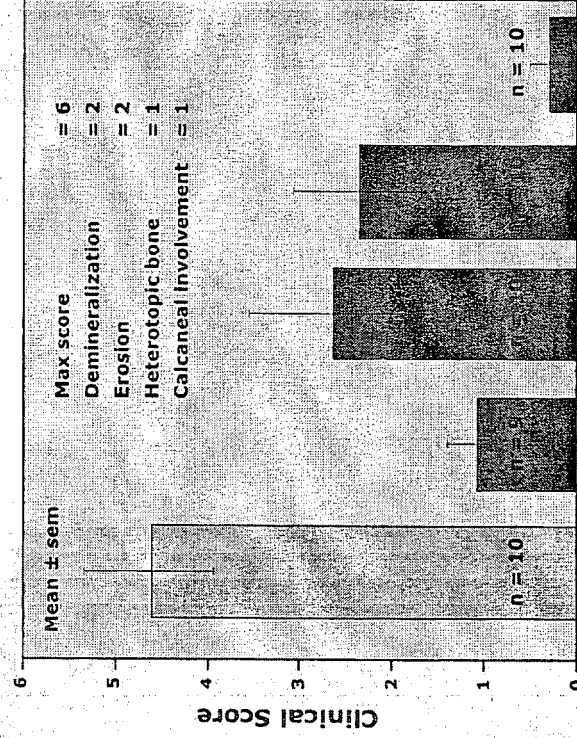
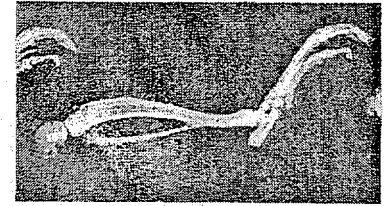
- In collaboration with Celgene's Signal Research Division, using high throughput screening followed by medicinal chemistry, we identified potent, reversible, orally active IKK-2 inhibitors

IKK-2 Inhibitor Project

- Active in the rat AIA* and mouse CIA models of rheumatoid arthritis after oral administration *(American College Rheumatology, 13 Nov 2001)
- Being tested in other animal models of inflammation and various autoimmune diseases. Positive results in EAE
- Entered preclinical development in Q1, 2001
- Planned first administration in humans mid-2003



Control



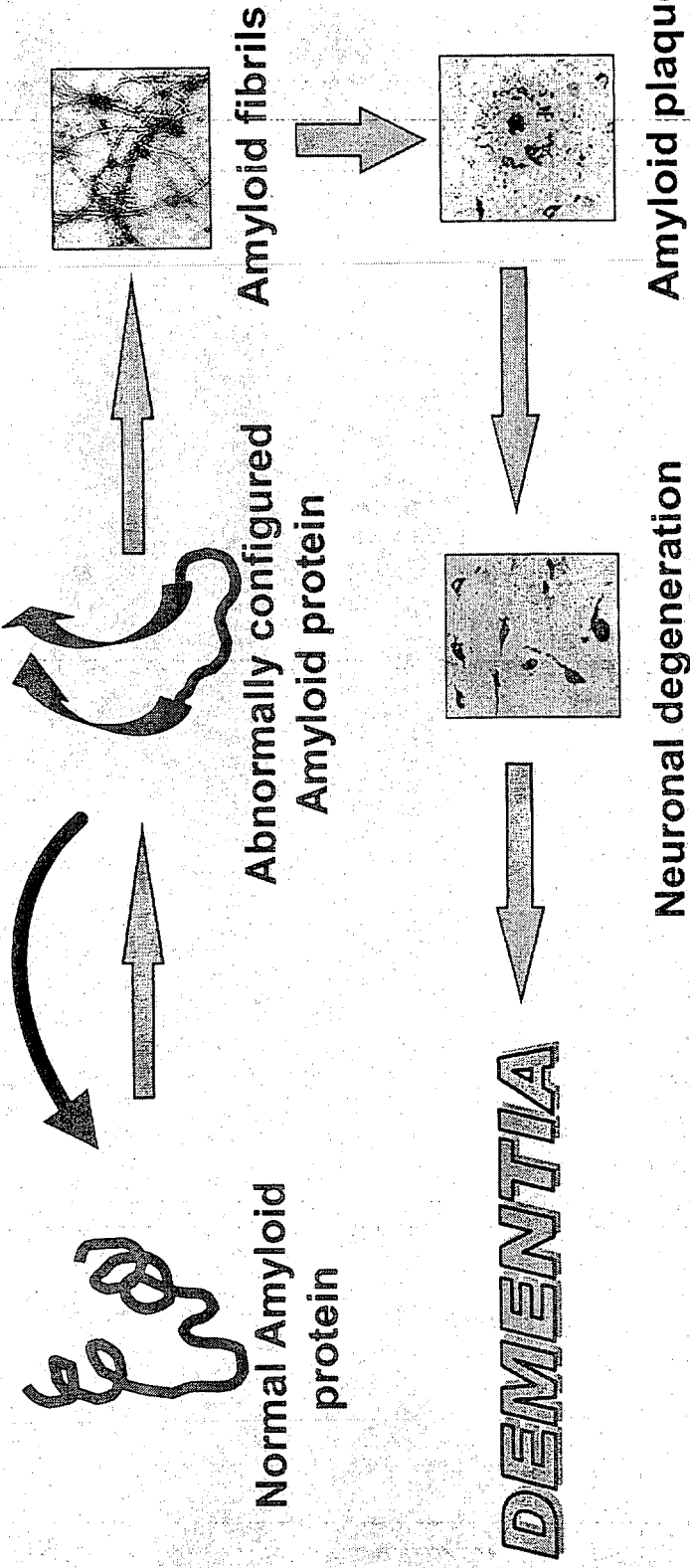
Vehicle Indomethacin AS602868 AS602868 AS602868
2 mpk p.o. 10 mpk p.o. 30 mpk p.o. 100 mpk p.o.

AS602868
100 mg/kg p.o.

Plaques rich in abnormal Amyloid protein may be central to pathology of Alzheimer's

- Alzheimer's is the most common form of dementia in later life
- Misfolding of the amyloid protein is a central event in the development of Alzheimer's disease
- Current drugs have modest effects on symptoms only

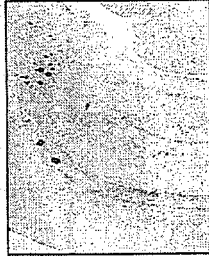
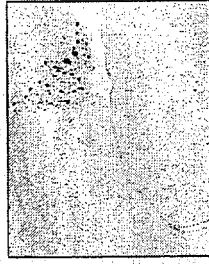
β -sheet breaker peptides



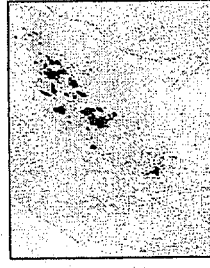
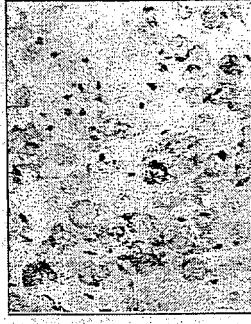
Amyloid beta-sheet breaker peptide:

active in a mouse model of Alzheimer's Disease

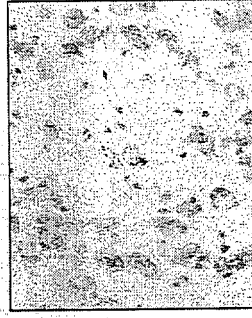
Peptide treated animals



Treated animals



Untreated controls



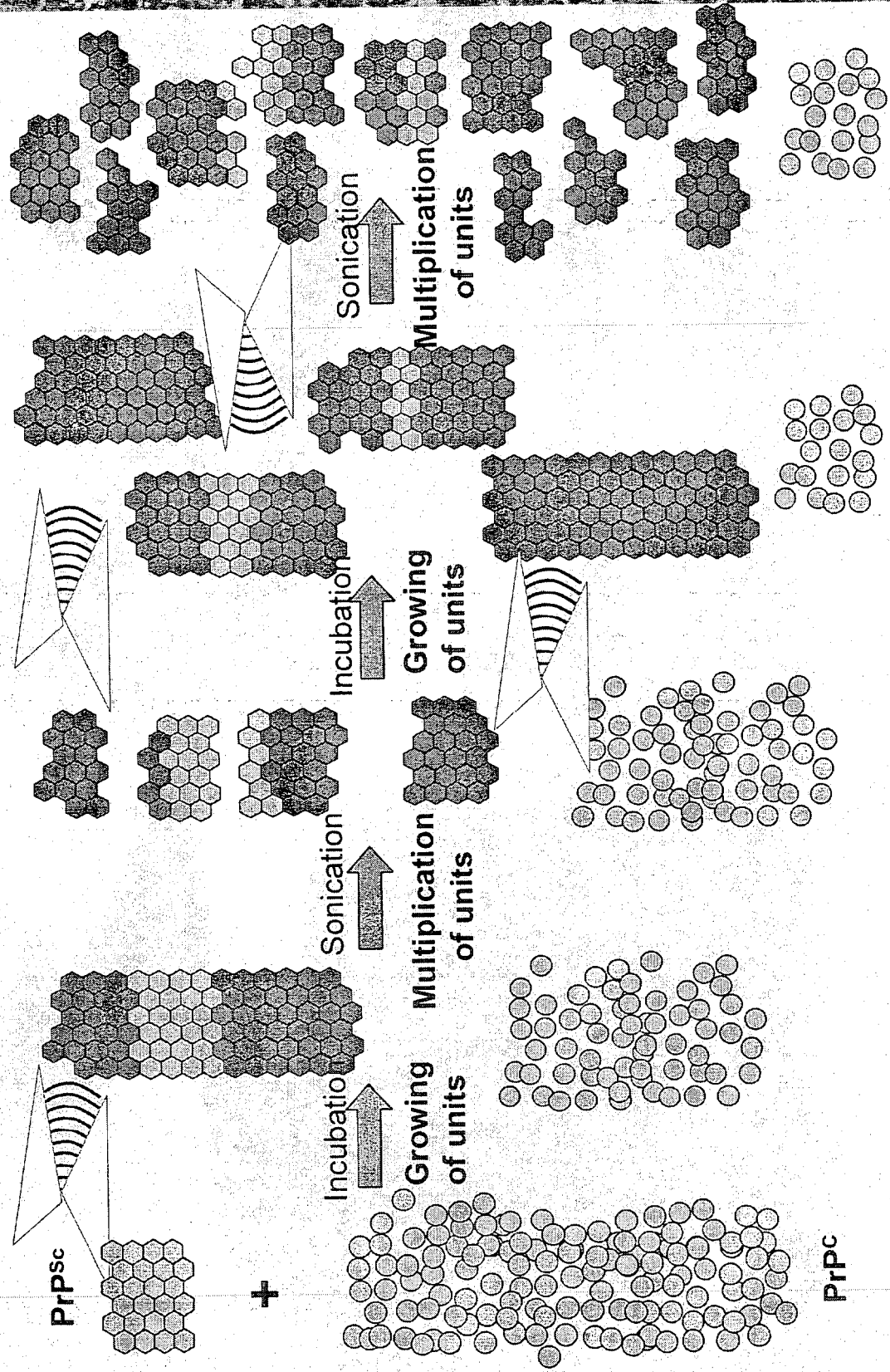
Untreated controls

Treatment decreases
amyloid load

Treatment increases
neuronal survival

- Optimized peptide in preclinical development. Phase 1 planned for early 2003.

Variant Creutzfeldt-Jakob disease: PMCA



Saborio et al, Nature June 2001, 411: 810-813

What are the implications of PMCA?

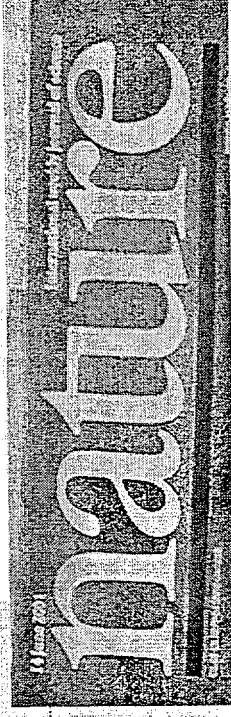
letters to nature

NATURE Vol 411, 14 June 2001

Sensitive detection of pathological prion protein by cyclic amplification of protein misfolding

Gabriela P. Saborio, Bruno Permanne & Claudio Soto

Serono Pharmaceutical Research Institute CH-1228, Geneva, Switzerland



■ Diagnosis

- Earlier and better detection of infected animals to limit entry into the food chain
- Pre-symptomatic diagnosis of living people (currently only in late-stage & confirmed post-mortem)

■ Research

- Helps basic research in CJD and facilitates testing of drug candidates

Therapeutic area	Preclinical phase	Phase 1	Phase 2	Phase 3
Reproductive health	oxytocin receptor antagonist • pre-term labour	microencapsulated r-FSH • to reduce the frequency of administration of r-FSH r-LIF • embryo implantation failure type 1 5-alpha reductase inhibitor • hirsutism associated with polycystic ovarian syndrome	r-LH (high dose) • ovulation trigger in female infertility (OI) r-TBP-1 • endometriosis (planned)	Phase 3 r-LH (high dose) • ovulation trigger in female infertility (ART)
Neurology	breaker peptide • Alzheimer's disease chemokine inhibitor • multiple sclerosis IKK-2 inhibitor • multiple sclerosis JNK inhibitor • central nervous system disorders	IFNAR-2 • to increase the half life of IFN β -1a PEG r-IFN β -1a • to increase the half life of IFN β -1a	r-IFN β -1a • Guillain-Barré syndrome	
Growth and metabolism	PEG GHRF • growth retardation		r-GH • HARS/lipodystrophy	
Gastroenterology		r-IL-18 bp • Crohn's disease	r-IFN β -1a • Crohn's disease r-IFN β -1a • ulcerative colitis r-TBP-1 • Crohn's disease	r-GH • short bowel syndrome
Inflammatory and autoimmune diseases	IKK-2 inhibitor • rheumatoid arthritis JNK inhibitor • ischemic and inflammatory conditions TACI • autoimmune conditions BCMA • autoimmune conditions	r-IL-18 bp • rheumatoid arthritis	r-IFN β -1a • rheumatoid arthritis r-TBP-1 • rheumatoid arthritis r-TBP-1 • psoriasis and psoriatic arthritis	
Oncology	itirelix nanospheres (GnRH antagonist) • prostate cancer	type 1 5-alpha reductase inhibitor • prostate disease	r-hCG • breast cancer	
Cardiology			r-TBP-1 • cardiac reperfusion injury	

TBP-1 (oncept) in Crohn's Disease

DDW, Atlanta, May 21, 2001

Recombinant soluble p55 TNF receptor induces remission, is non-immunogenic and is well tolerated in active Crohn's disease: results of a randomized pilot trial

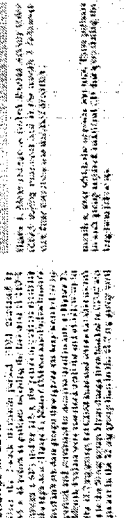
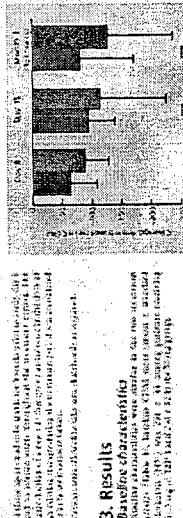
Paul Rutgeerts¹, Lisbeth Lemmens¹, Ger Van Assche¹, Maja Noman¹, Isabelle Borghini-Fuhrer², René Gansdorp²
¹University Hospital Gasthuisberg, Leuven, Belgium; ²Serono International SA, Geneva, Switzerland

1. Introduction
 Active Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) characterized by recurrent episodes of inflammation and ulceration of the gastrointestinal tract. The disease is characterized by a chronic relapsing and remitting course. The pathogenesis of CD is still unknown, but it is thought to be a multifactorial disease involving genetic, environmental, and immunological factors. The mainstay of treatment is corticosteroids and immunosuppressants, but these drugs are associated with significant side effects. Therefore, the development of new therapeutic strategies is a high priority.

2. Methods
 The study was a randomized, double-blind, placebo-controlled trial. The study population consisted of 20 patients with active CD, defined as a Crohn's Disease Activity Index (CDAI) score of 150 or higher. The patients were randomized to receive either TBP-1 (n=10) or placebo (n=10). The primary endpoint was the proportion of patients achieving clinical remission (CDAI score < 150) at week 12. Secondary endpoints included the proportion of patients achieving partial remission (CDAI score < 250) and the proportion of patients tolerating the treatment without significant side effects.

3. Results
 The results of the study are summarized in Table 1. At baseline, the mean CDAI score was 180. At week 12, the proportion of patients achieving clinical remission was significantly higher in the TBP-1 group (60%) compared to the placebo group (20%). The proportion of patients achieving partial remission was also significantly higher in the TBP-1 group (80%) compared to the placebo group (40%). The proportion of patients tolerating the treatment without significant side effects was similar in both groups (80%).

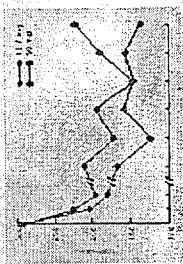
4. Conclusions
 The results of this study demonstrate that TBP-1 is an effective and well-tolerated treatment for active Crohn's disease. TBP-1 induces clinical remission and partial remission in a significantly higher proportion of patients compared to placebo. These findings suggest that TBP-1 may be a promising new therapeutic strategy for the treatment of active Crohn's disease.



Parameter	TBP-1 (n=10)	Placebo (n=10)
Mean CDAI score at baseline	180	180
Mean CDAI score at week 12	80	140
Proportion of patients achieving clinical remission (CDAI < 150)	60%	20%
Proportion of patients achieving partial remission (CDAI < 250)	80%	40%
Proportion of patients tolerating treatment without significant side effects	80%	80%

Table 1. Clinical remission and partial remission at week 12

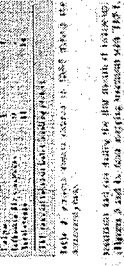
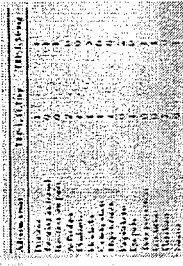
Group	n	Clinical remission (CDAI < 150)	Partial remission (CDAI < 250)
TBP-1	10	60%	80%
Placebo	10	20%	40%



Parameter	TBP-1 (n=10)	Placebo (n=10)
Mean CDAI score at baseline	180	180
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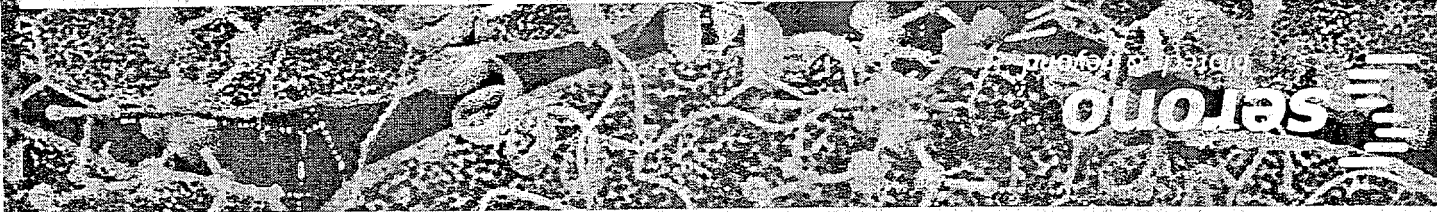
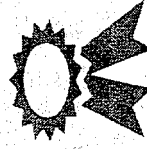
Abstract
 Objective: To evaluate the efficacy and safety of TBP-1, a recombinant soluble p55 TNF receptor, in the treatment of active Crohn's disease. Design: Randomized, double-blind, placebo-controlled trial. Setting: University Hospital Gasthuisberg, Leuven, Belgium. Patients: 20 patients with active Crohn's disease, defined as a Crohn's Disease Activity Index (CDAI) score of 150 or higher. Interventions: TBP-1 (n=10) or placebo (n=10). Main Results: The proportion of patients achieving clinical remission (CDAI score < 150) at week 12 was significantly higher in the TBP-1 group (60%) compared to the placebo group (20%). The proportion of patients achieving partial remission (CDAI score < 250) was also significantly higher in the TBP-1 group (80%) compared to the placebo group (40%). The proportion of patients tolerating the treatment without significant side effects was similar in both groups (80%).

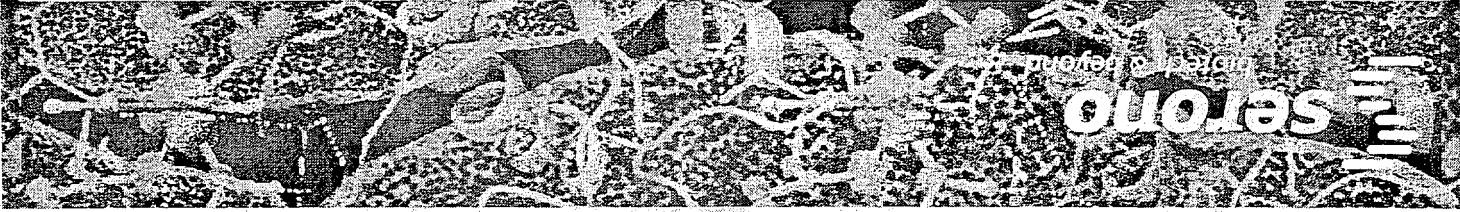
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 The results of this study demonstrate that TBP-1 is an effective and well-tolerated treatment for active Crohn's disease. TBP-1 induces clinical remission and partial remission in a significantly higher proportion of patients compared to placebo. These findings suggest that TBP-1 may be a promising new therapeutic strategy for the treatment of active Crohn's disease.

References
 1. Rutgeerts P, Lemmens L, Van Assche G, Noman M, Borghini-Fuhrer I, Gansdorp R. Recombinant soluble p55 TNF receptor induces remission in active Crohn's disease: results of a randomized pilot trial. *Gastroenterology* 2001;120:1050-1058.

DDW Atlanta 2001

« Poster of Distinction » Award





Crohn's Disease

■ TBP-1

- Multicenter, DBPC, dose-finding (10, 25, 35, or 50 mg TIW, SC, onercept)
- 200 patients
- 30-35 centers in Australia, Belgium, Canada, Denmark, Germany, Hong Kong, Israel, Singapore, Spain, Switzerland, The Netherlands, US, Yugoslavia
- Study initiated Q4, 2001. Outcome expected mid-2003

■ IFN beta-1a

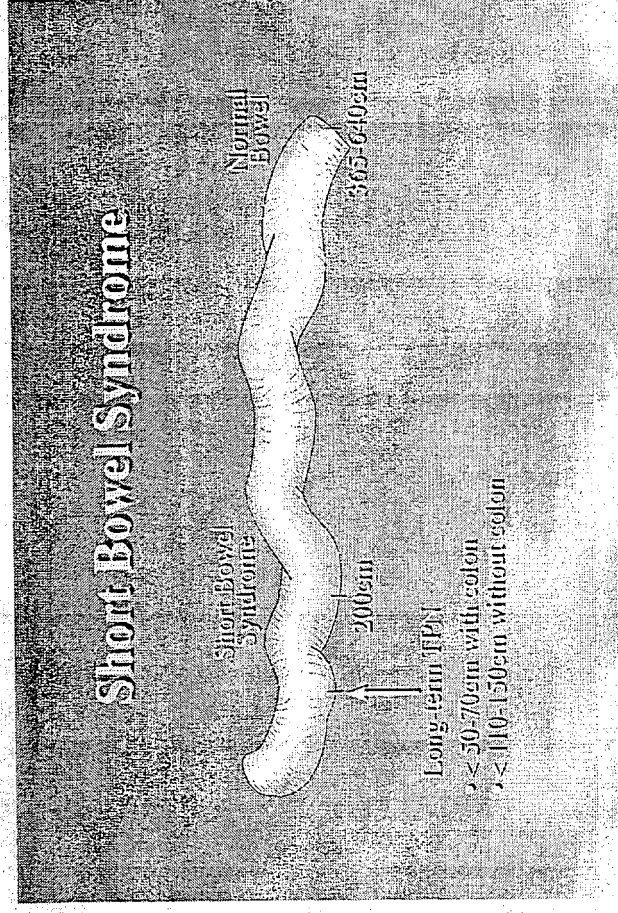
- Multicenter, DBPC, dose-finding (44 mcg BIW, 44 mcg TIW or 66 mcg TIW, SC, IFN beta-1a). Long-term follow-up
- 192 patients
- 35-40 centers in Belgium, Canada, Germany, Italy, Norway, Sweden, UK, USA, Yugoslavia
- Study initiated Q3, 2001. Outcome expected Q3, 2003

IFN beta-1a in Ulcerative Colitis

- Multicenter, double-blind, placebo-controlled, dose-finding study (44 or 66 mcg TIW, SC, IFN beta-1a)
- 168 patients
- 35-40 centers in Belgium, Denmark, Germany, Israel, Norway, Singapore, Spain, Sweden, Switzerland, Taiwan, Thailand, Netherlands, UK, US, Yugoslavia
- Long-term follow-up study for patients who completed the previous double-blind study
- Study initiated Q3, 2001. Enrolment on-going. Outcome expected Q3, 2003

rGH in Short Bowel Syndrome (SBS)

- Double-blind, placebo-controlled trial
- To investigate the effect of Serostim in reducing the requirements for iv parenteral nutrition (IPN) in SBS
- 45 patients with short bowel syndrome dependent on IPN
- Randomized to Serostim, glutamine or the combination
- Duration 2 weeks baseline; 4 weeks treatment.
- Single daily sc injection 0.1 mg/kg (maximum 8.0 mg/day)
- Change in weekly IPN volume from baseline to study week 6
- Outcome expected Q3, 2002



HARS

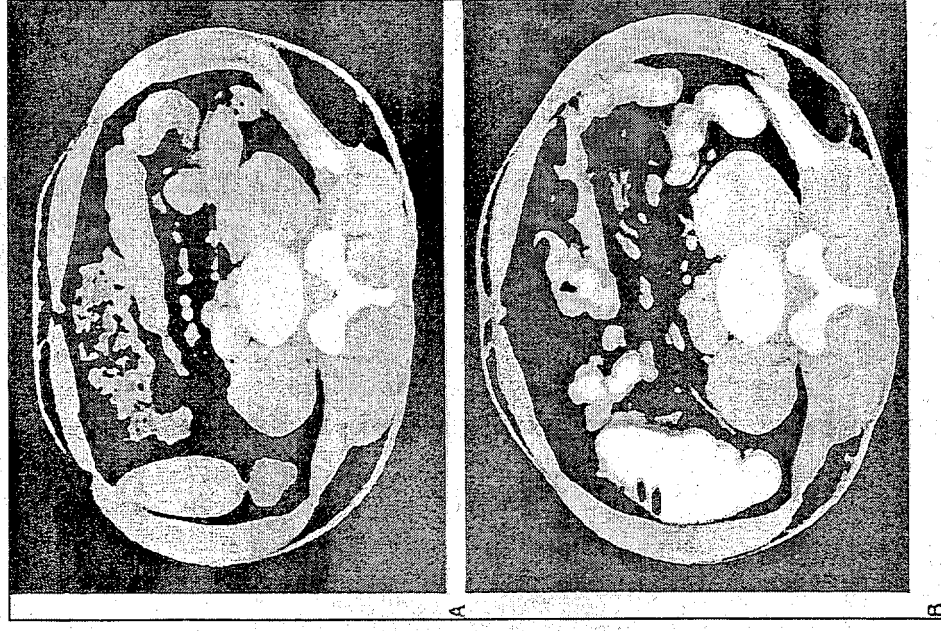
■ HIV-associated **Adipose Redistribution Syndrome**

- Abnormal adipose tissue accumulation
- With or without adipose tissue depletion
- With or without metabolic complications

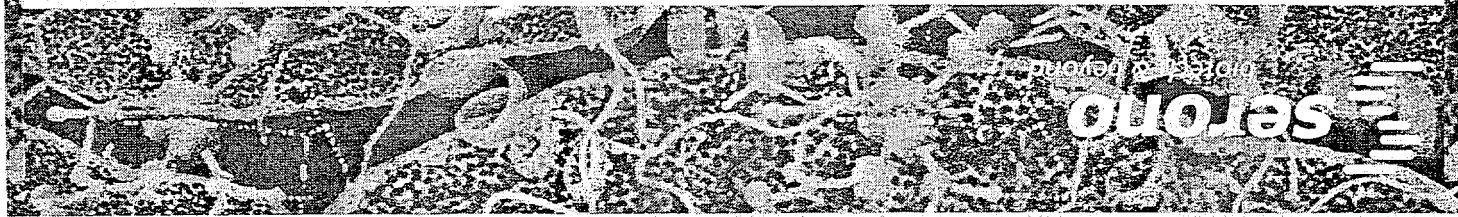
■ Appearance is distressing to patients, stigmatizing & ↓QOL

■ A cause of poor antiretroviral adherence

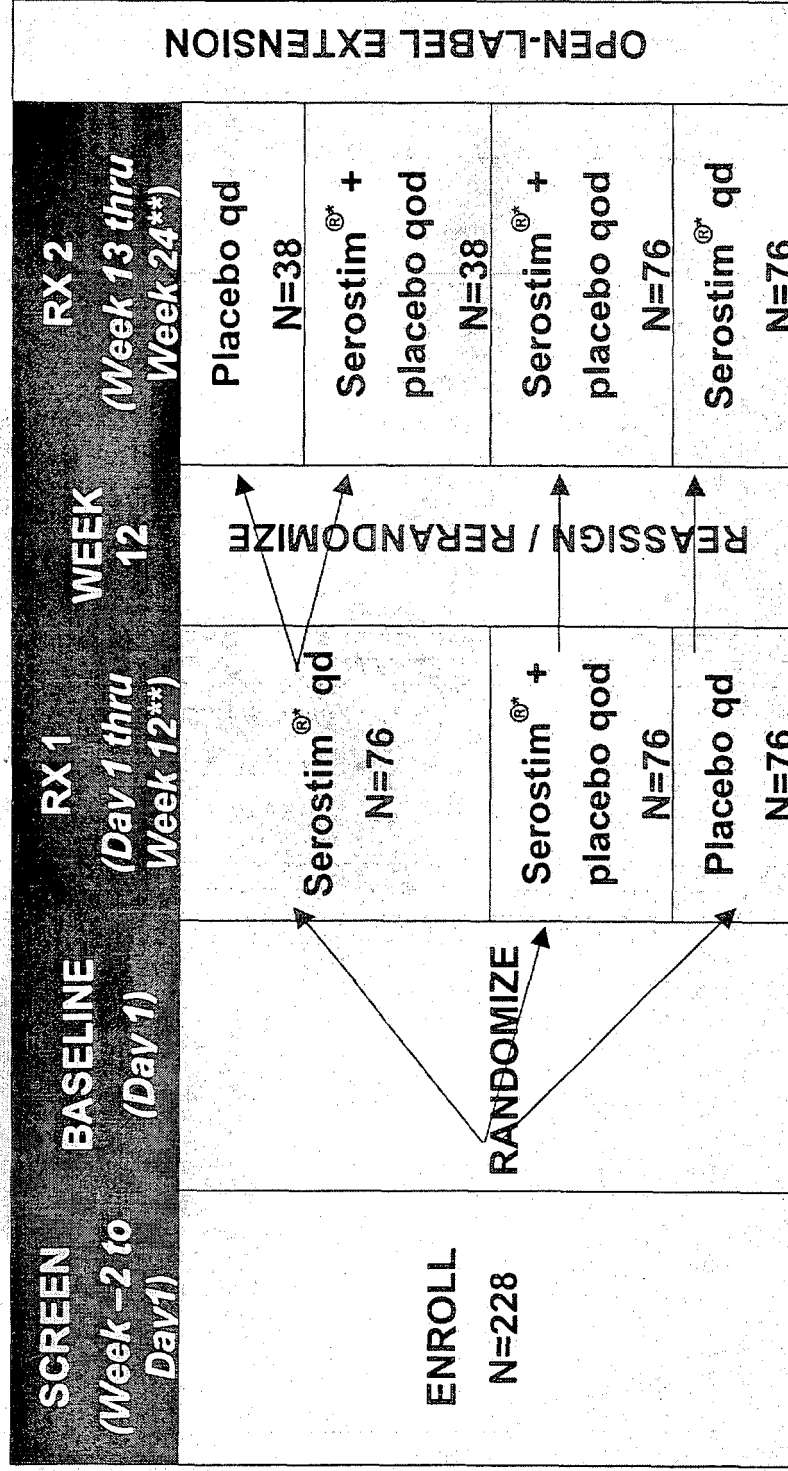
■ Excess visceral fat is an independent cardiovascular risk factor



Abdominal CT scans before and 5 months after starting indinavir



Serostim in HARS/ Lipodystrophy – Phase 2/3 study design



*Maximum dose is 4mg

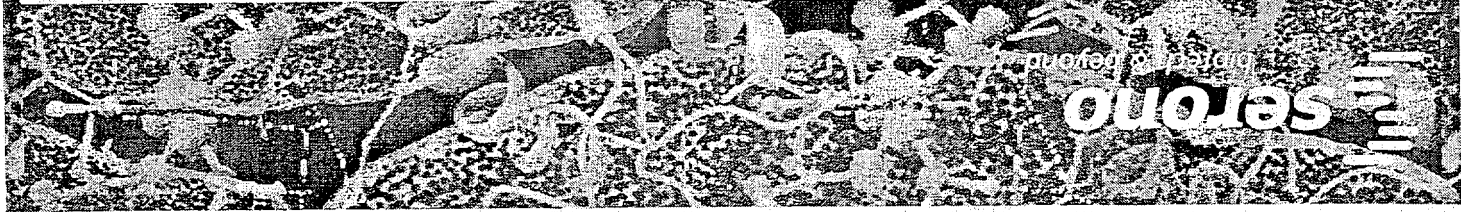
**Interim visits are scheduled at Weeks 2, 4, 14 and 16

- Efficacy measures: DEXA, CT scans, measurements, QOL
- All patients on therapy. Outcome Q3, 2002

Therapeutic area	Preclinical phase	Phase 1	Phase 2	Phase 3
Reproductive health	oxytocin receptor antagonist • pre-term labour	microencapsulated r-FSH • to reduce the frequency of administration of r-FSH r-LIF • embryo implantation failure type 1 5-alpha reductase inhibitor • hirsutism associated with polycystic ovarian syndrome	r-LH (high dose) • ovulation trigger in female infertility (OI) r-TBP-1 • endometriosis (planned)	Phase 3 • r-LH (high dose) • ovulation trigger in female infertility (ART)
Neurology	breaker peptide • Alzheimer's disease chemokine inhibitor • multiple sclerosis IKK-2 inhibitor • multiple sclerosis JNK inhibitor • central nervous system disorders	IFNAR 2 • to increase the half life of IFNβ-1a PEG r-IFNβ-1a • to increase the half life of IFNβ-1a	r-IFNβ-1a • Guillain-Barré syndrome	
Growth and metabolism	PEG GHRF • growth retardation		r-GH • HARS/Lipodystrophy	
Gastroenterology		r-IL-18 bp • Crohn's disease	r-IFNβ-1a • Crohn's disease r-IFNβ-1a • ulcerative colitis r-TBP-1 • Crohn's disease r-IFNβ-1a • chronic hepatitis C – a genotypic subgroup of patients	r-GH • short bowel syndrome
Inflammatory and autoimmune diseases	IKK-2 inhibitor • rheumatoid arthritis JNK inhibitor • ischemic and inflammatory conditions TAGI • autoimmune conditions BCMA • autoimmune conditions	r-IL-18 bp • rheumatoid arthritis	r-IFNβ-1a • rheumatoid arthritis r-TBP-1 • rheumatoid arthritis r-TBP-1 • psoriasis and psoriatic arthritis	
Oncology	itirelix nanospheres (GnRH antagonist) • prostate cancer	type 1 5-alpha reductase inhibitor • prostate disease	r-hCG • breast cancer	
Cardiology			r-TBP-1 • cardiac reperfusion injury	

TBP-1 in Psoriasis and Psoriatic arthritis

- Multicenter, DBPC study
- 126 patients with at least a 6 month history of disease and having failed a recognised psoriasis treatment/ at least 1 DMARD
- Study sites in North America, Canada, Europe and Far East
- Patients randomized to one of three treatment groups:
 - 50 mg r-hTBP-1 sc, three times per week
 - 100 mg r-hTBP-1 sc, three times per week
 - Matching placebo sc, three times per week
- Primary endpoint (week 12) :
 - Psoriasis - % of PASI responders
 - Psoriatic Arthritis - % of PsARC responders
- Outcome H1 2003



Phase II studies in Rheumatoid Arthritis

■ IFN beta-1a

- Multicenter, DBPC dose finding in poor responders to methotrexate (MTX)
- 209 patients on MTX randomized to one of three treatment groups: 2.2mcg, 44mcg or placebo, sc, TIW
- Endpoints: radiological progression of disease, improvement according to ACR criteria
- Outcome expected mid-2002

■ TBP-1 (onercept)

- Multicenter, DBPC dose finding
- 132 patients randomized to one of five treatment groups: TBP-1 at 10mg, 25mg, 50mg TIW, 50mg BIW or placebo
- Endpoints: improvement according to ACR criteria
- Outcome expected Q3, 2002

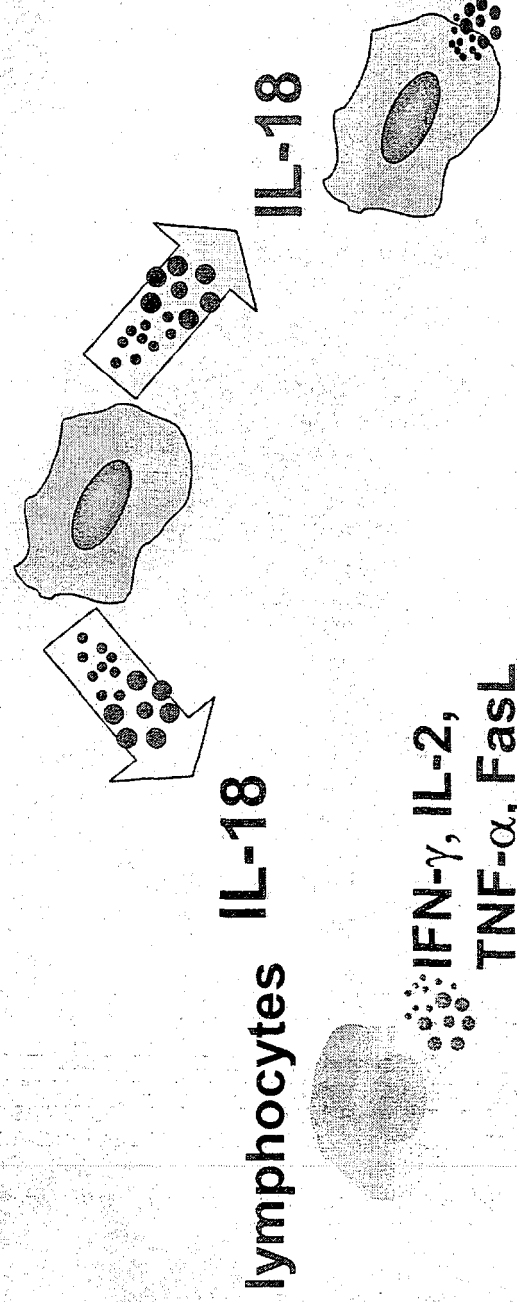
United & beyond

serono

Immunology

IL-18 binding protein

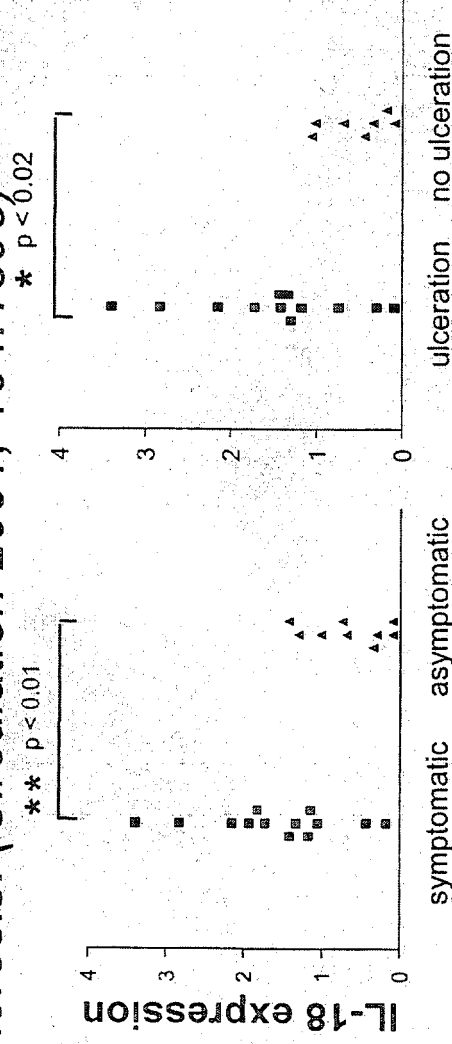
- IL-18bp is a natural circulating protein which binds and neutralizes IL-18



- Possible indication: Rheumatoid arthritis - IL-18bp decreases disease severity & cartilage erosion (*J. Clin. Invest* 2001; 108: 1825)
- Possible indication: Crohn's disease - IL-18bp decreases severity and mucosal ulceration (*Gastroenterology* 2001; 121: 1372)

IL-18 binding protein

- Possible indication: Atherosclerosis. Raised levels of IL-18 in atherosclerosis. (*Circulation* 2001; 104:1598)



- IL-18bp inhibits plaque formation in disease models (*Circ Res.* 2001; 89: 41)

Control



IL-18bp



- Status: Phase 1 (announced Q1, 2002)

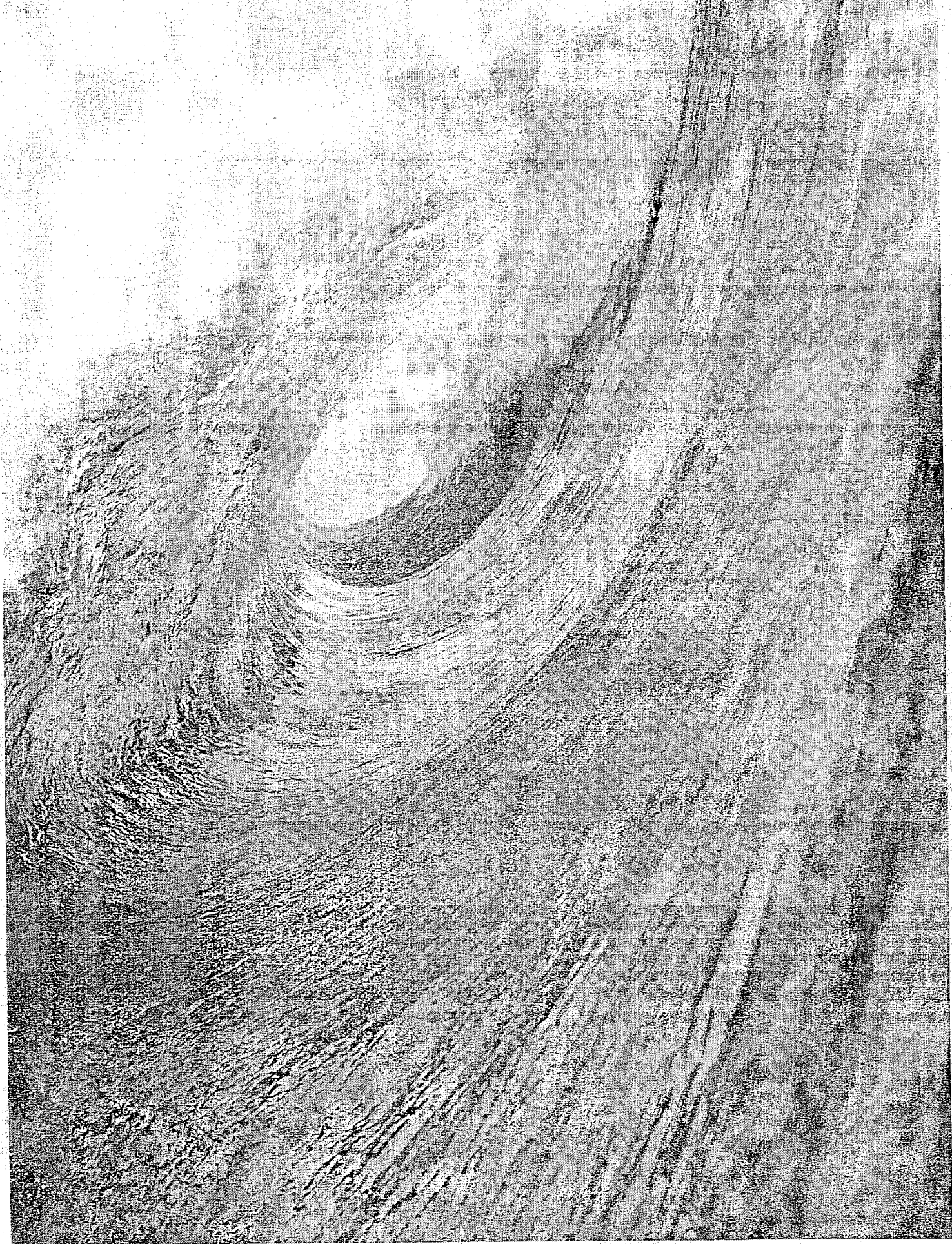
2002 Newsflow

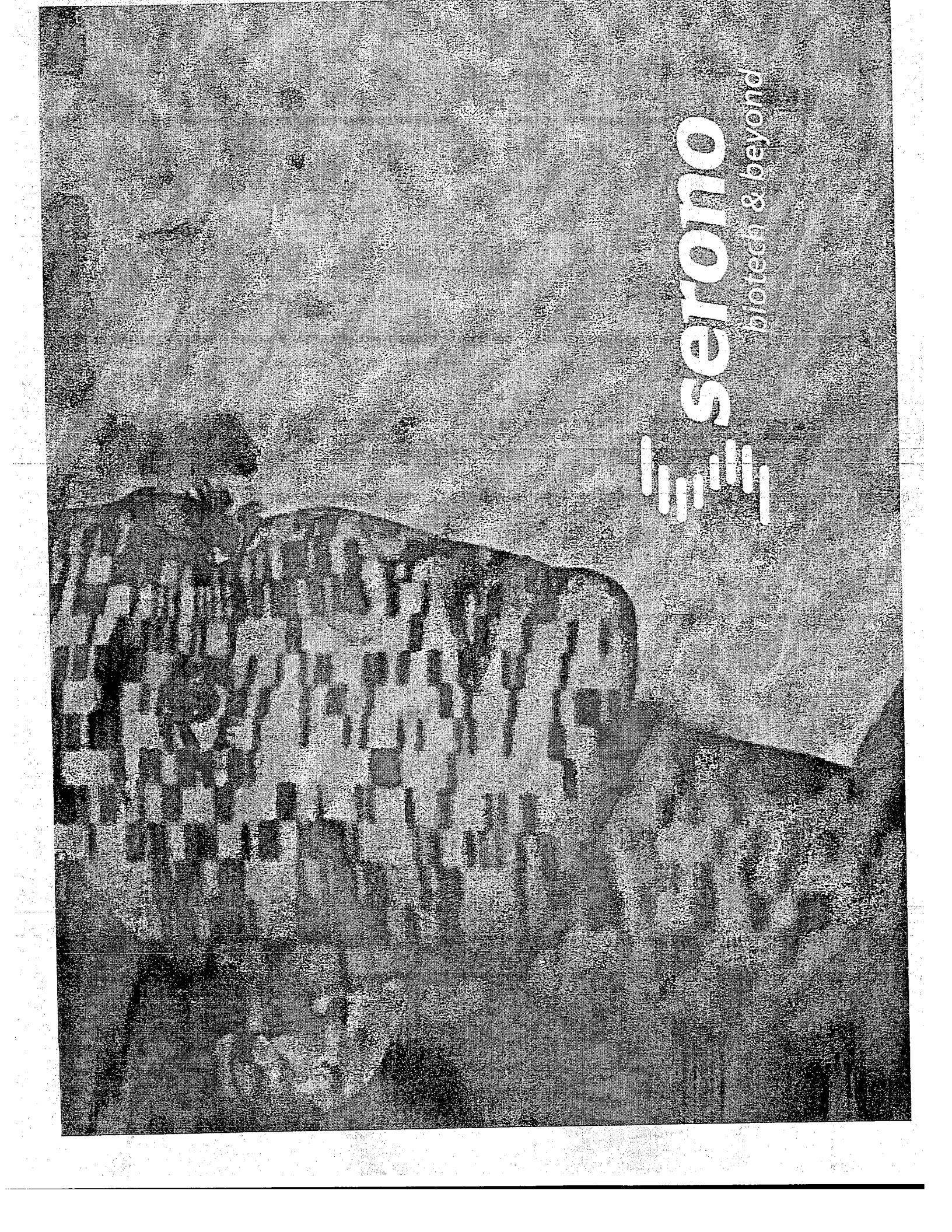
Event	Announced	H1	H2
Rebif FDA approval	✓		
Rebif US launch	✓		
Crinone relaunch (US)	✓		
Outcome of IFN-beta in RA (phase 2)		✓	
Outcome of TBP in cardiac reperfusion (phase 2)		✓	
Outcome of LIF (phase 1)		✓	
FDA decision on Luveris NDA			✓
Outcome of TBP-1 in RA (phase 2)			✓
Outcome of IFNAR-2 (phase 1)			✓
Outcome of PEG-IFN-beta (phase 1)			✓
Outcome of HCG in breast cancer (phase 2)			✓
Outcome of Serostim in AIDS wasting study (9037)			✓
Outcome of Serostim in HARS (phase 2/3)			✓
Outcome of GH in short bowel (phase 3)			✓
Start of FSH microsphere (phase 2)			✓

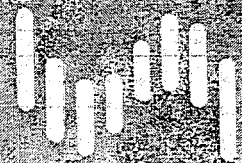
Pharmacia & Upjohn

serono







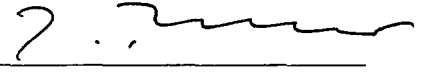
 **serono**
biotech & beyond

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SERONO S.A.
a Swiss corporation
(Registrant)

March 25, 2002

By: 

Name: Jacques Theurillat

Title: Chief Financial Officer