

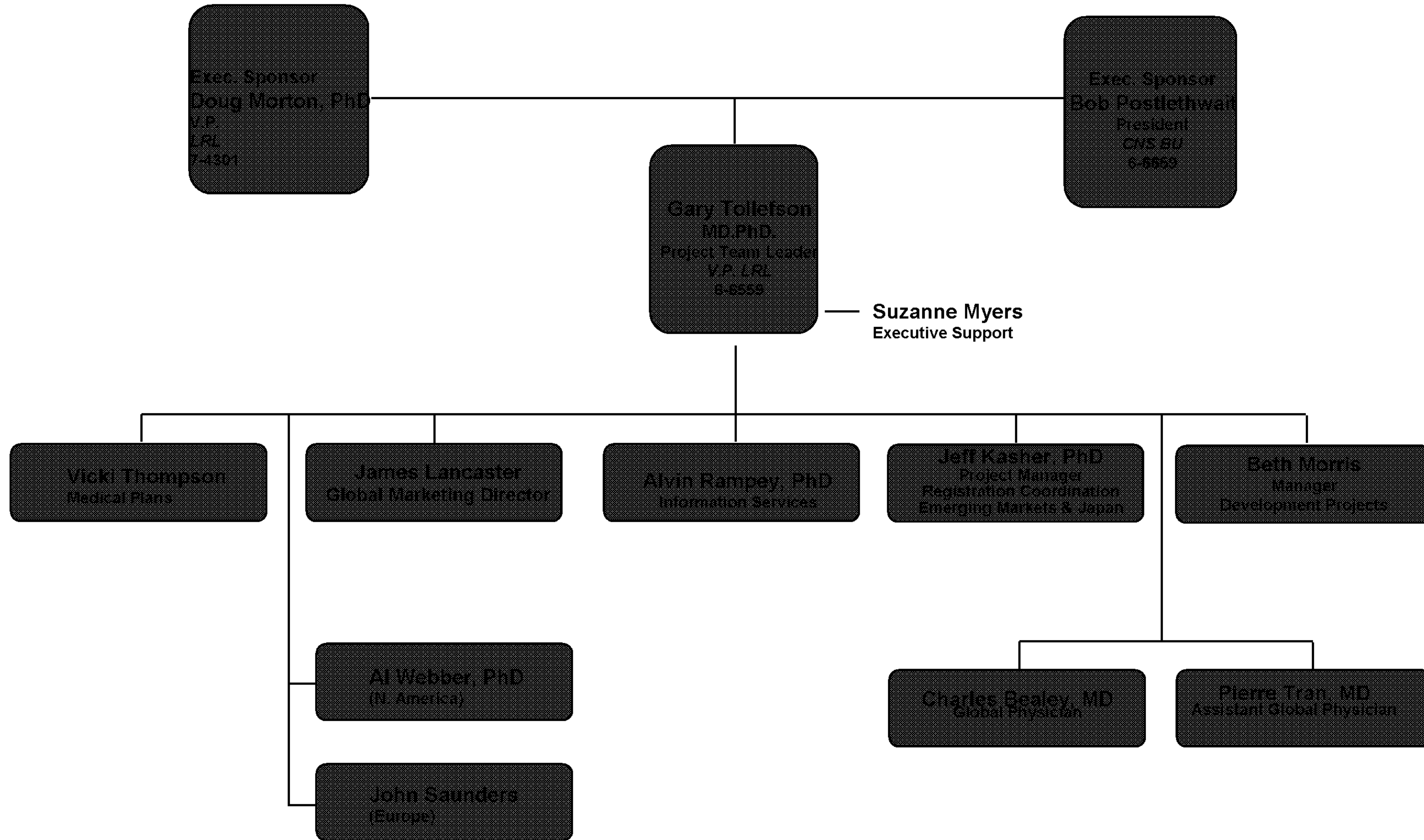
# **Zyprexa - A Major Step Toward A Health Care Solution For Psychosis**

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July 20, 1995



# Olanzapine Core Impact Team



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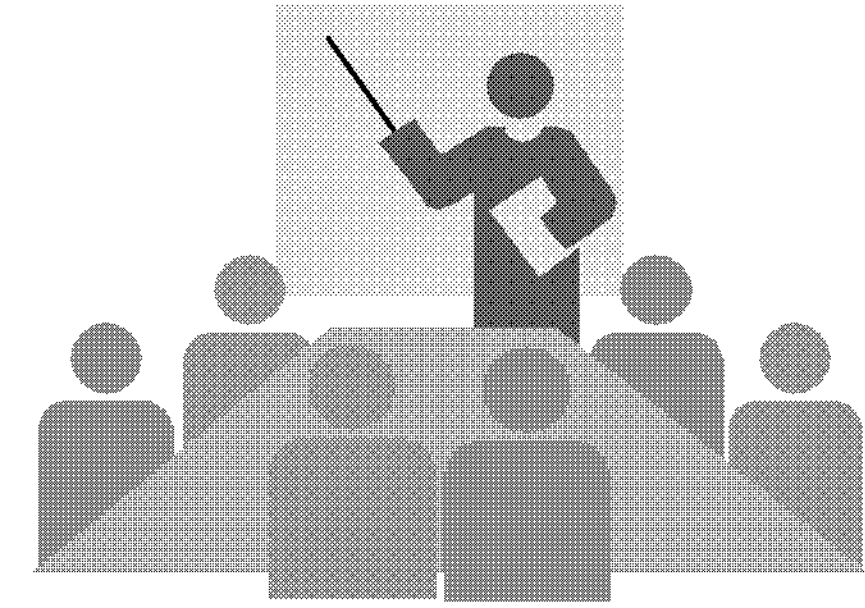


# Presentation Outline

- I. Overview Module
- II. Concept of the HWT "Lifecycle" and a "Deliverables Matrix"
- III. Phased Deliverables by HWT Components
- IV. HWT Learning Points
- V. Resource Requirements
- VI. Issues
- VII. Conclusions
- VIII. Question Wrap-Up

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## **Presentation Objectives**

- **The customer**
- **Recognition of the strategic importance of Zyprex to Lilly shareholders**
- **Road to major market submissions**
- **From submission to launch (and beyond)**
- **HWT approach enhanced both quality and speed; efficiency, and employee satisfaction/ownership**

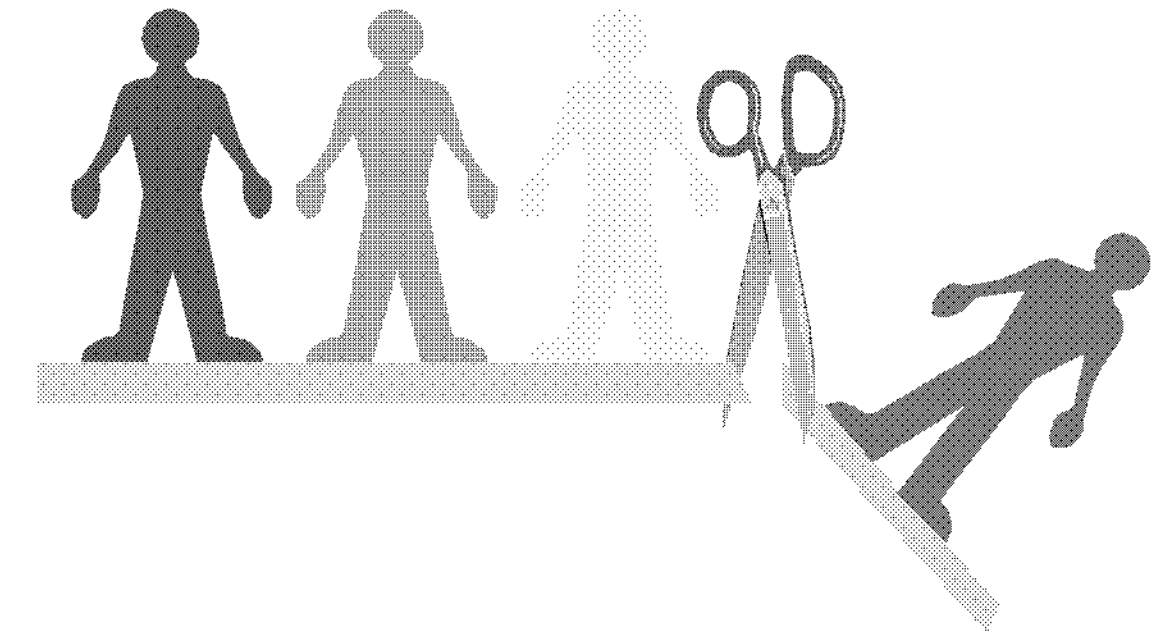
GDT/dle

**[approved for 2 category one credits by the ZMA]**

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# Schizophrenia



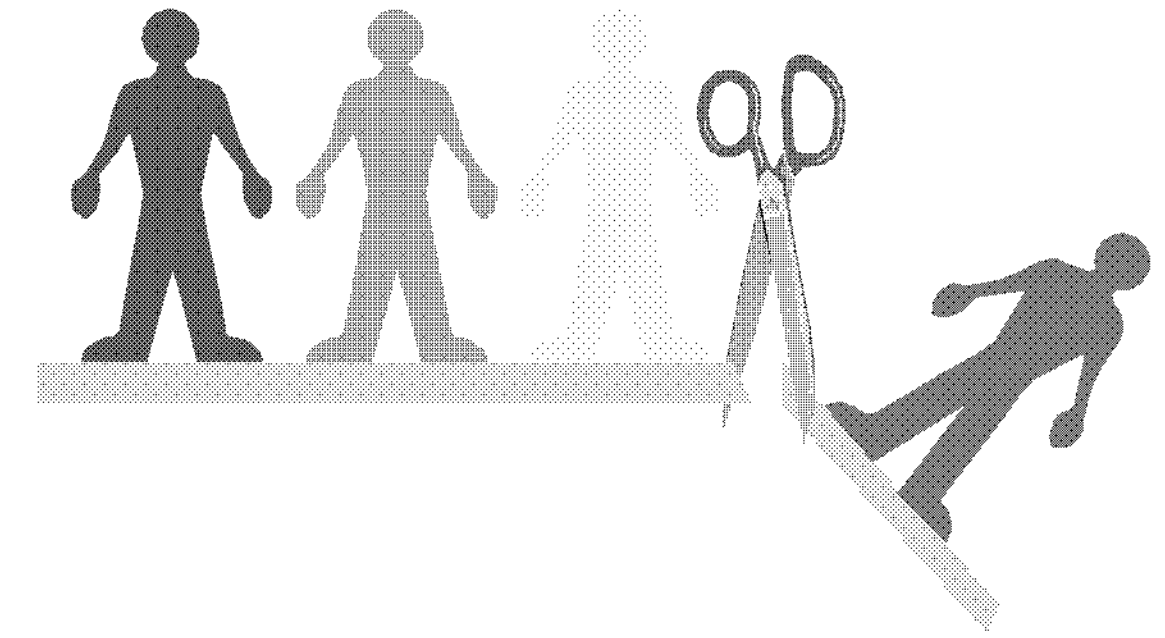
**“In schizophrenia, all of the normal mental processes - sensation, perception, language, emotion, interpersonal relationships - appear to go complete awry. People with the disorder lose touch with the real world. They hear voices that are not there, speak a language that does not exist, laugh for no reason, or sit motionless for hours on end. *The entire human personality is laid waste, and the psychological and social building blocks of every day life are crushed, often beyond recognition.*”**

**Natl. Advisory Mental Health Council - 1988**

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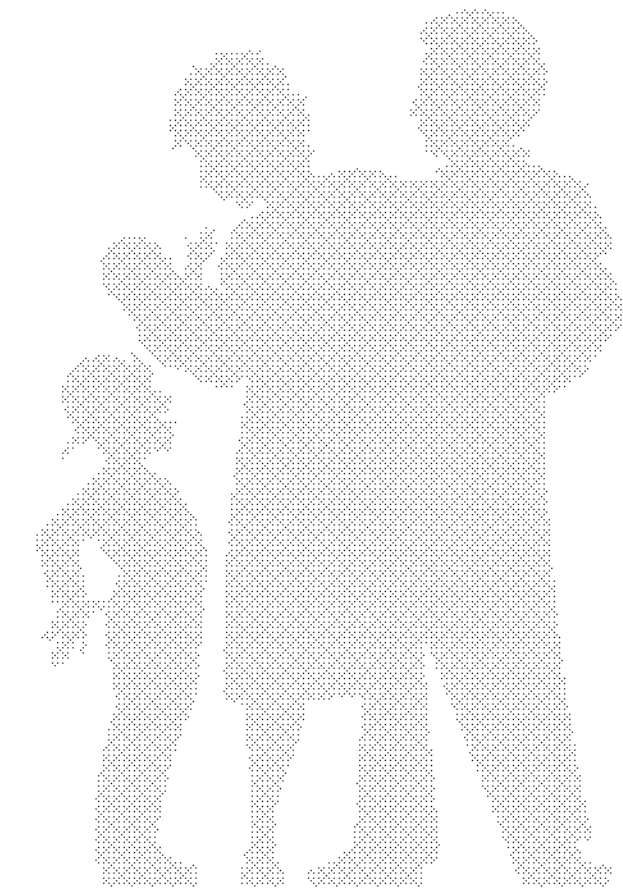
# Schizophrenia



## I. Background

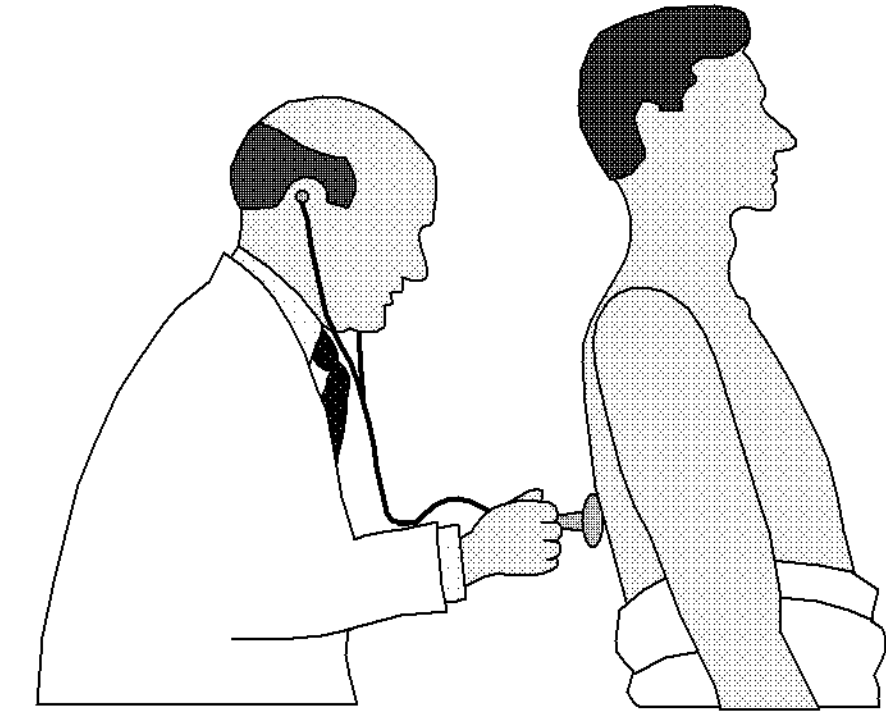
- worldwide prevalence - 1 percent
- neurochemistry - disturbance of select regional 5-HT and/or DA activity - 1<sup>0</sup> or 2<sup>0</sup>??
- pathophysiology - “intrinsic wiring abnormality”
- onset - mid-teens to young adulthood
- course - chronic in more than half of victims

# Schizophrenia



- **Assessing the burden**
  - **370,000 years of lost productivity for U.S. men**
  - **accounts for nearly 3% of total health care expenditure**
    - » **ex. half the cost of MI annually despite 1/12th as common**
  - **per patient costs - exceed \$20,000 per year**
  - **approximately 10% of the totally and permanently disabled in the U.S. are people with schizophrenia**

# Schizophrenia



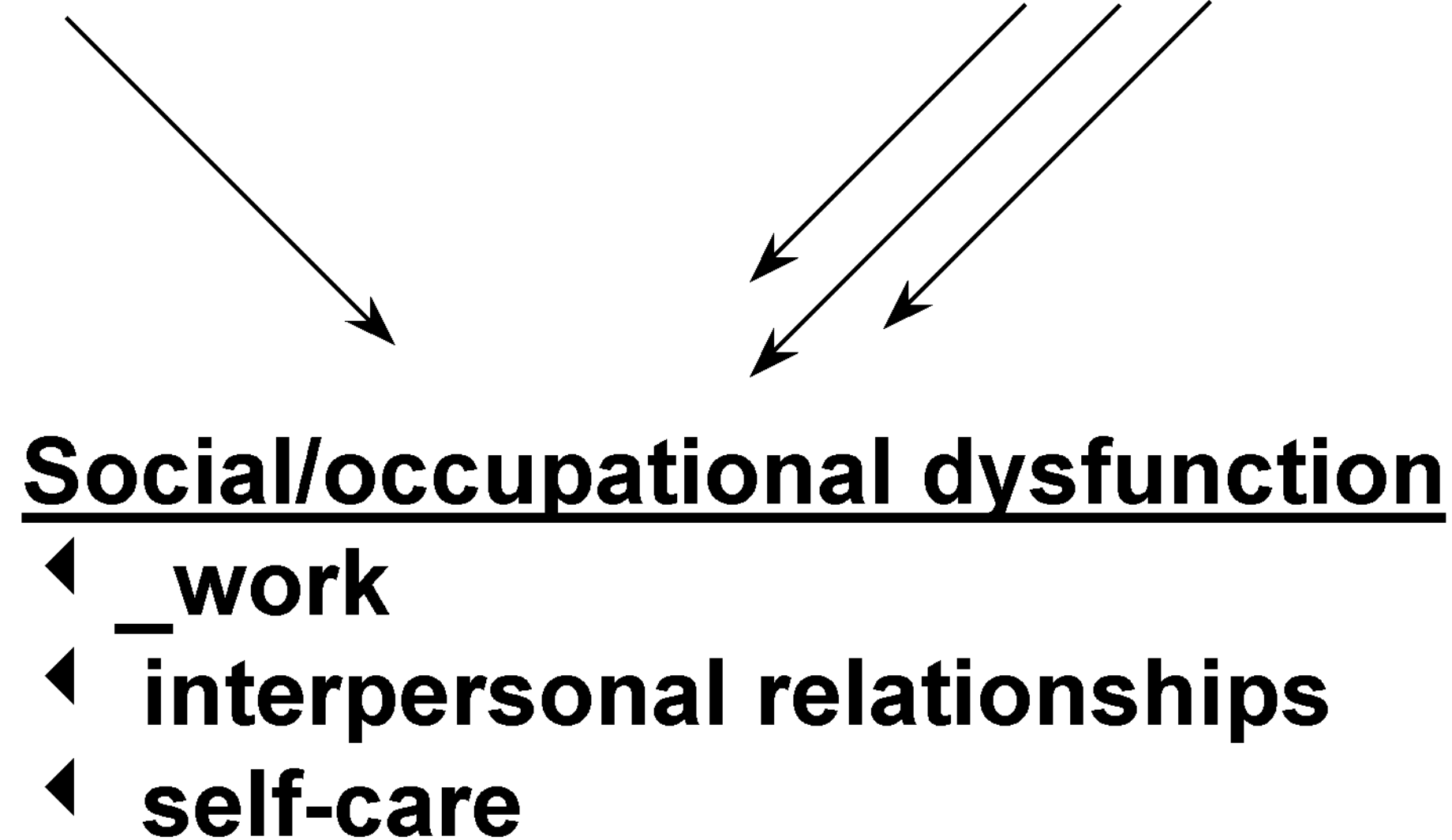
## II. Symptomatic Presentation

### Positive

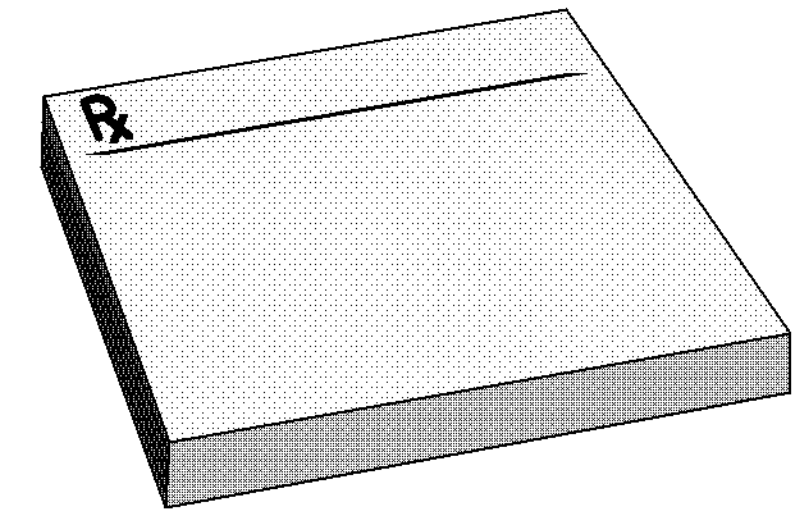
delusions  
hallucinations  
disorganized speech  
catatonia

### Negative

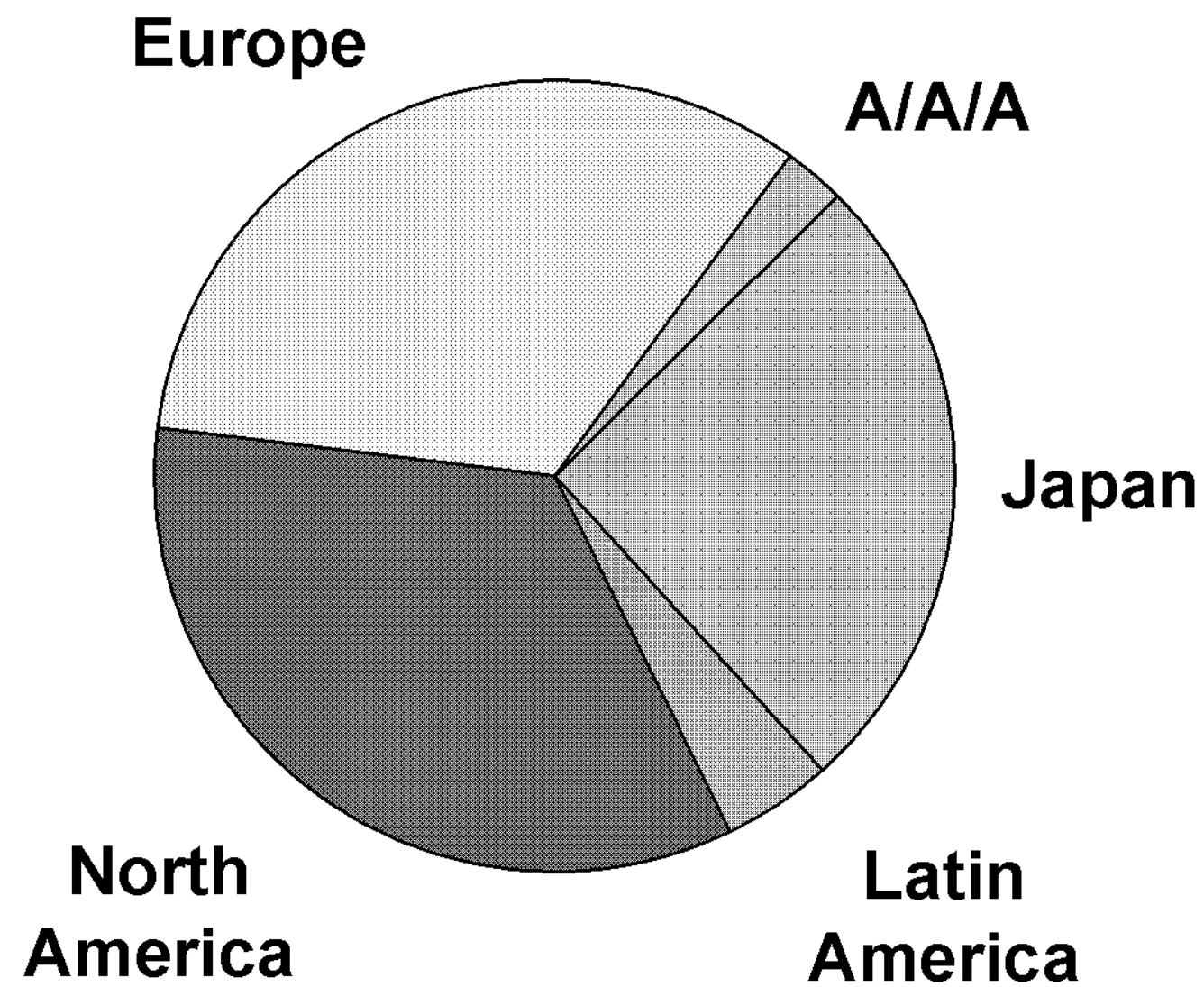
affective flattening  
alogia  
avolition  
anhedonia



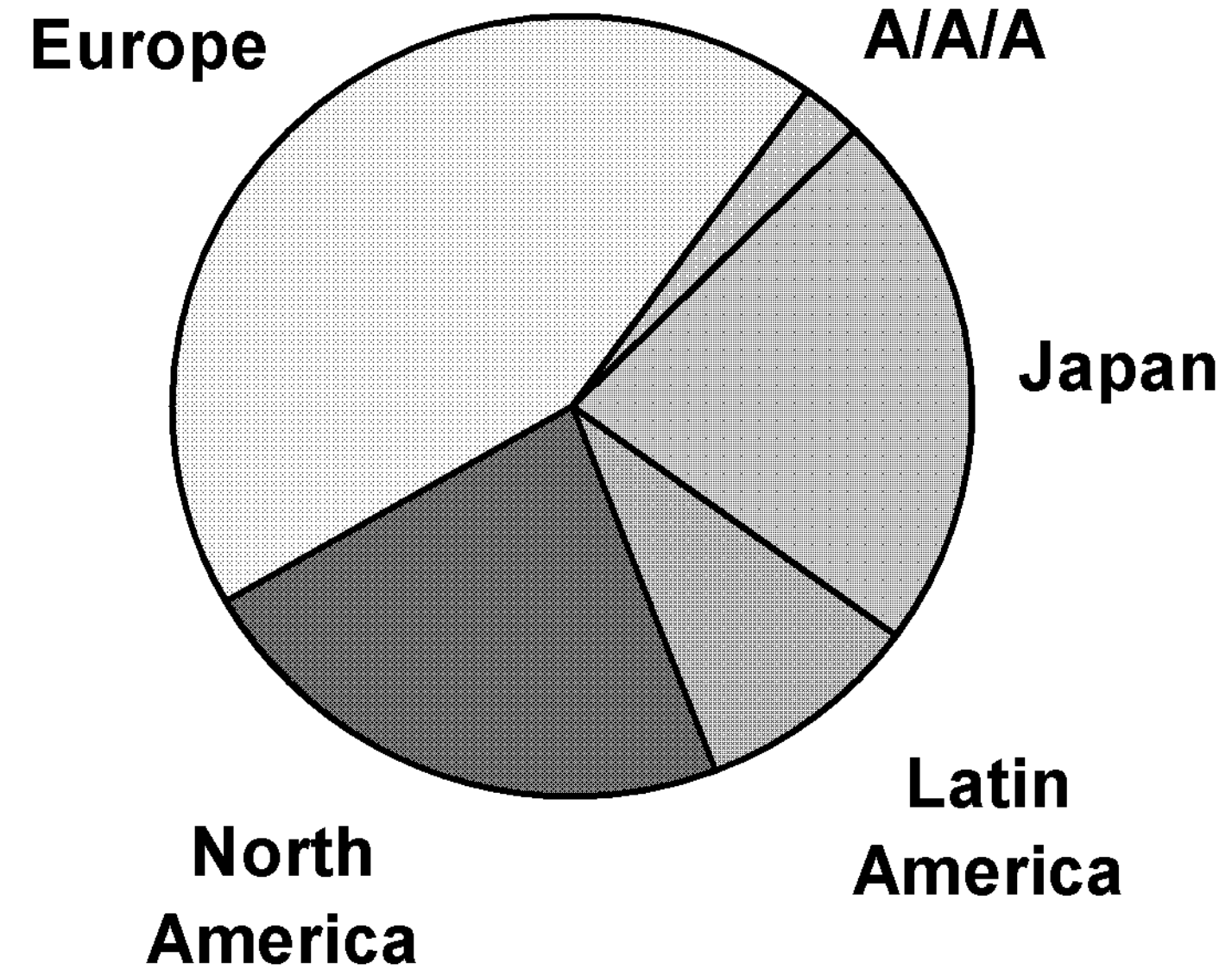




# The Neuroleptic Market



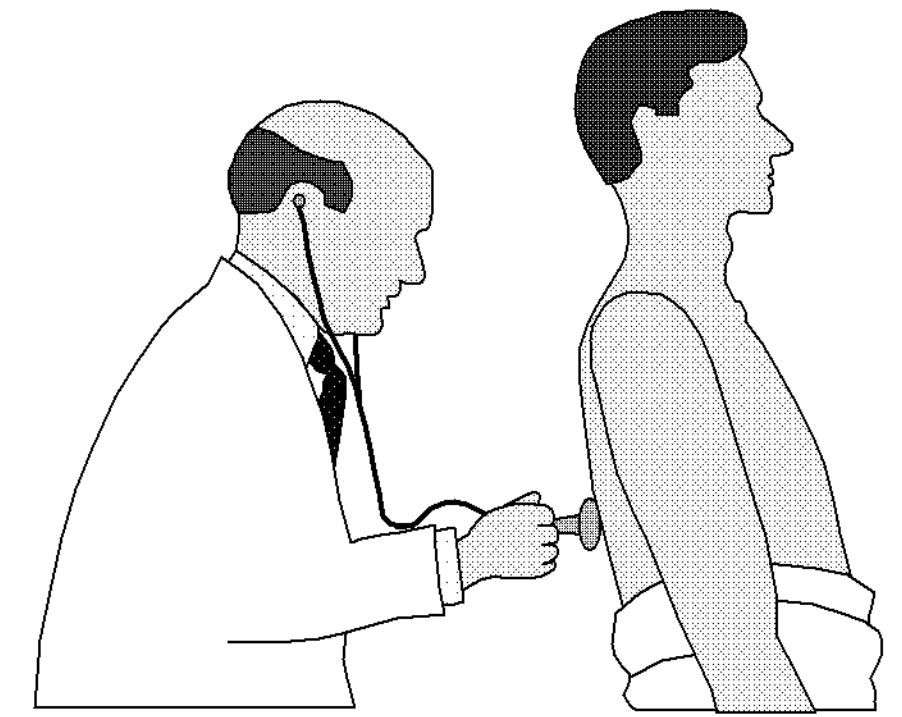
**\$1406**  
**WW USD Sales (millions)**  
**1993 WW USD Growth = 5%**



**2665 DOT (millions)**  
**1993 WW Growth = 4%**

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# Market Opportunity: The Patient's Perspective

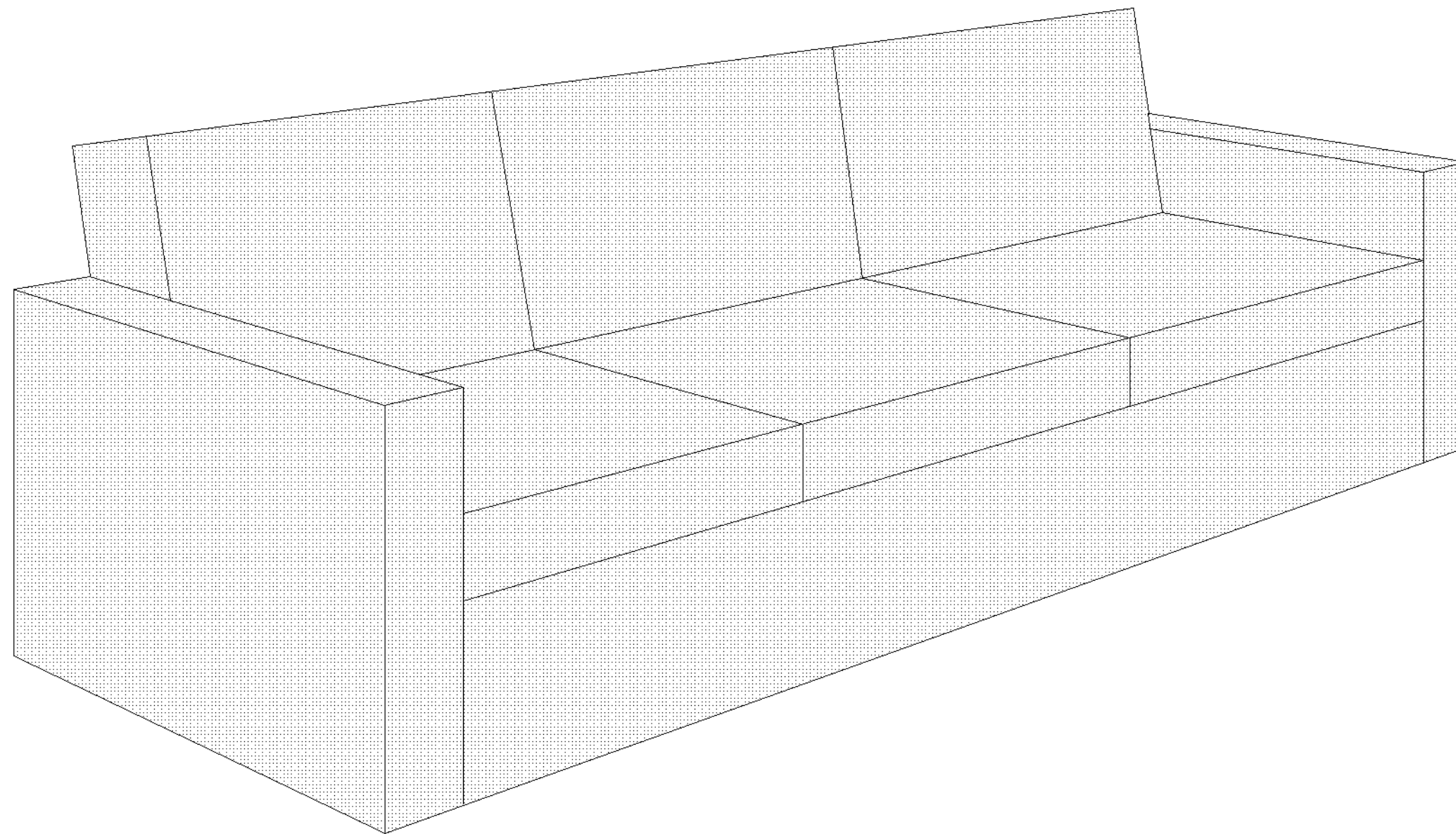
- **Superior efficacy for negative symptoms**
- **A lower incidence of adverse events eg, EPSE, hematotoxicity**
- **Reversal of poor compliance leading to relapse, rehospitalization, and “downward drift”**

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# Market Opportunity: The Analyst's View



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# A Major New Market Opportunity

- **The market for schizophrenia drugs appears to be underserved and highly dissatisfied with existing drugs.**
- **Currently a one billion dollar market but the potential to be an estimated \$3.5 billion market by 2000.**
- **Abbott Labs, Eli Lilly, Pfizer and Zeneca appear to be in a close race to introduce the next major drug. “We believe that Eli Lilly’s olanzapine is the best overall new drug on the horizon.”**

**1994**

**Richard R. Vietor, CFA  
First Vice President U.S.A.**

**Nigel J. G. Barnes  
First Vice President U.K.**

**Merrill Lynch & Co.  
Global Securities Research & Economics Group  
Global Fundamental Equity Research Department**

**GDT/dle**

**July 20, 1995**



**Stover Haley Burns, Inc. June 26, 1995**

A horizontal banner graphic with a light gray background and a black border. The banner has a ribbon-like shape with pointed ends. The text "Investment Recommendation: Strong Buy" is centered within the banner in a bold, black, sans-serif font.

**Investment Recommendation: Strong Buy**

**“We continue to believe that olanzapine will be a drug of major importance for Lilly and likely will emerge as the antipsychotic drug of choice. It could do for the treatment of schizophrenia what Prozac has done for depression.”**

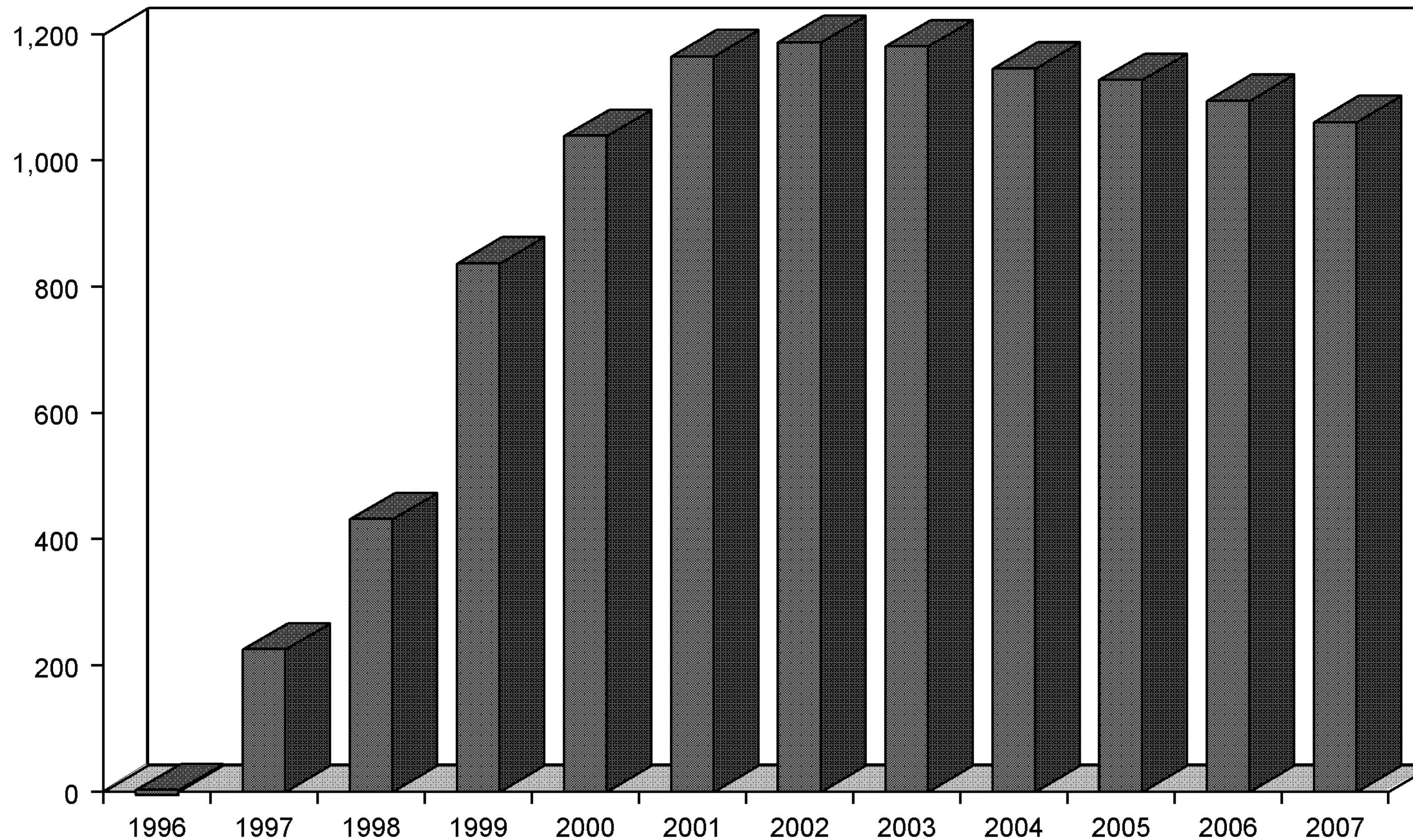
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# Olanzapine Global Forecast



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# Forecasted Sales (\$mil) in Year 5 (2000)

	<u>Base Case</u>
North America	\$621
Total Europe	\$332
Japan	\$69
<u>R.O.W.</u>	<u>\$17</u>
<b>Total</b>	<b>\$1,039</b>

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# Competitive Update

## I. Marketed Competition - Generic Neuroleptics

### Mechanisms

- conventional D<sub>2</sub> antagonists of varying potency/specificity without A<sub>9</sub>:A<sub>10</sub> selectivity

### Advantages

- known to the practitioner
- cost
- effective against positive symptoms for some patients
- multiple formulations

### Drawbacks

- absent to limited treatment response in 35-50% of patients
- no demonstrable long term benefit in negative symptoms
- no effect or exacerbation of comorbid mood symptoms
- high incidence of EPSE leading to over 50% non-compliance during maintenance therapy
- 15% tardive dyskinesia

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# Competitive Update II

## 2. Marketed Competition - Recent

### a. Clozaril (Sandoz)

- mechanism - 5-HT<sub>2</sub>, D<sub>1</sub>, D<sub>2</sub>, D<sub>4</sub>, M<sub>1-5</sub>, alpha<sub>1,2</sub>
- indication - patients refractory to conventional treatment
- safety - agranulocytosis (1.3%); orthostasis  
seizure (5.0%); hypersalivation
- cost - monitoring ex. first year U.S. \$10,500
- annual sales - \$148 million

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## Competitive Update II

### b. Risperdal (JNJ/Janssen)

- mechanism - 5HT<sub>2</sub>, D<sub>2</sub>
- advantages -
  - may benefit negative symptoms
  - lower incidence of EPSE at bottom of the dose range
- drawbacks
  - curvilinear dose: response (2 - 16 mg)
  - haloperidol-like  $\geq$  6 mg
  - requires titration
  - administered bid.
  - inhibitor of CYP450IID6
- first year sales \$149 million (February launch)

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# Competitive Update III

## Compounds in Development (N = 80)

### Closest to Market

### Phase of Development

Product	Mechanism	Company	U.S.	O.U.S.	Critical Assessment
Roxindole EMD49980	D <sub>2</sub> , 5-HT <sub>1A</sub> Agonist	E Merck	?	Phase III (early)	<ul style="list-style-type: none"> <li>• early efficacy (OL) with low response rate</li> <li>• possible negative sx. effect (OL)</li> <li>• antidepressant effect (OL)</li> <li>• nausea/dizziness</li> </ul>
Zotepine	“balanced” dopamine agonist	Fujisawa Licensed to Boots in U.S.	Reportedly in Phase II/III	Launched Japan	<ul style="list-style-type: none"> <li>• BPRS - like haloperidol</li> <li>• SANS - superior to Hal</li> <li>• EPSE - superior to Hal</li> <li>• ADR - ↑LFT</li> </ul>
Seroquel™ IC1204636	A weak D <sup>2</sup> blocker.	Zeneca	Phase III; NDA submission- end of 1995.	Phase III.	<ul style="list-style-type: none"> <li>• 1 positive placebo study - weak</li> <li>• 1 comparable to chlorpromazine</li> <li>• insomnia/sedation</li> <li>• sinus tachycardia/LFT</li> <li>• ?tox above 500 mg/day</li> </ul>
Sertindole LU23174	high affinities for D <sub>2</sub> , 5HT <sub>2</sub> , and α-1 receptors- antagonist	Lundbeck, Abbott (US), Shionogi (Japan)	III	III (II Japan)	<ul style="list-style-type: none"> <li>• two high dose studies separating from placebo (20 mg)</li> <li>• titration</li> <li>• male sexual dysfunction</li> <li>• headache/congestion</li> <li>• insomnia/somnolence</li> </ul>
Ziprasidone CP-88059	5HT <sub>2</sub> /D <sub>2</sub> , antagonist	Pfizer	III	?	<ul style="list-style-type: none"> <li>• conventional D2 occupancy (85%) by PET</li> <li>• 5T<sub>1/2</sub> 4-6 hours</li> <li>• hi dose comparable to HAL</li> <li>• EPSE at higher doses</li> <li>• headache</li> </ul>

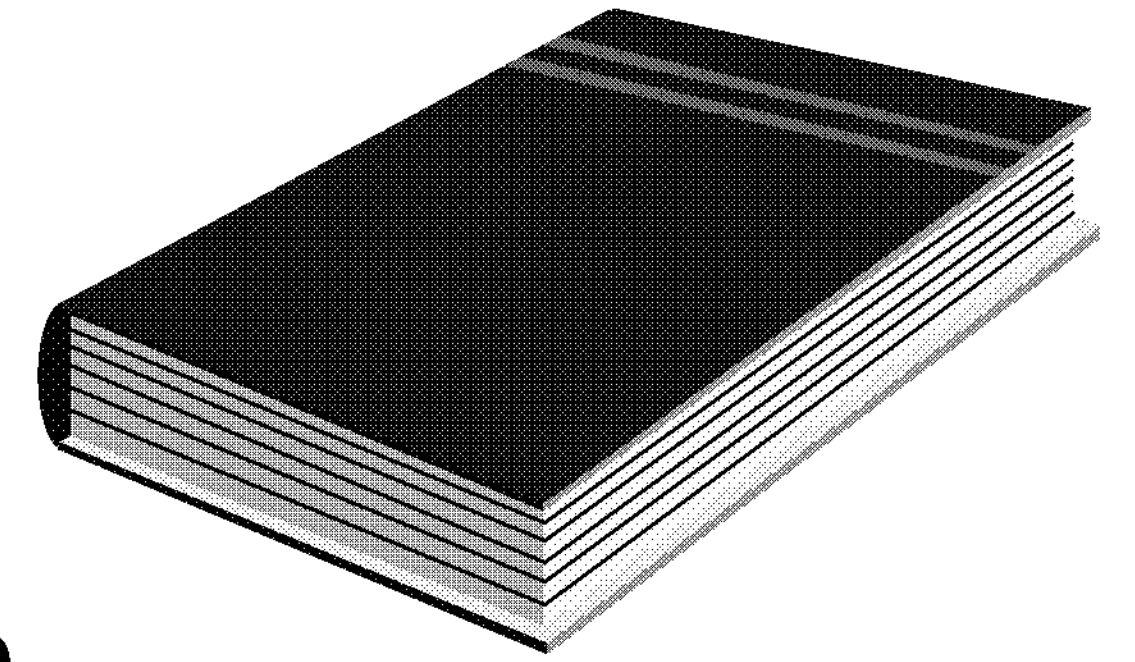


# Background Milestones

	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995
<i>Compound Synthesized</i>	▲													
<i>Project Team Formed</i>				▲										
<i>First Human Dose</i>					▲									
<i>First Efficacy Dose</i>							▲							
<i>Development Initiated in Japan</i>								▲						
<i>Registration Phase GPAC Review</i>											▲			
<i>Patent Issued</i>												▲		
<i>Product Decision</i>													▲	
<i>HWT Team Formation</i>														▲

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## **Primary Indication**

**Olanzapine is indicated for the management of the manifestations of psychotic disorders\* which consist of both positive and/or negative psychotic signs and symptoms.**

**\*"Schizophrenia and related..." in Europe**

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## Critical Success Factors

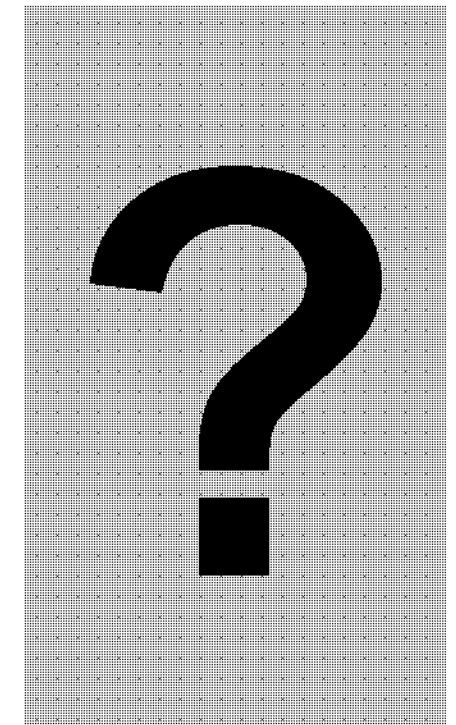
- **Efficacy with respect to positive symptoms**
  - decrease in BPRS > placebo
  - percent responders  $\geq$  haloperidol
- **Efficacy with respect to negative symptoms**
  - decrease in PANS subscale and SANS statistically significant relative to baseline and > haloperidol
- **Safety**
  - Incidence of tardive dyskinesia < haloperidol
  - Elevation of liver enzymes transient and non-progressive
  - No “Black Box” or mandatory monitoring requirement

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# Question



**Does a heavyweight team have a  
half-life that is longer than**

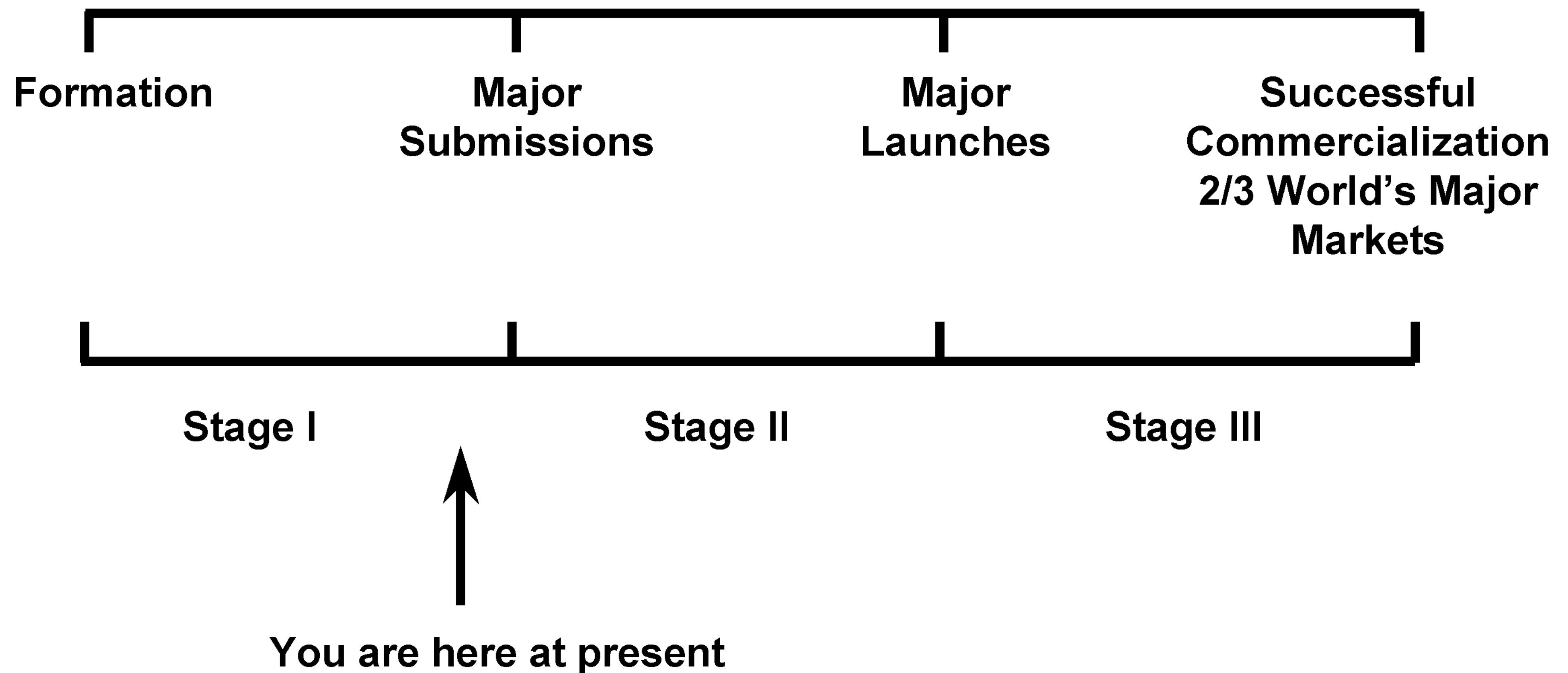
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# The Concept of a HWT's Life Cycle



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# Key Component Strategies Vary Over The HWT's Life Cycle

- Visualize HWT deliverables over time via a matrix plan

	Stage 1	Stage 2	Stage 3
Component 1			
Component 2			
Component 3			

**Key component strategies are integrated to maximize efficiency and ROI**



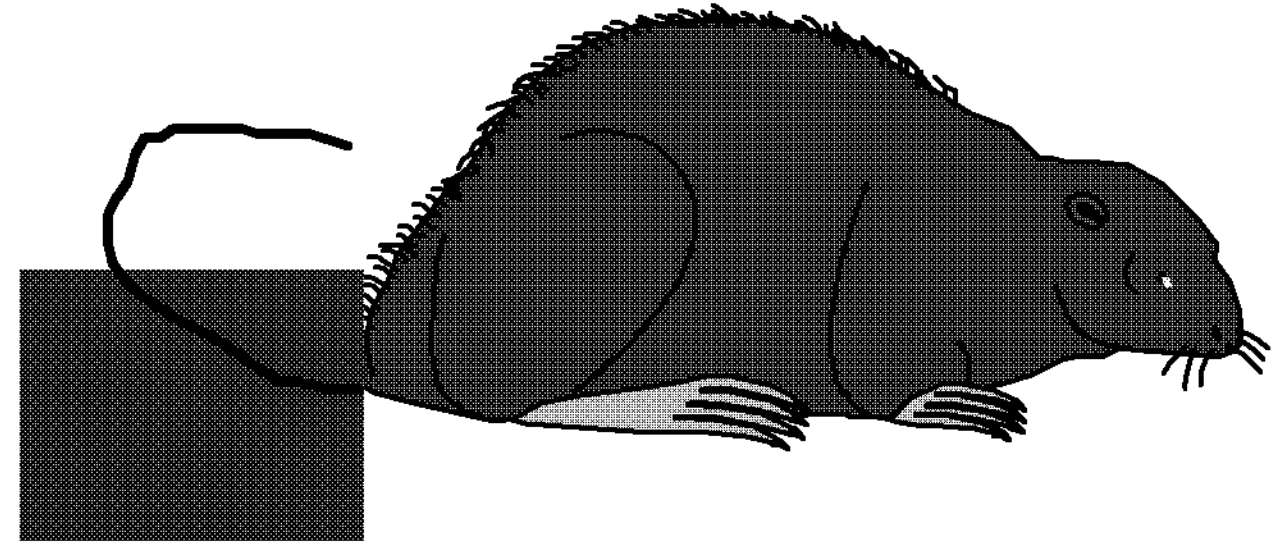
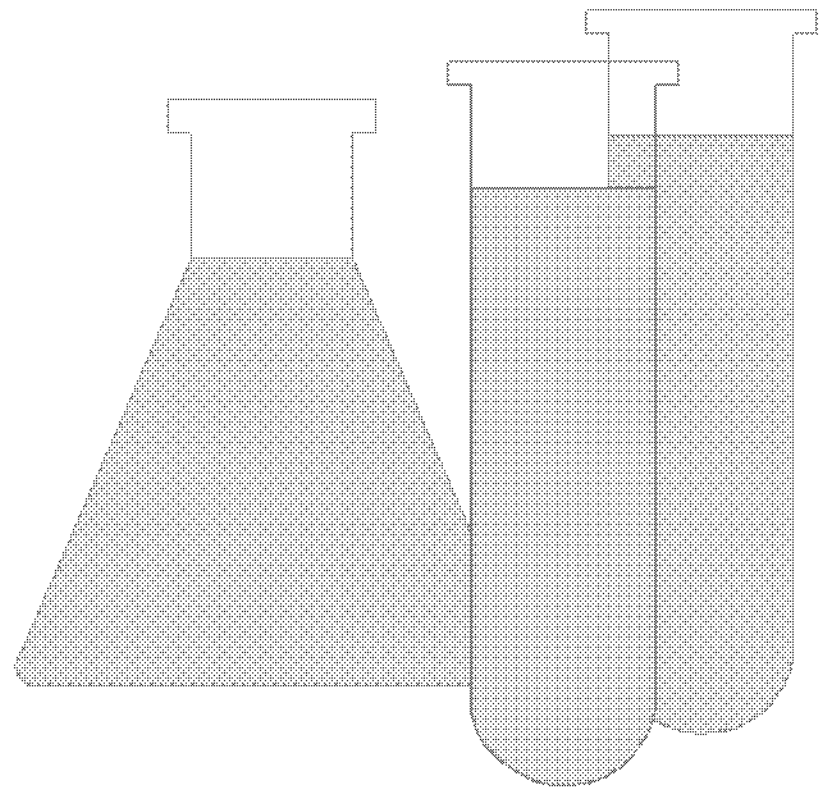
# **Deliverables Support the Zyprex Heavyweight Team Strategic Initiatives**

- **Speed to global markets**
- **Customer focused product development plan**
- **Redefine standard of care and position  
Zyprex as the standard for a cost-effective  
pharmaceutical solution**
- **Aim for rapid and broad market penetrations**
- **Accelerate presence in emerging markets**

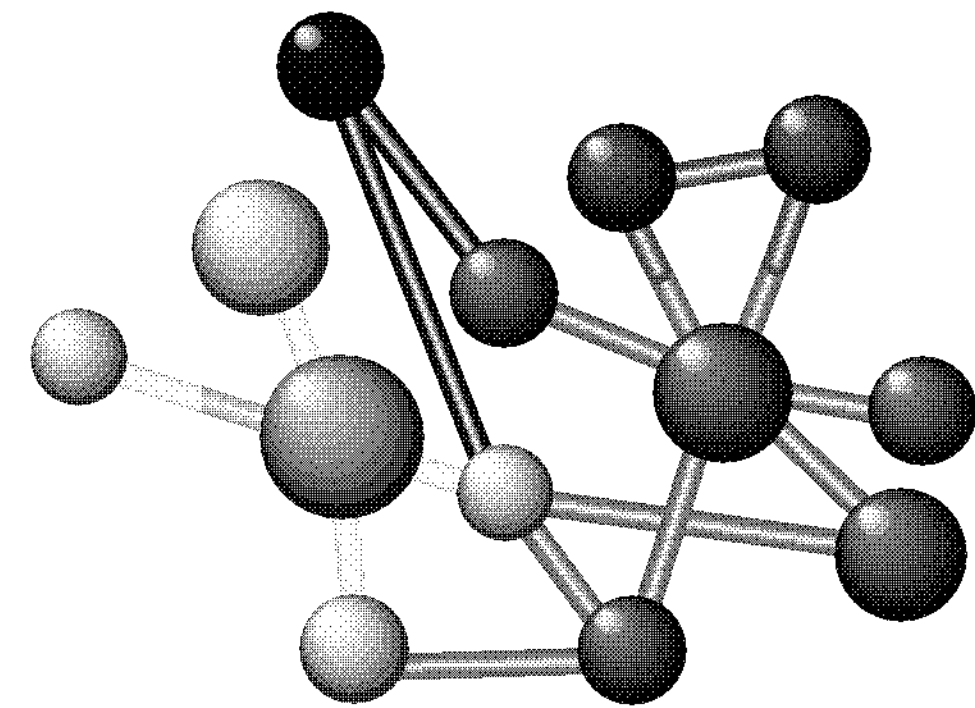
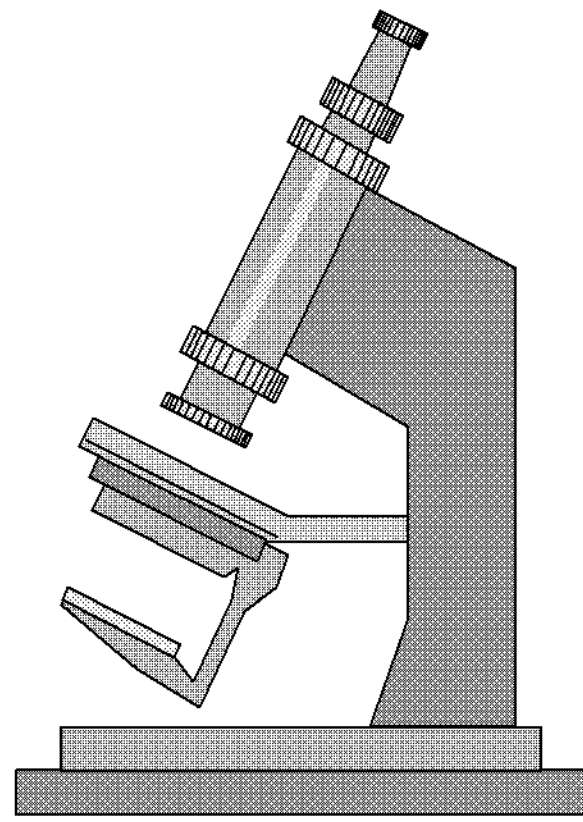
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**ZYPREX**  
Olanzapine



# *Preclinical*



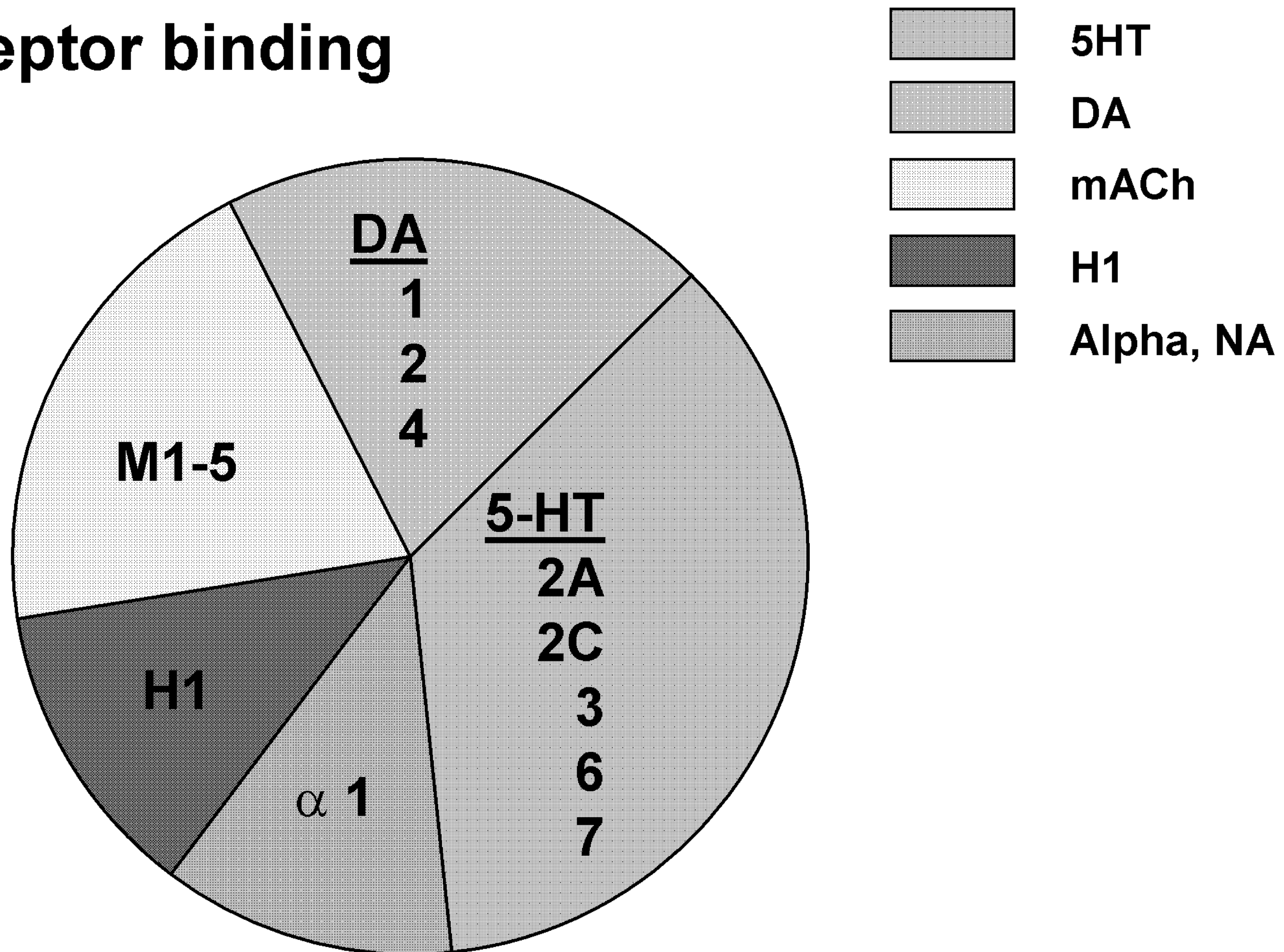
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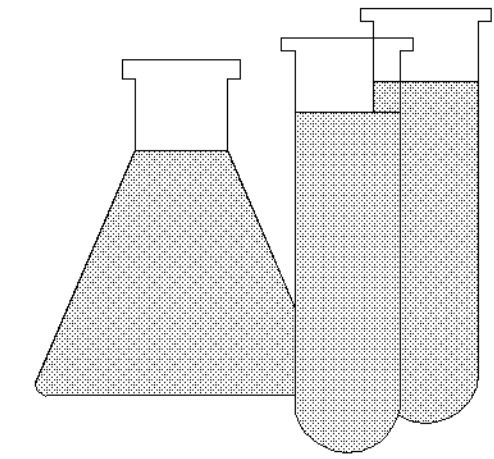
# Olanzapine

- In vitro receptor binding



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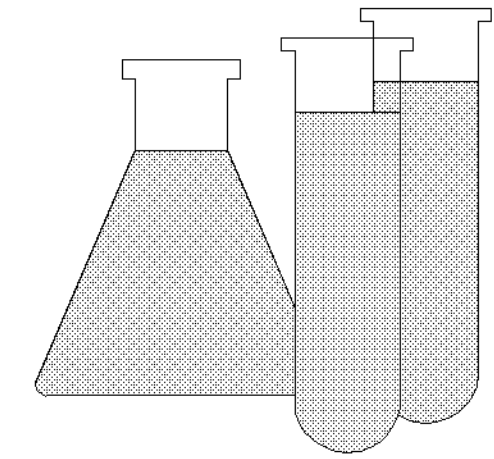
## Preclinical

- **In vivo behavioral pharmacology**
  - CAR to CAT ratio 4:1
  - increase in punished responding
  - A<sub>10</sub> mesolimbic selectivity
- **Blocks NMDA antagonist neurotoxicity**
- **Identification/characterization of parent/metabolite profiles**

redacted

- **No behavioral activity from metabolites evident**





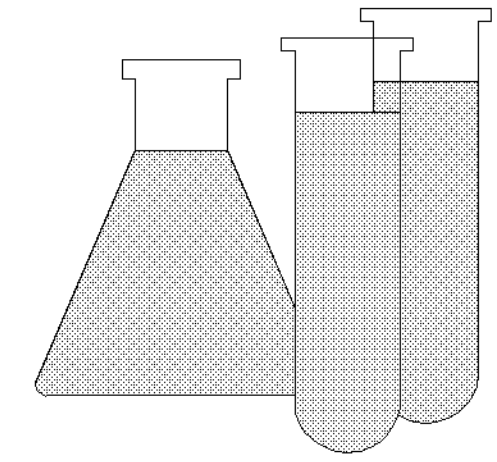
## Stage II

# Preclinical Strategy - “Leverage The Neuroscience Explosion”

- **Potential blockage of NMDA antagonist-induced neurotoxicity**
- **Atypical neuroleptics and central amygdaloid membrane properties and synaptic potentials**
- **Olanzapine in a conflict response model**
- **In vitro binding profiles across regions/subtypes**
- **Restoration of PCP-induced deficits in prepulse inhibition (sensorimotor gating)**



## Stage III



**Preclinical Strategy - “Better Living (SOPA) Through Chemistry (and Biology)”**

**More of a good thing**

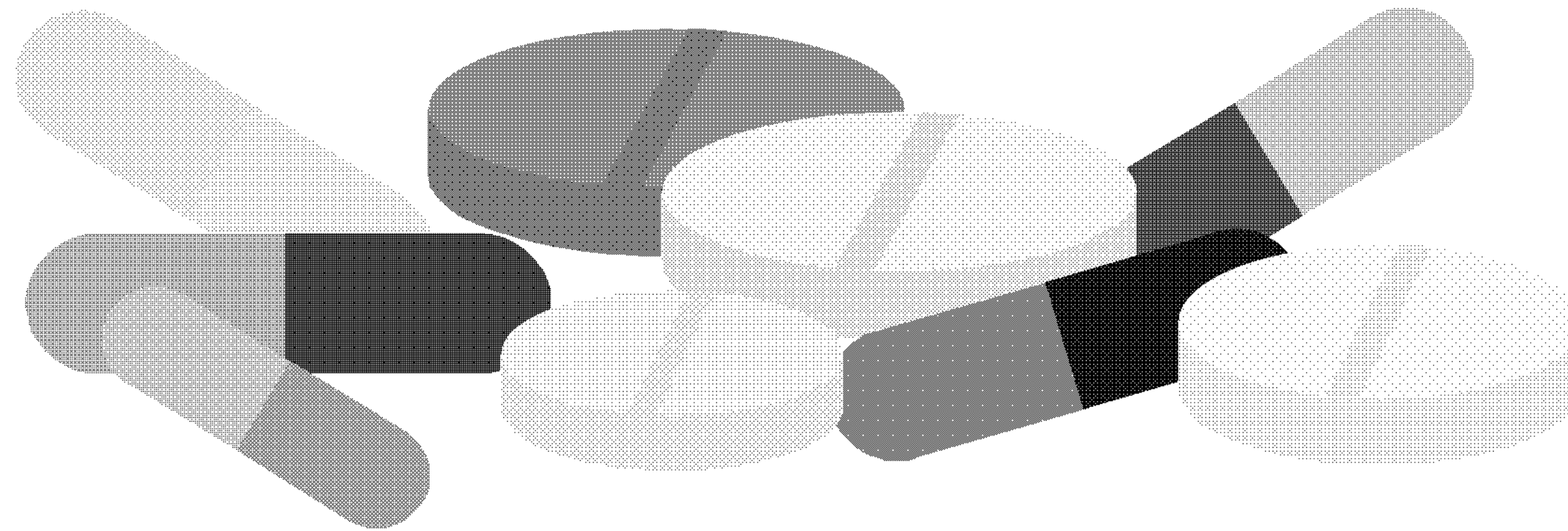
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# OLANZAPINE CLINICAL DEVELOPMENT:

## Molecule To Drug Candidate



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Zyprex HWT  
Bldg 48-3  
Lilly Corporate Center  
Indianapolis, IN USA



**Clinical Deliverables - Stage I  
Global Regulators  
Anywhere, World**

# Clinical Deliverables

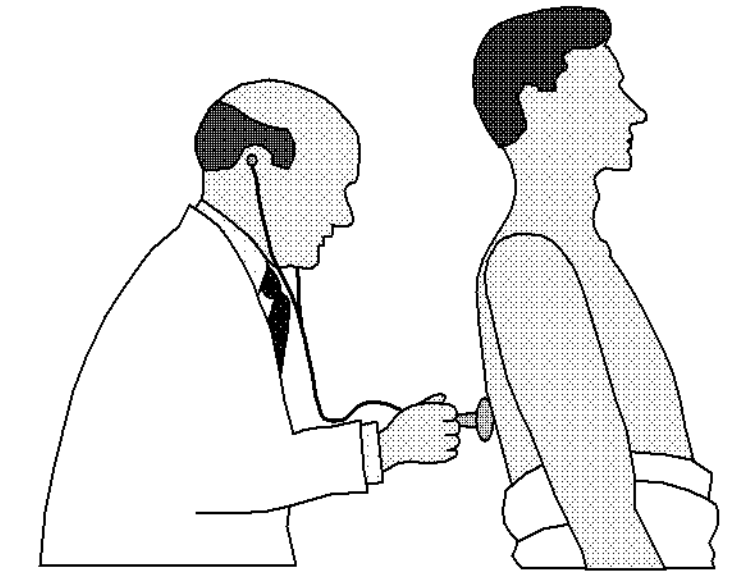
- **Execute, analyze, and write up a series of core registration studies designed to illustrate olanzapine's superior profile (safety, efficacy, functional well being, economics) to both**
  - (a) placebo and
  - (b) a representative conventional antipsychotic (haloperidol)

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# Olanzapine



## Human Exposure (2/14/95)

**$\geq$  1 Dose: 3,100**

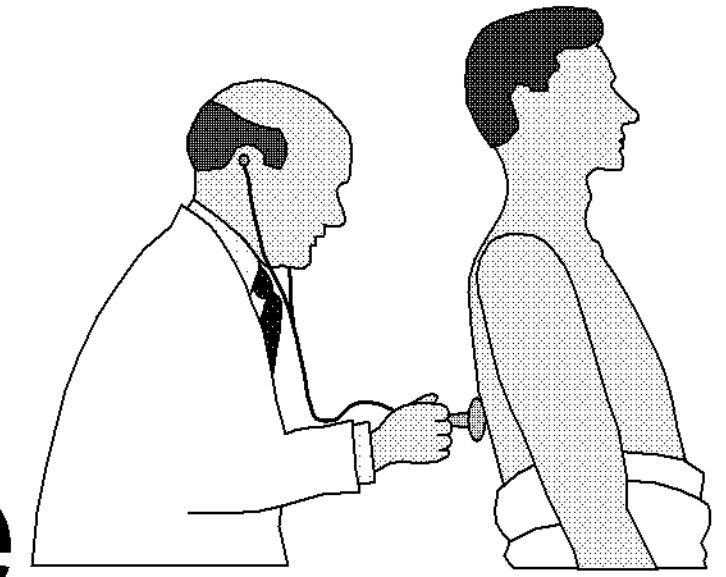
**$\geq$  6 Weeks: 1,867**

**$\geq$  6 Months: 880**

**$\geq$  1 Year: 321**

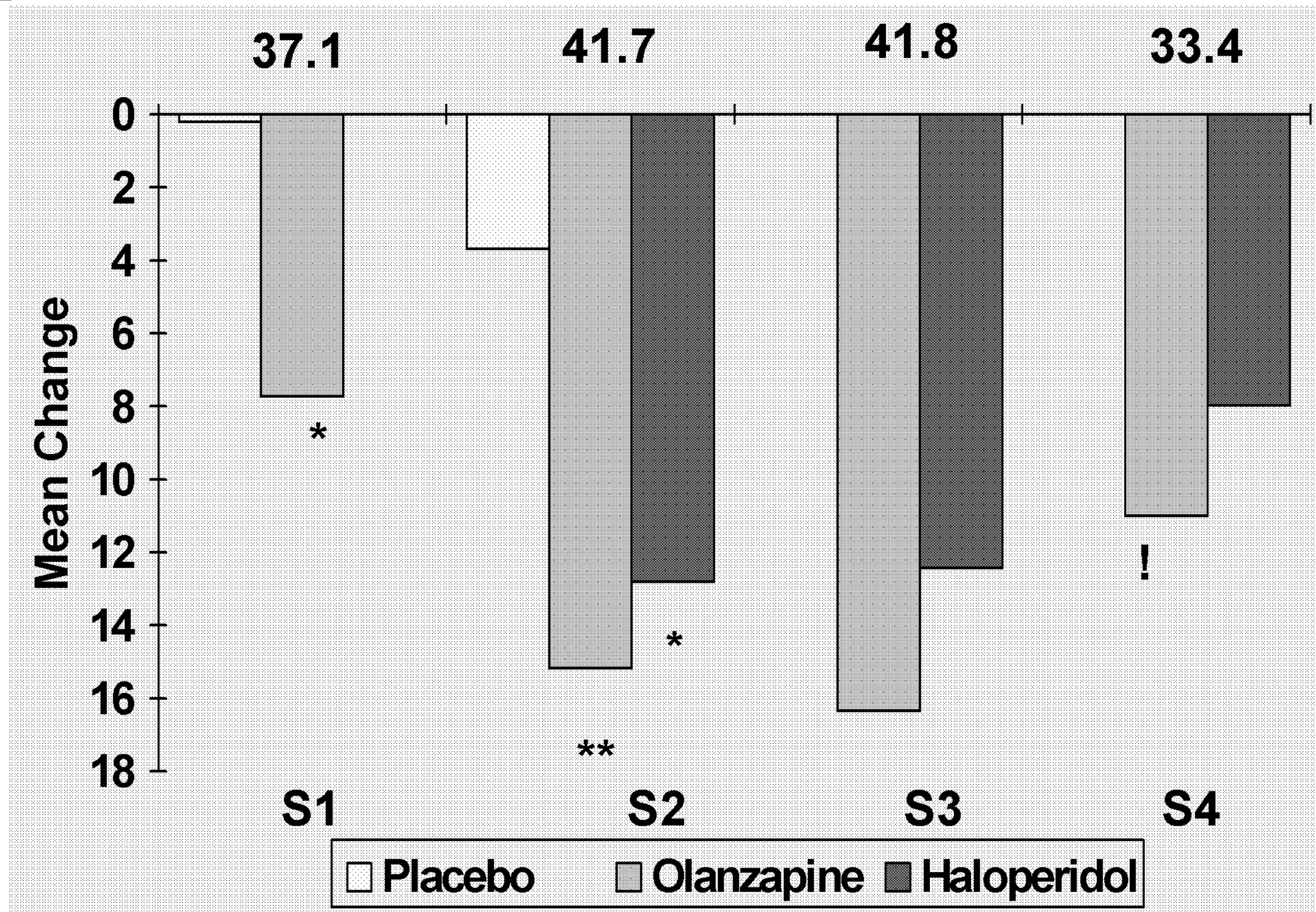
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# Efficacy: BPRS - Total Score (Mean change, LOCF)

Baseline

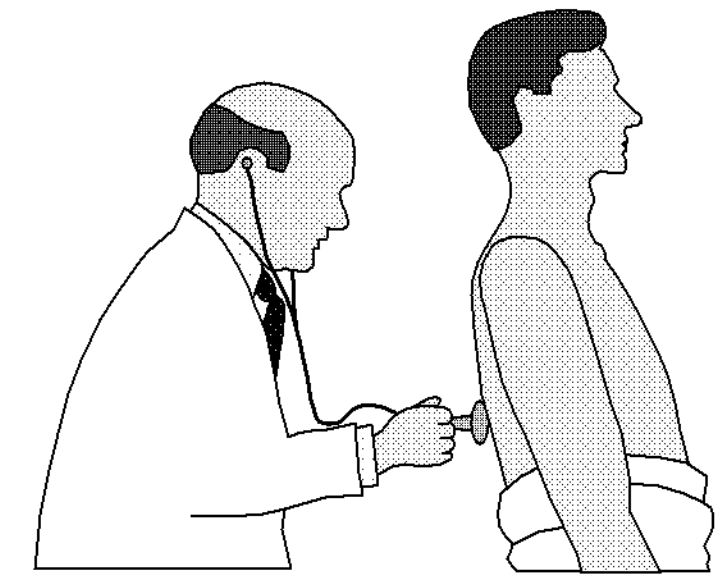


\*p ≤ .050 vs placebo  
 \*\*p ≤ .001 vs placebo  
 !p ≤ .050 vs haloperidol

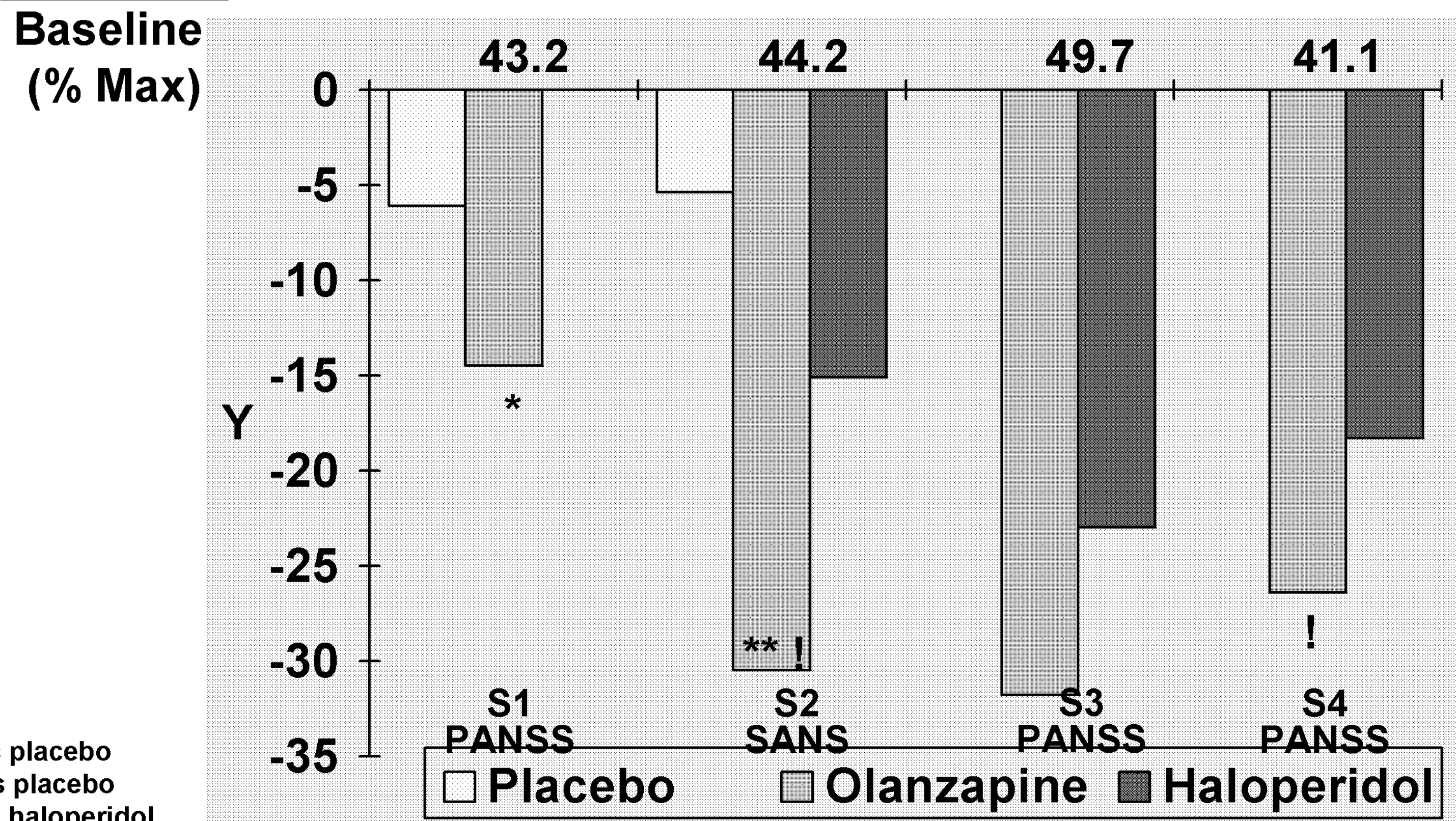
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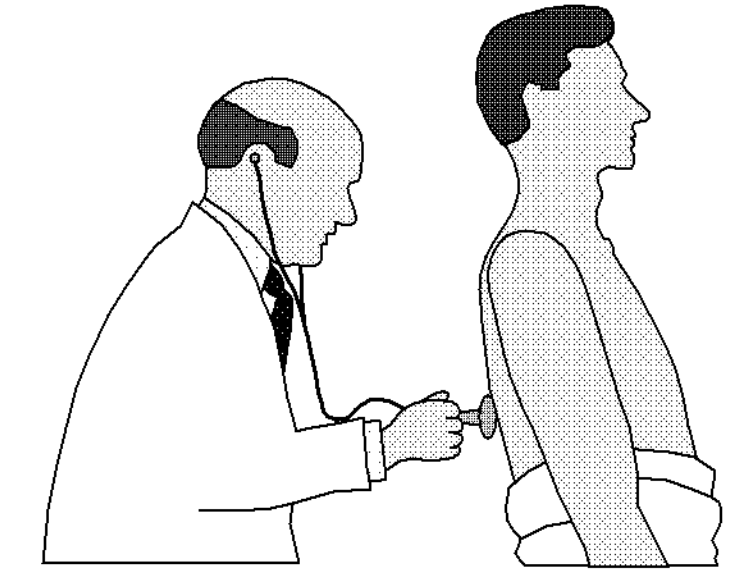
# Efficacy: Negative Symptom Scales (Mean change [%], LOCF)



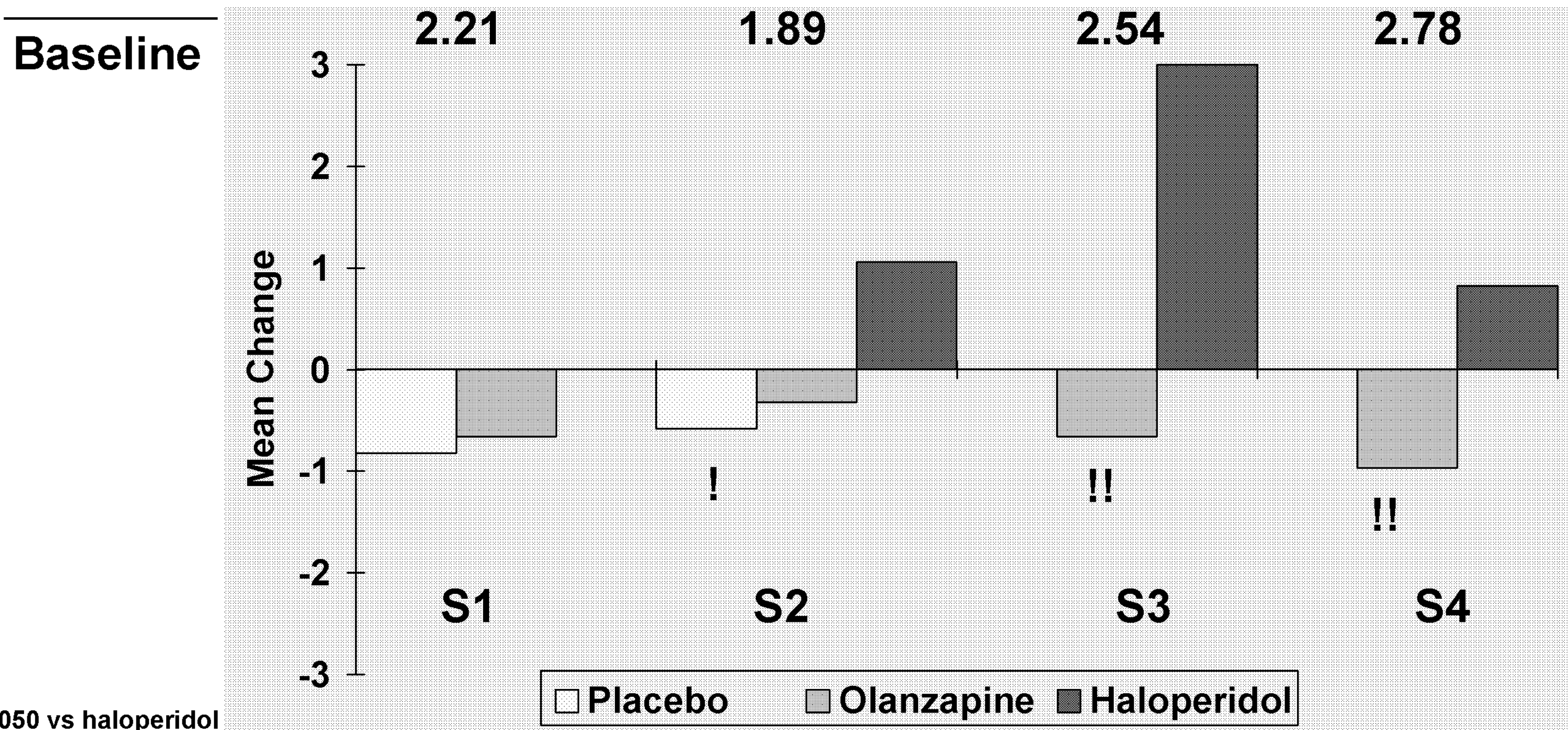
\*p ≤ .010 vs placebo  
 \*\*p ≤ .001 vs placebo  
 !p ≤ .050 vs haloperidol

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# Acute EPSE: Simpson-Angus Scale (Mean change, LOCF)



!p ≤ .050 vs haloperidol  
!!p ≤ .001 vs haloperidol

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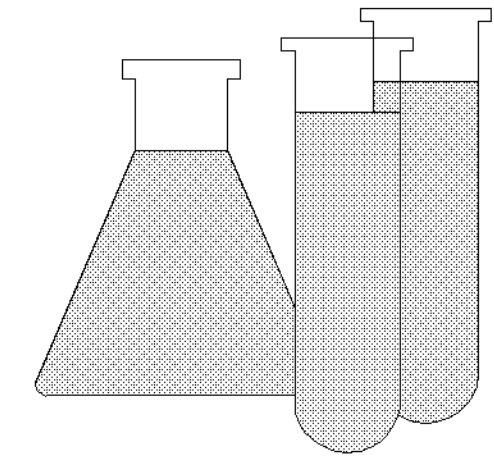


## Clinical Safety Summary

- **Only three events occurred  $\geq 2\%$  which were statistically significantly more common than Haldol**
- **Early discontinuations due to ADR comparable to placebo**
- **No change in resting vital signs**
- **Significantly less tx. emergent T.D. than with Haldol**
- **Weight gain dose related; early plateau**
- **ECG: no clinically significant changes**

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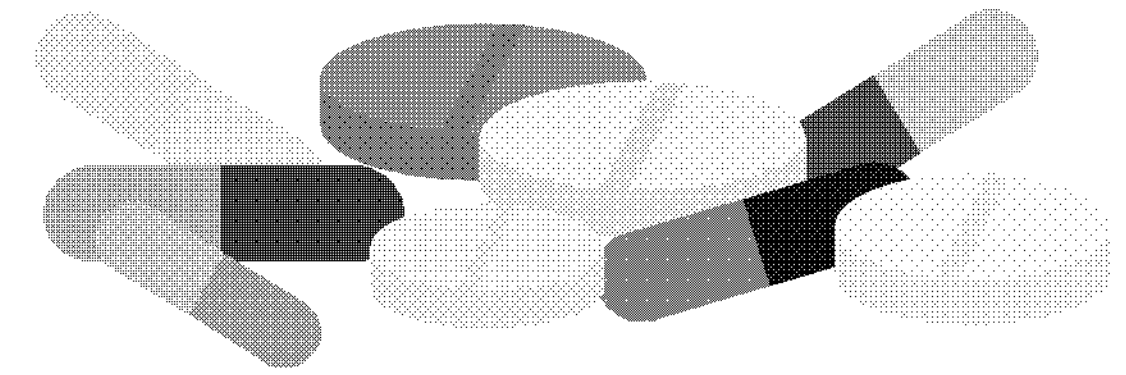
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## Laboratory Analytes

- **Transient, possibly dose-related increase in hepatic transaminases**
  - No clinical symptoms
  - No discontinuations during acute phase of S4 (N = 1995)
- **No evidence of hematotoxicity**
- **Mild, transient dose-related increase in prolactin**
- **Substantially less prolactin elevation than with haloperidol**





## Conclusions:

### Atypical Profile

- **Greater efficacy against negative symptoms than haloperidol. Dose range 5-20 mg once daily. Optimal dose 10-15 mg. No titration to an effective dose.**
- **Rare dystonic reactions and significantly less parkinsonism and akathisia than with haloperidol**
- **Superior long term compliance during maintenance therapy with significantly fewer re-hospitalizations**





# Clinical Deliverables Stage II and III

## I. Clinical Plan

- Institute a “second wave” of clinical investigation ('96, '97) for the following purposes:

**goal 1      optimize pricing decisions**

**goal 2      prepare for timely launch in selected type  
II countries**

**goal 3      differentiate product attributes of  
olanzapine from key competitors**

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## **Clinical Deliverables Stages II and III**

- goal 4**      **leverage the recent explosion of clinical and neuroscience activity in the schizophrenias to position Olz as the innovator**
  
- goal 5**      **select and implement “new indications” capable of significantly growing the market potential**
  
- goal 6**      **recognizing local market idiosyncrasies, provide funding to engage key opinion leaders in publication**

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# Clinical Studies Stages II and III

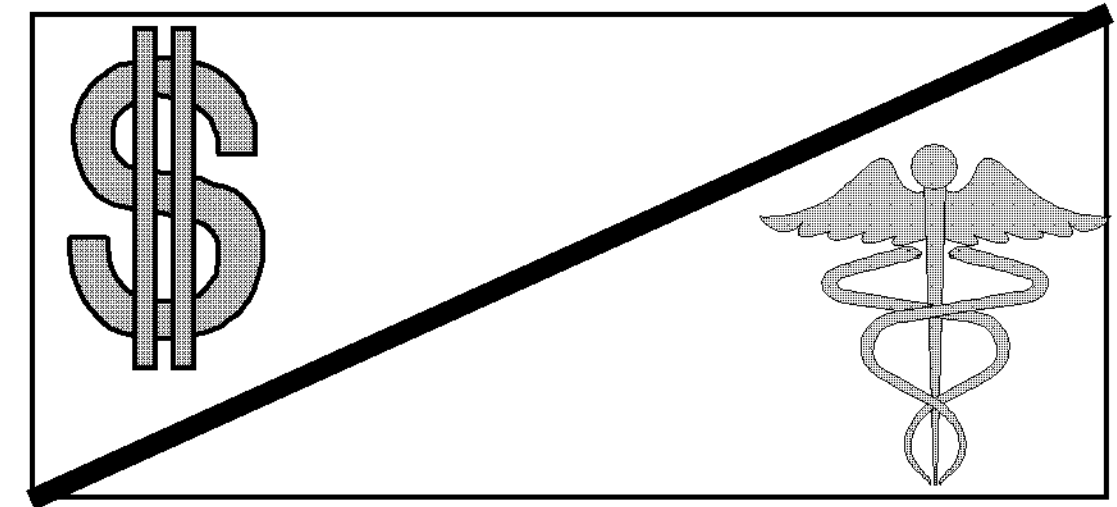


## Examples - 1996 Plan

Objective	Locale	PI
• Emerging market registration	Hong Kong/China Mexico	Lieh-Mak
• New indication	global	many
– mania – psychosis in Alzheimer's	global	many
• Expand the package insert wording	U.S.	Lieberman, et al,
– relapse prevention – refractory	Neth U.S.	Kahn Tamminga
• Commercialization -	multistate	many
• Local opinion leader involvement - templates	global	many

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# Health Economics

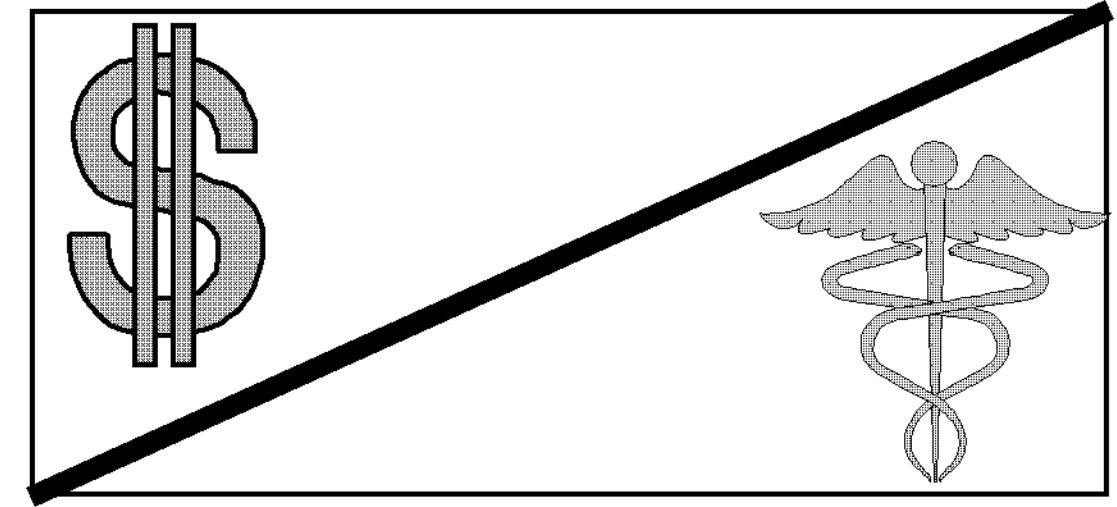
## Overall Strategy

The overall objectives of the Health Economics global plan are several-fold:

- Create a greater *awareness* about the prevalence of the disease, its *poor prognosis* in a significant number of patients and the large *medical and societal costs* attributed to the various stages of the disease

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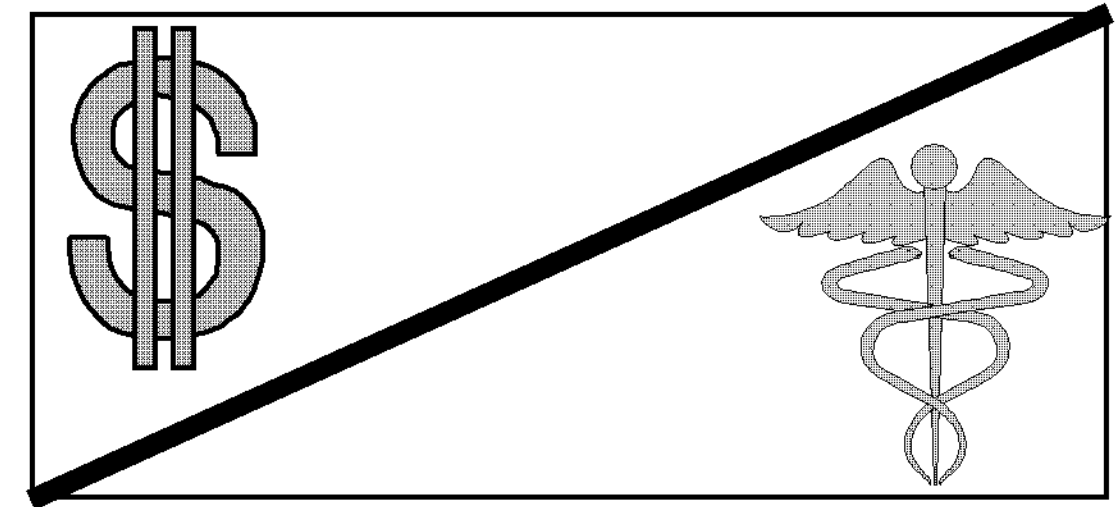
# Health Economics

## Overall Strategy

- Provide authorities with the necessary health economic data to document olanzapine's *value* regarding registration, formulary inclusion, level of reimbursement, and pricing negotiations
- Publications in *support* of olanzapine's advantage in *patient outcomes*

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# Health Economics

## Studies

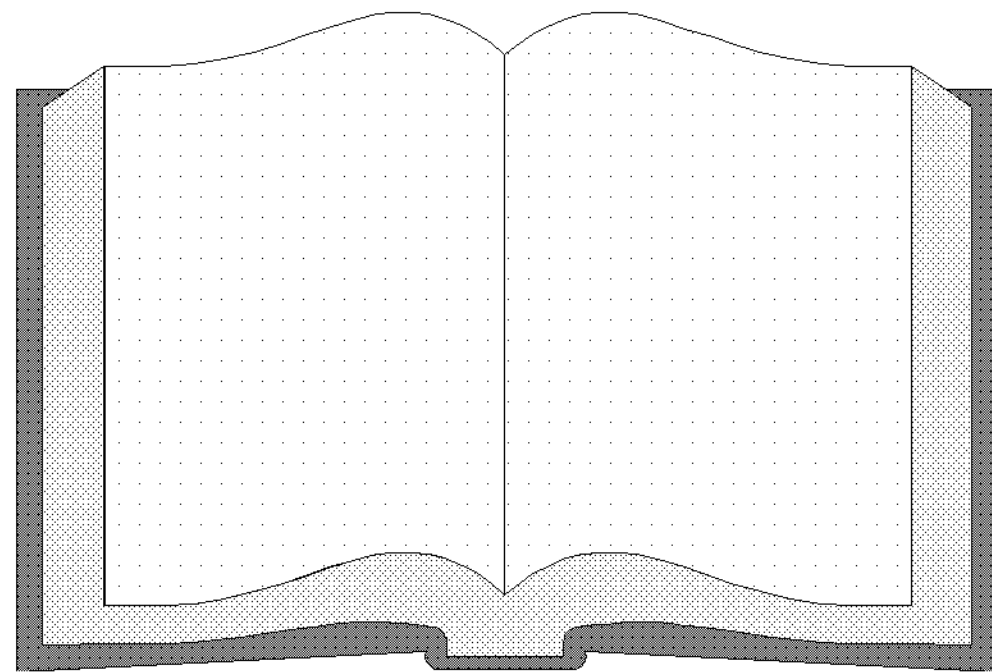
- **Cost of illness**  
Spain, Germany, Italy Belgium/Australia/France
- **Quality of life (QLS)**  
HGAD, E003, HGAJ, amisulpride-France
- **Targeted resource utilization**  
HGAJ
- **Treatment-resistant patients**  
US; Austria/Spain
- **Family burden**  
Italy

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# *Regulatory*



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## **Regulatory Strategy - Stage I (road to initial submissions)**

- **Simultaneously prepare and submit dossiers in the US, EU, and Canada on October 1, 1995. Remaining Type I submission will take place within a 30-day window (except Japan)**
- **Cultivate key relationships with global affiliates and regulatory agencies to facilitate speed of review**
- **Electronic plus paper submissions where desired**

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## **Regulatory Strategy - Stage II (Submission to Major Launches)**

- **Prioritize a submission strategy for FSC countries to implement within 60 days of UK approval**
- **Prepare/submit pricing dossiers**
- **Rigorous preparation for FDA Advisory Panel meeting**
- **Anticipate/rapid response to regulatory questions**
  - **central query database**
- **High quality 120 day safety update (FDA)**
- **Prompt printing of labels**

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## **Regulatory Strategy - Stage III**

### **Post Marketing**

- **Liaison with regulatory agencies on new indication, labeling expansion, and line extensions**
- **Help coordinate safety update**
  - DEN
  - PMS
- **Work with marketing to optimize promotional materials within local guidelines**

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# Japan



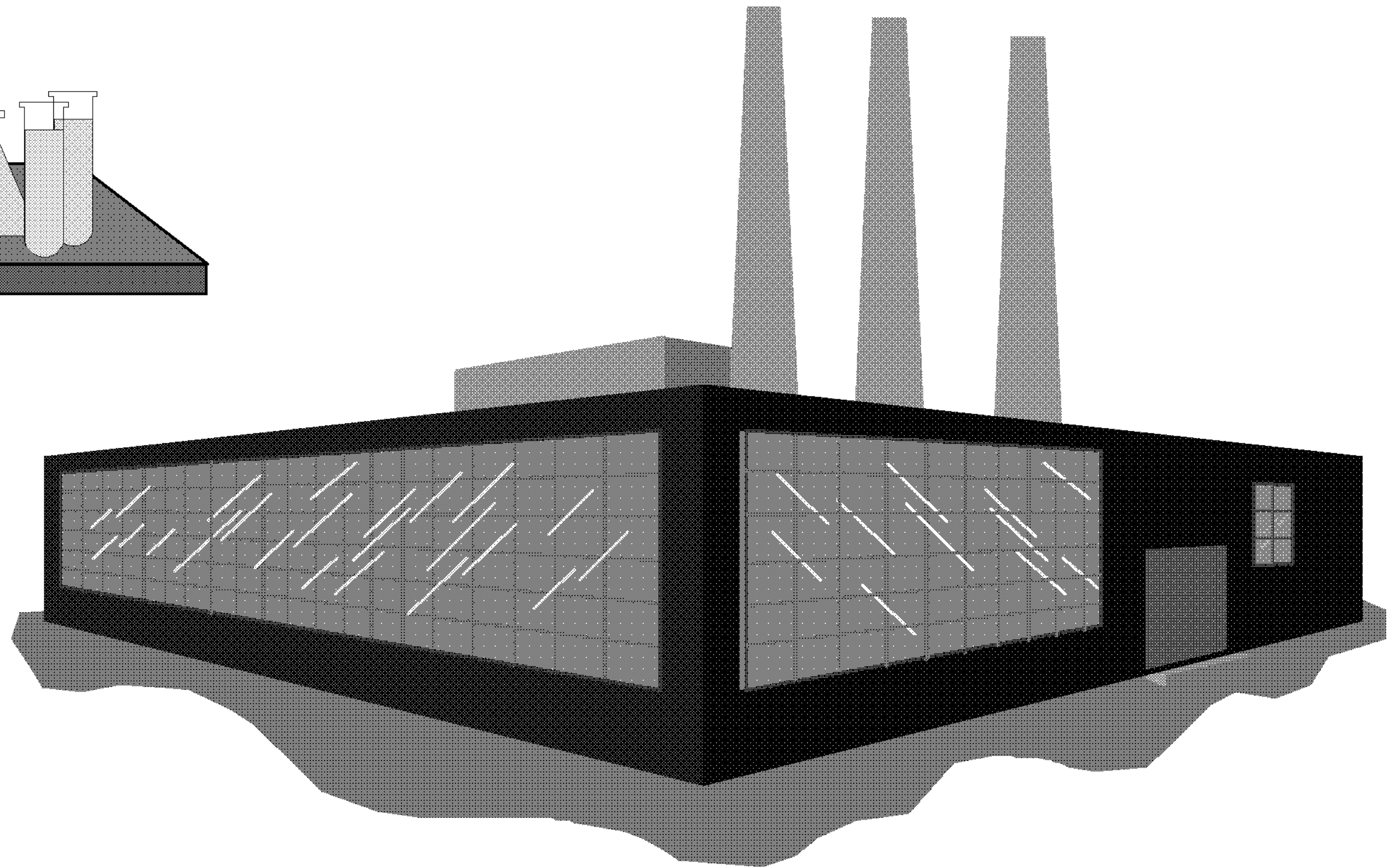
- **Early Phase II/Late Phase II results encouraging**
- **Inadequate resources in ELJJK, earthquake and many competitors have resulted in project delays**
  - current NDA target of July '97 very doubtful
- **Heavyweight Team visits/meetings with opinion leaders being planned for Q4 '95**

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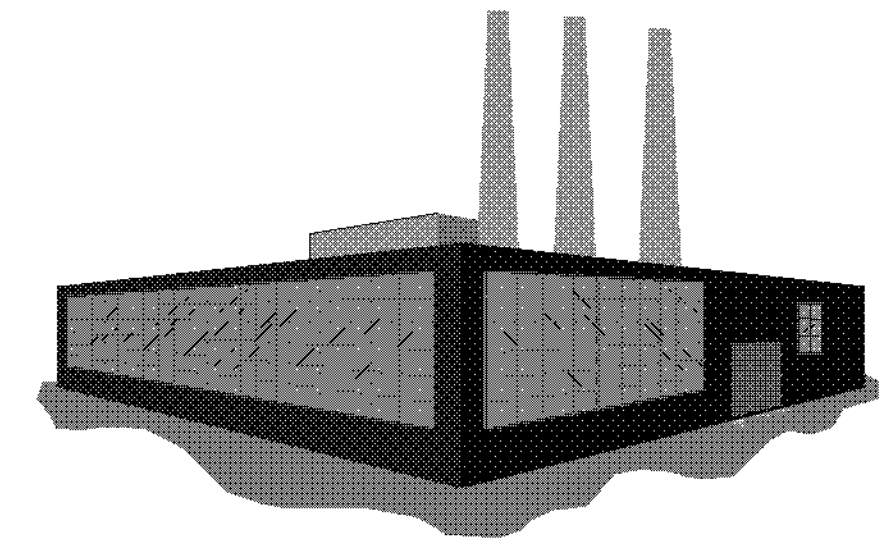
**ZYPREX**  
Olanzapine

**CM&C**



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## **CM&C General Strategy - Stage I**

**Bulk Drug: 4 step synthesis**

**Tablets: white, round, globally acceptable  
2.5, 5, 7.5, 10 mg**

**Granules: “Fine Granules” for Japan  
Doubles as reconstitutable solid  
for R.O.W. in 2.5, 7.5, and 10 mg  
sachets**

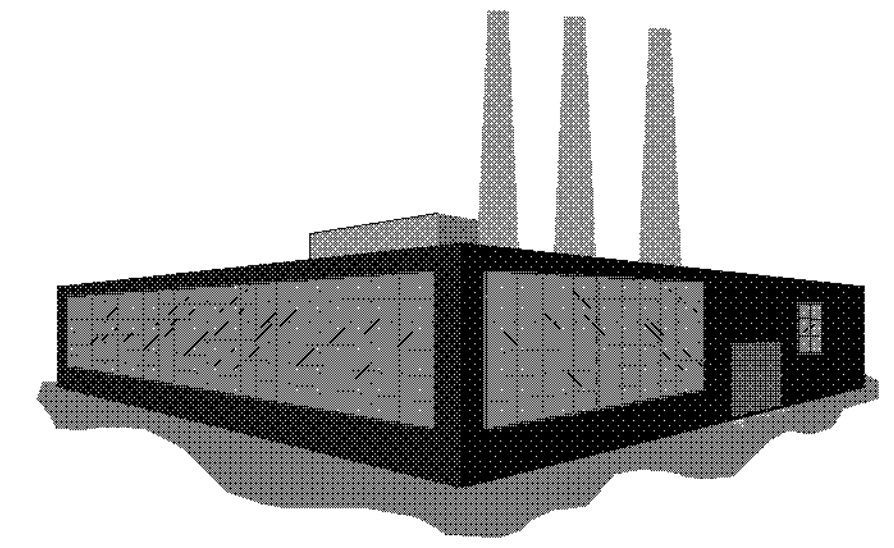
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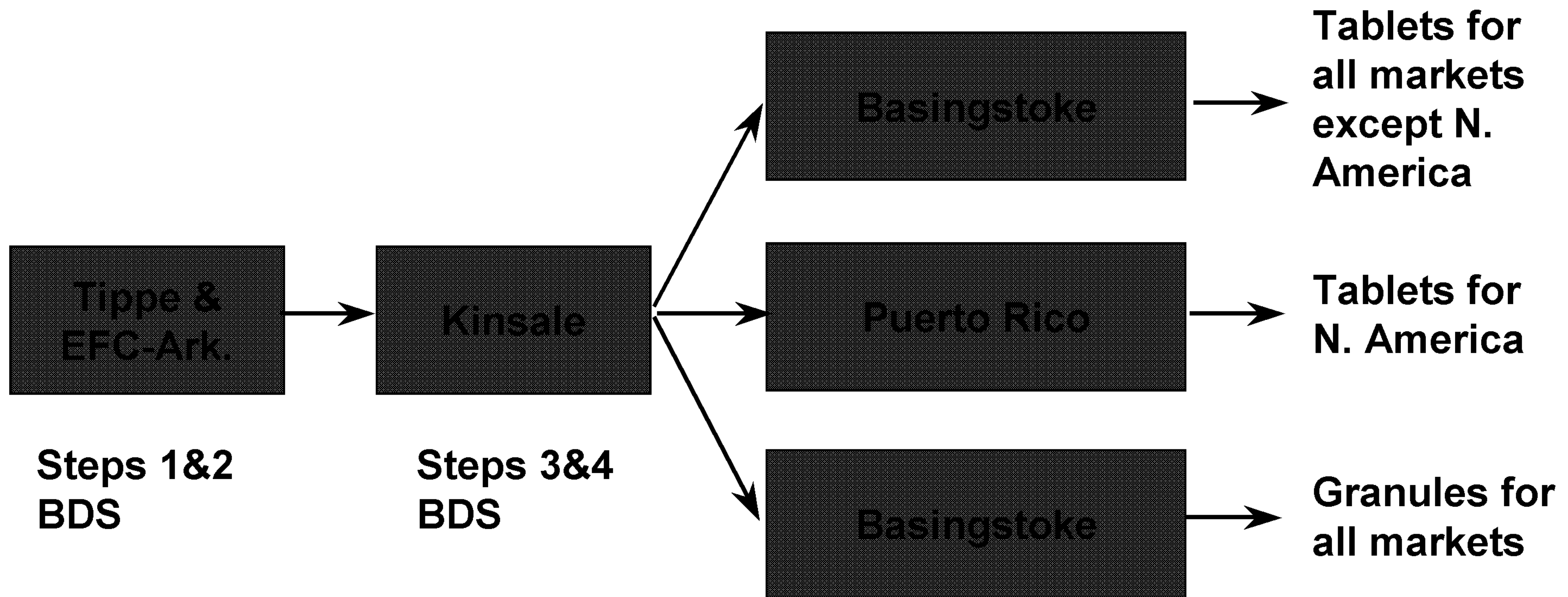




# CM&C Strategy



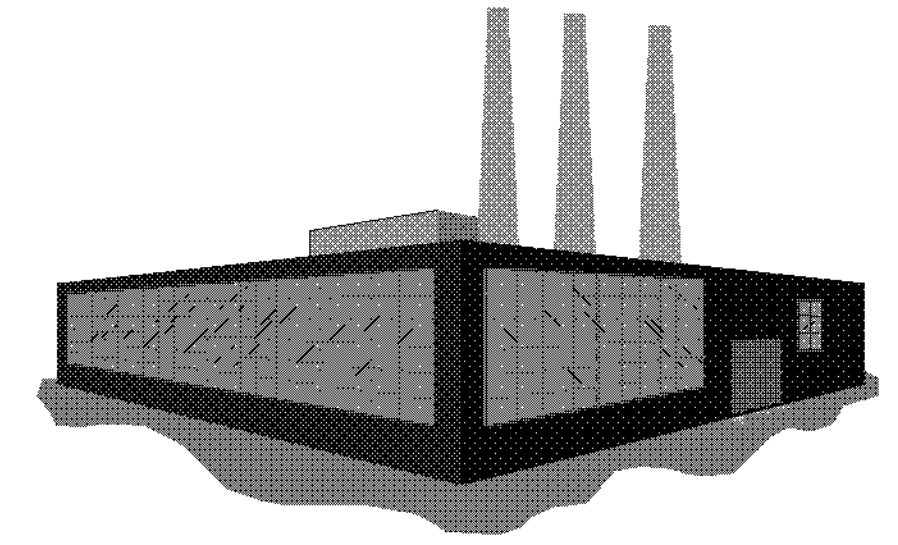
## Sourcing Strategy for Marketed Products at Launch



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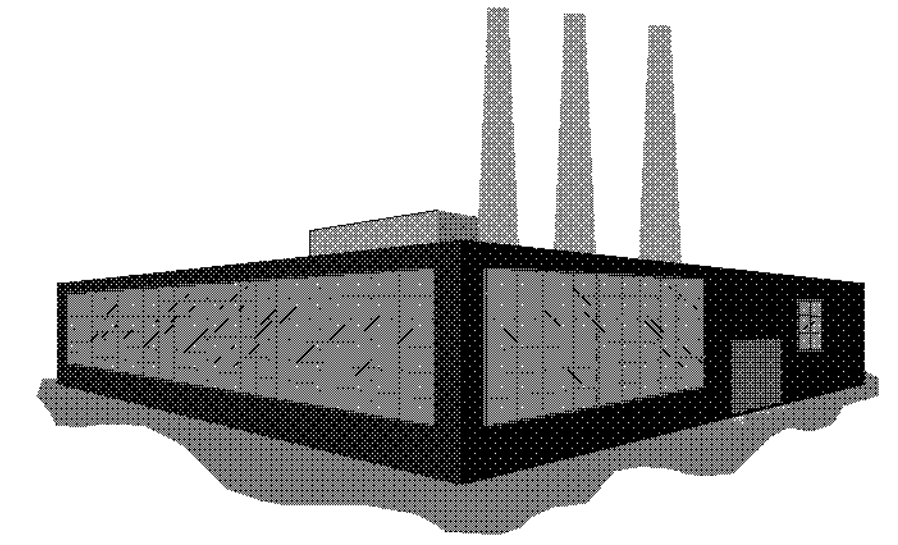


## CM&C Key Strategies

- **Early site involvement in process and method development**
- **Early validation of bulk and product**
- **Generate stability data for submission on validation lots**
- **Use validation lots to supply CT's where possible**
- **Bracket dosage strengths for validation/stability**

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## **CM&C Deliverables - Stage I**

- **Validate BDS at Kinsale**
- **Validate tablets at Carolina and Basingstoke**
- **Manufacture granule stability lots at Basingstoke**
- **Generate stability data**
- **Complete CM&C packages  
(NDA, dossier, Canadian NDA)**

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## **CM&C Deliverables - Stage II**

- **Validate granules at Basingstoke**
- **15 mg tablet NDA amendment strategy based on current formulation**
- **Assure manufacturing sites prepared for FDA pre-approval inspection and launch**
- **Participate in formation/action steps of cross-functional launch team, including emerging market strategy**
- **Investigate cost-benefit of developing 20 mg tablet and alternative smaller 15 mg tablet**
- **Pursue customer -focused line extension plan**
- **Support aggressive CT needs for commercialization studies**

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# CM&C Line Extensions - Status

<u>Formulation</u>	<u>Strategic Partner(s)</u>	<u>Status</u>
Zydis rapid-dissolving tablet	Scherer DDS AAI	Agreement signed, Poor performance from Scherer so far
Short-Acting IM injection	Cook Imaging (AAI?)	Formulation development in progress
15 mg tablet	-----	Project plan roughed out Stability lots in PR 10/95
Depot Injection	1. Atrix 2. Polymicrospheres 3. Southern Biosystems 4. Others?	Feasibility studies in progress; test lead formulations in dogs 1Q96? High degree of technical difficulty and uncertainty
Patch	1. Lohmann Therapie Sys. 2. Cygnus Therapeutics	Feasibility studies to be completed 3Q95. Select strategic partner 4Q95
Granules	B - L	Stability ongoing validation 4Q95
15 and 20 mg tabs GDT/dle	?	Business case pending

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# Additional Formulations Approximate Timeline

<u>Formulation</u>	<u>Target Submission Date</u>
Granule	1996
15 mg Tablet	amend NDA?
Zydis Tablets	1997
Short-Acting IM.	1997
Patch	1998
Depot Injection	1999

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## Line Extension Team

- **Co-chairs:** Tom VanAbeelee (DPM) and Paula Franz (PPM)
- **Focus:** Develop and implement plans to successfully register those line extensions important to our customers
- **Team will function much like a project team**
- **May need additional support from Tippecanoe Development for some line extensions**

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## Global Launch Team

- **Co-chairs:** Beth Morris (DPM) and Rob Schmid (Marketing)
- **Focus:** Prepare global readiness and strategies to have product available in minimal time at optimal quantity ASAP after approval

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# ***HWT***

# ***Commercialization***

# ***Strategy***

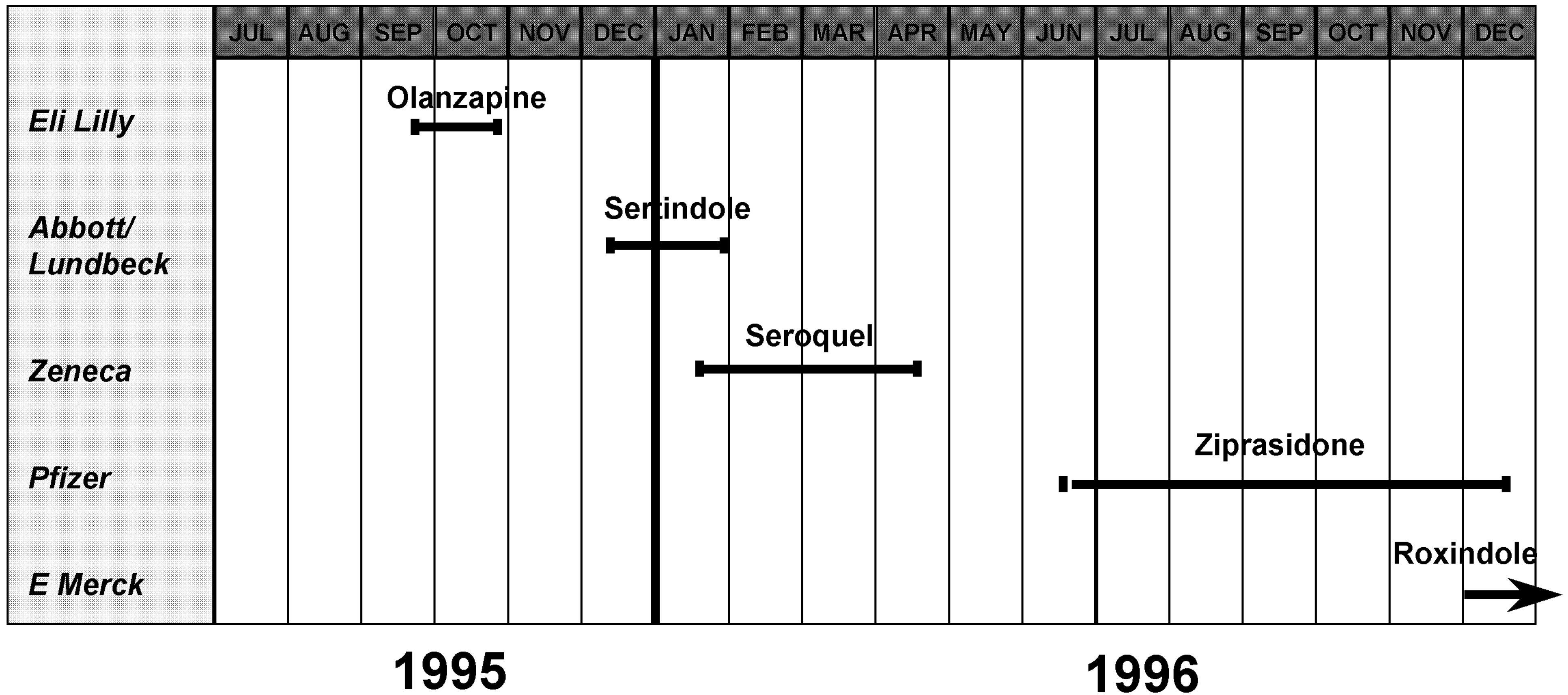
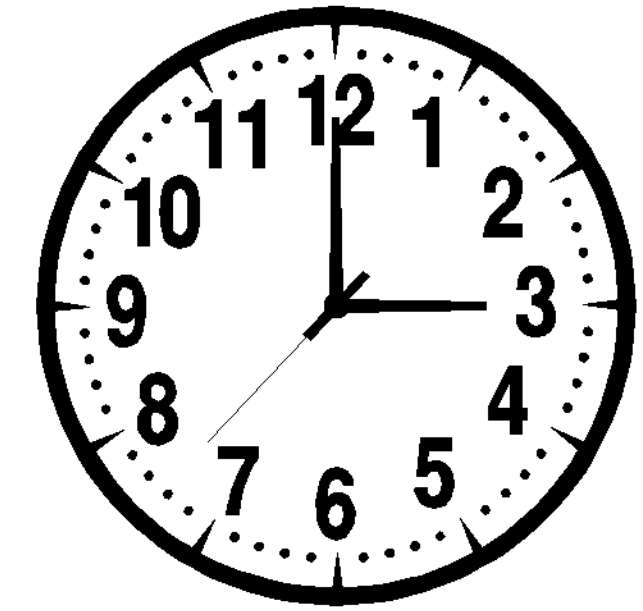
- **Be next**
- **Be better**
- **Be global**

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# Be Next!



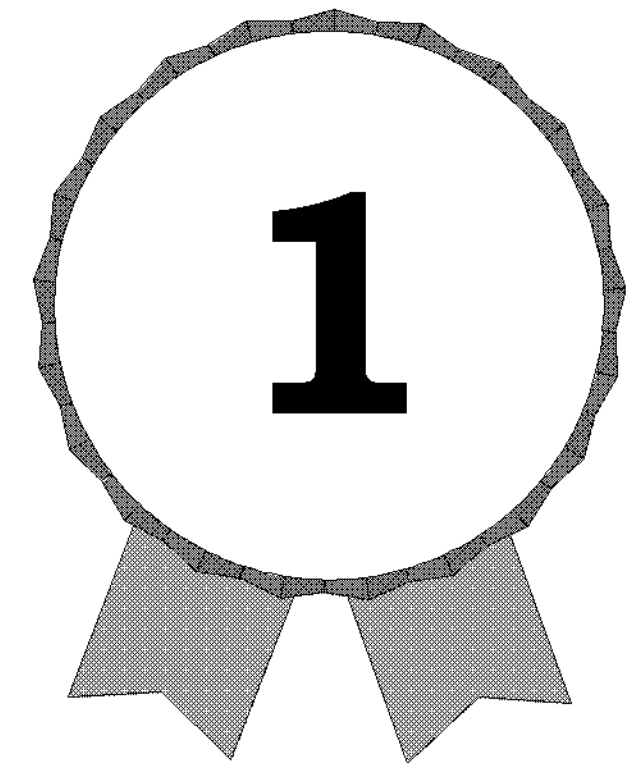
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# Be Better!

## Olanzapine/Schizophrenia Strategy



### Goal:

**Customers worldwide will recognize Lilly/olanzapine as the company/antipsychotic that delivers optimal therapeutic and economic outcomes.**

### Strategy:

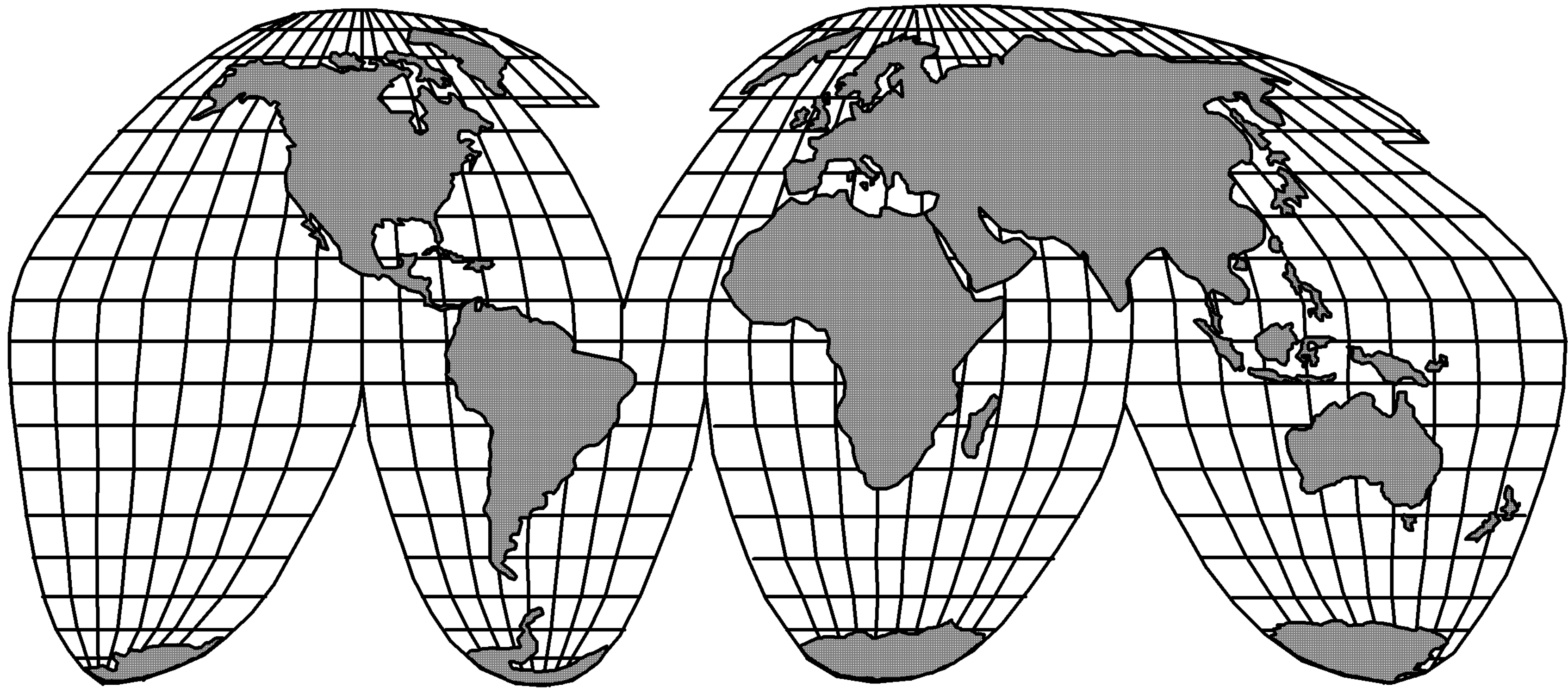
- Speed to global markets
- Customer focused product development plan
- Redefine standard of care and position olanzapine as the standard of pharmaceutical care
- Aim for rapid and broad market penetrations
- Participate in emerging markets

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# Be Global!



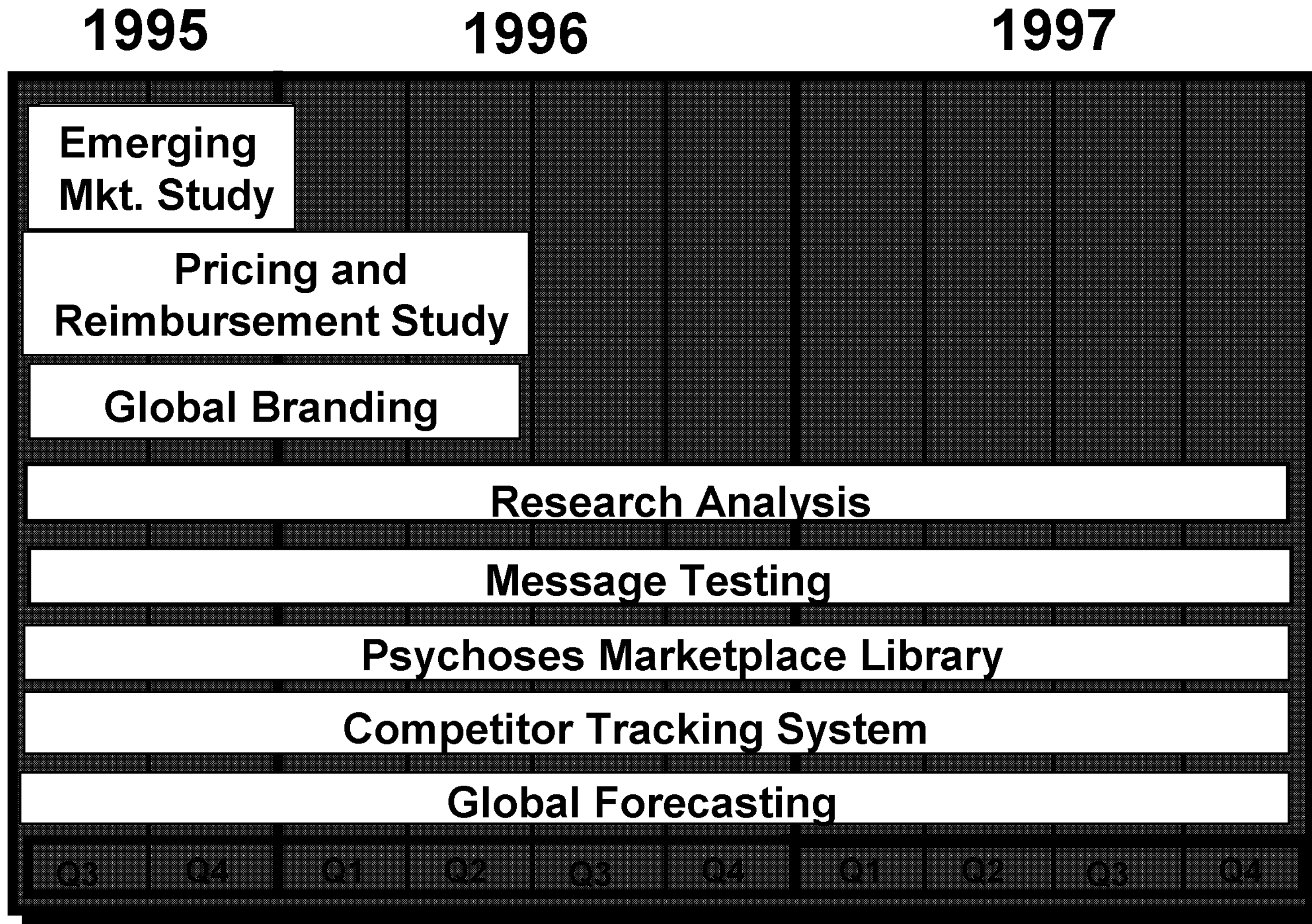
**Develop a global marketing strategy around a consistent brand name and image that is shared by all of our affiliates and recognized by all of our customers**

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# Olanzapine Market Process Timeline



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# Stage I

## Commercialization: Positioning For Rapid and Broad Market Penetration

- **Undertake aggressive pre-launch marketing activities**
  - energize affiliates to commit resources to implement pre-marketing strategies and programs
  - initiate market research studies
  - craft a product image/branding
  - evaluate opportunities for additional indication
  - develop publication/symposia plan
  - initiate global pricing studies

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## **Stage II**

# **Commercialization: Putting The Strategy Into Place**

- **Finalize global branding**
- **Achieve consensus on a global price(s) that optimizes economic return and assures access to as many global patients as possible**
- **Complete development of preapproved promotional materials**
- **Finish an emerging market analysis**
- **Integrate Japanese market planning into the global strategy**



## Stage III

# Achieve Rapid and Broad Market Penetration and Implement an Aggressive Growth Plan

- **Implement post-launch marketing strategy to gain broad market access and maximize shareholder benefit**
  - do what it takes (i.e., strategic alliances, bundling products/services, risk sharing)
  - manage global brand
  - maximize clinical opportunities through Plan D process
  - introduce line extensions in planned manner
  - ongoing competitive analysis and aggressive strategy
- **Manage effective corporate communications plan**



# Zyprex

- **Global branding strategy**
- **Globally pre-approved materials provided to affiliates**
- **Pricing**
- **Packaging**
- **Market research**
- **Communication strategies**

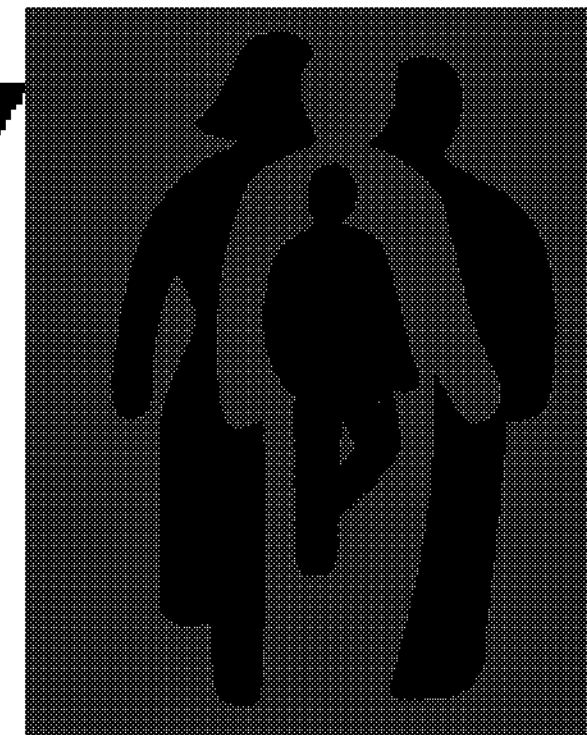
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**ZYPREX**  
Olanzapine

*Making re-integration the standard. . .*

**ZYPREX**



Olanzapine - Lilly

*Antipsychotic power for routine use*

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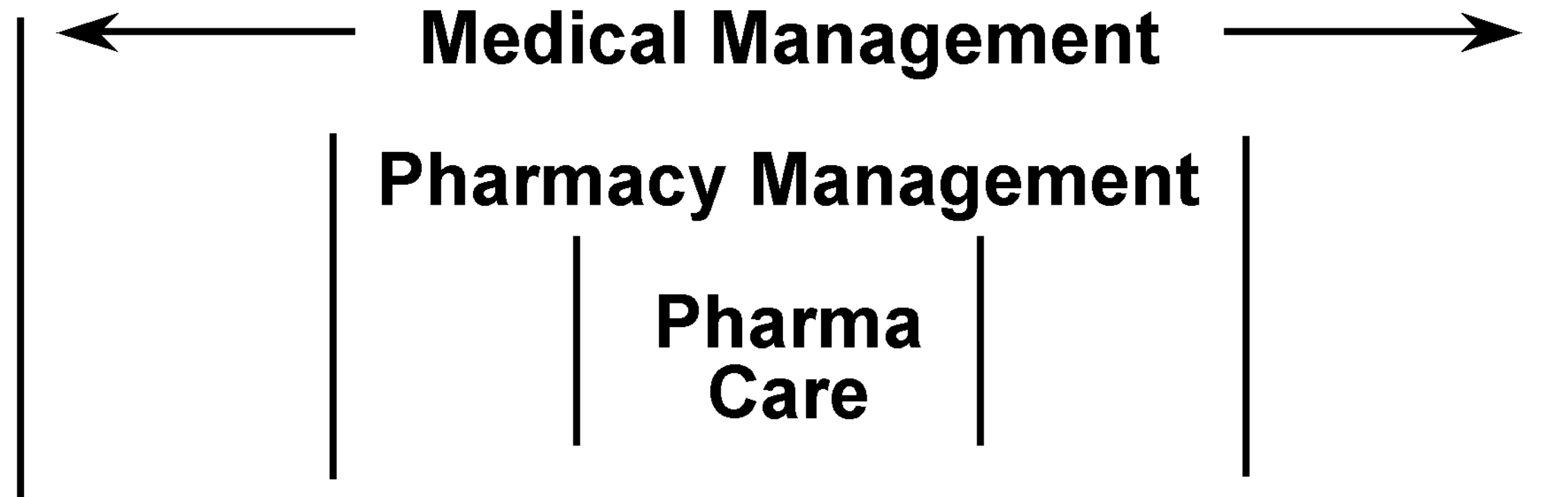
# *Healthcare Solutions*

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# Lilly Disease Management Offerings



<b>Pharmaceutical Care</b>	<b>Lilly products and interventions/services that pull Lilly products</b>
<b>Managed Pharmaceutical Care</b>	<b>Core services, connectivity, and interventions/services and management for total pharmaceutical care</b>
<b>Medical Management</b>	<b>Delivery of interventions/services and management for the clinical delivery of care to provide specific outcomes</b>

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# Program Goals

- **Improve treatment outcomes**
  - Enhance symptom control
  - Manage relapse
- **Lower cost of care**
  - Minimize re-hospitalizations and LOS
- **HRQL outcomes**
  - Optimize functional level
  - Enhance social reintegration
  - Decrease caregiver burden

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# Program Structure

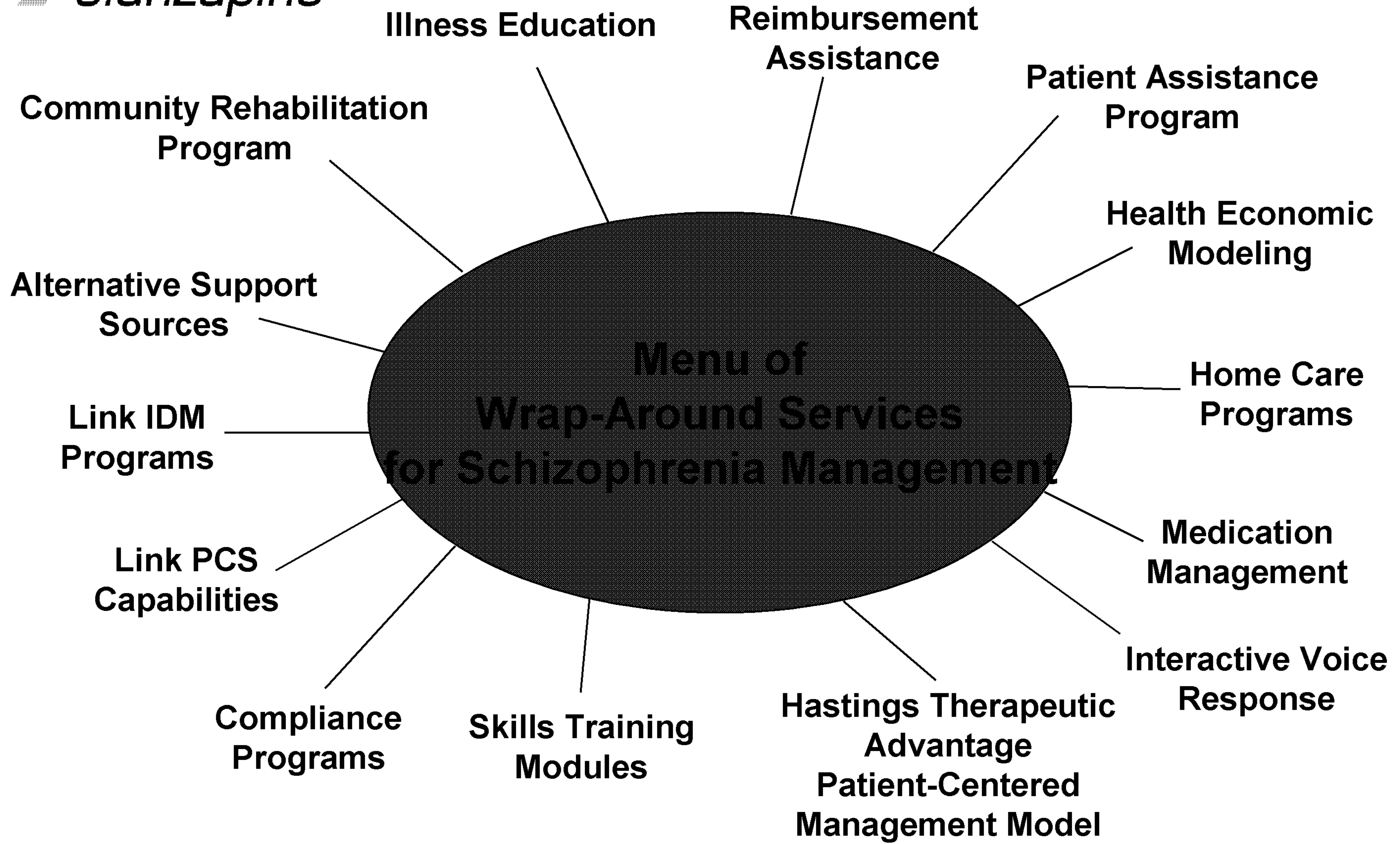
- **Comprehensive group of tools and resources**
- **May be used either independently or as an integrated system**
- **Accessible to providers, caregivers and consumers**
- **Flexible**
  - **Work within all after-care system organizations**
    - » **Mental health care-out/in**
      - e.g., Charter hospital
    - » **STAR/partial hospitalization**
    - » **CMHC/clubhouse**
    - » **Adaptable for international use and with other products**

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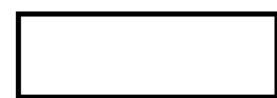
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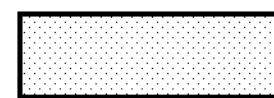
# Flexible Service Offerings



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Available Launch



Post Launch

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# *Key HWT Points*

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# Two Aspects of the Heavyweight Team

## Team's Mission

1. Expedite launch in two-thirds of the global major markets
2. Optimize the early commercialization of the product

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# HWT Innovations/Learning Points

- **Product leadership**
  - focused accountability
  - vision - creating it/realizing it
  - rapid response to opportunities
  - product champions set the example
    - » ex. core team sets priority, gets buy-in, problem solved
- **Co-location**
  - quicker resolution of issues
    - » more ownership of total project
    - » more team spirit
    - » shared goals
    - » enhanced communication
    - » Olanzapine database vs redacted at same time point in life cycle shows improved quality

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## **HWT Innovations/Learning Points - cont'd.**

- **Reallocation**
  - apply a resource when and where it is needed
  - one priority, achieving product milestones
    - » ex. reallocation of systems analysts to cover a 14 day slip in the creation of the HGAO reporting database
- **Decision making**
  - delayed
  - concentrated
  - prompt
    - » ex. Pharmaco database error; required rerunning 300 reports. No project delay despite initial optimistic view minimum one month delay in re-creating reporting database.

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## **HWT Innovations/Learning Points - cont'd.**

- **Efficiency**
  - ability to re-engineer methods in response to unexpected challenges/complications
    - » ex. parallel report writing
- **Having Core Team member on each “work group” facilitates getting things done**
- **Work Team “removes layers”**
  - allows upper management to see issues early on and take action

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## **HWT Innovations/Learning Points - cont'd.**

- **Cross-functional team involvement earlier in process**
  - catch issues earlier and save time
    - » ex. Canada Study  
In review of an amendment for this study by a cross-functional group, data quality issues became apparent and we averted a possible incomplete database

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## **HWT Innovations/Learning Points - cont'd.**

- **Quality of the work environment**
  - “before some people didn’t even know others on the project”
  - a more relaxed atmosphere
  - “has given everyone an identity they didn’t have back in their functional areas”
  - “more influence/greater responsibility” to the individual
  - individuals have a “better overview of the entire project and a better understanding of what their colleagues are doing”

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## **HWT Innovations/Learning Points - cont'd.**

- **Launch strategy**
  - dedicated global launch team leader instead of having multiple launch teams should provide focus yielding quality and speed to launch planning and execution
- **Earlier dedication of resources to commercialization studies than in old paradigm**
  - quicker market penetration
  - earlier submission in Type II countries

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## **Process Improvement - Registration Planning**

**Develop a registration strategy to ensure submission by October 1995 in North America, Europe, Israel, South Africa, and Australia. Submit in Japan by October 1996.**

- **Hold all non-essential, nonregistration activities until after submission.**
- **Identify current resources and headcount for registration in all affiliates and compare with the level of resources needed to address critical registration issues. Resource adequately to meet registration milestones.**
- **Aggressively expedite filling of open requisitions across countries and components and recruit for expertise in the process.**
- **Utilize routine teleconferences to proactively identify resource issues across countries and components.**

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# Process Improvement - Registration Planning

- Early regulatory summits { info sharing  
trouble shooting
- Got approval from FDA to not submit paper CRF's (reduced submission by 200 volumes or 100 trees saved. Reduced assembly time/quicker review.
- Dialog with FDA to initiate pre-submission early review. Expedite review.
- Data browser (user-friendly review)
- Pre-submission rapporteur discussion with EMA (optimize choice - shorten review/minimize issues)

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# **HWT Innovations/Learning Points - Conclusion**

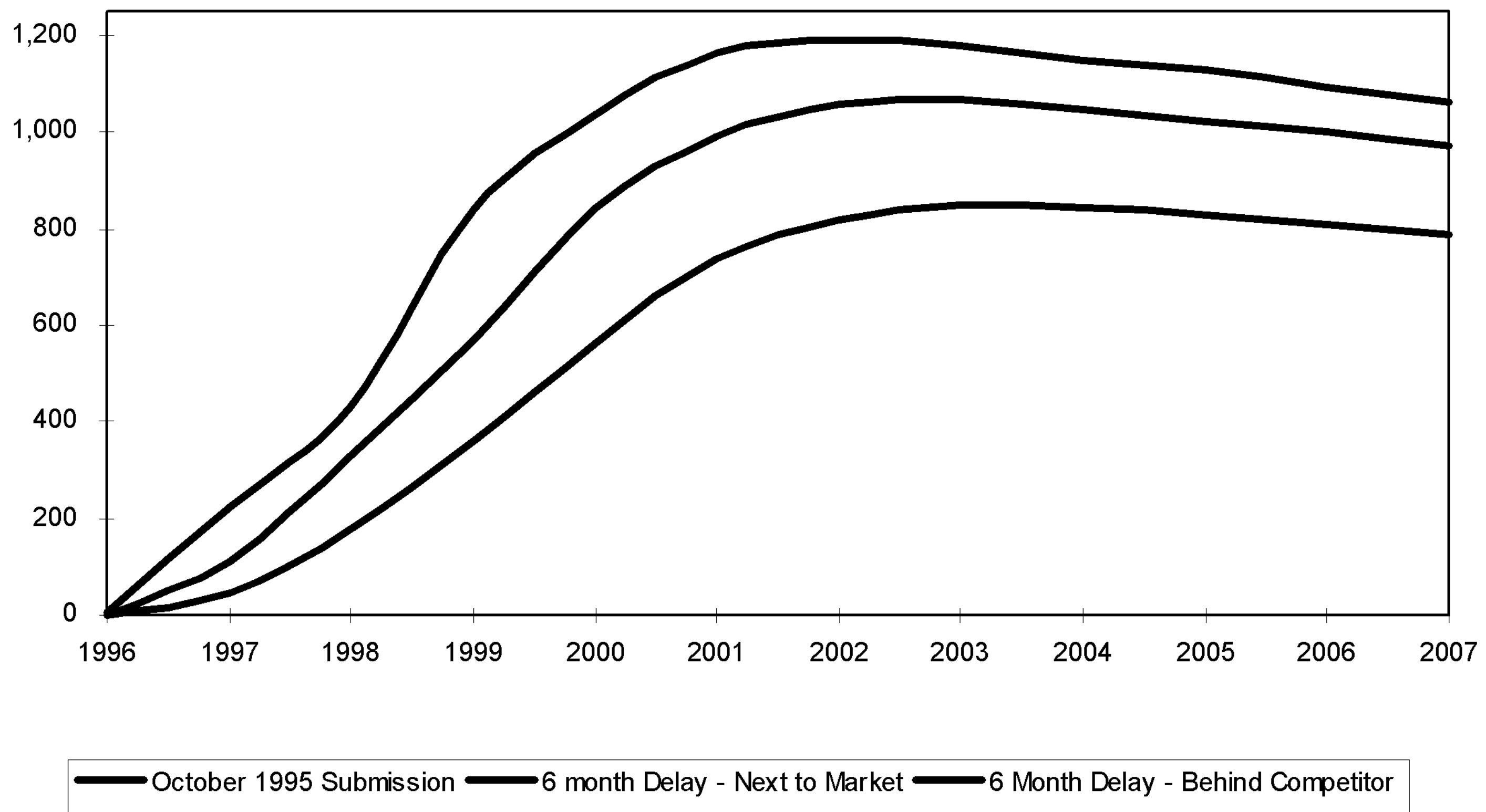
**In a superior work milieu, a HWT can better employ valuable and finite resources to deliver both quality and speed resulting in a superior EVA to Lilly shareholders**

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## Effects of 6 Month Launch Delay

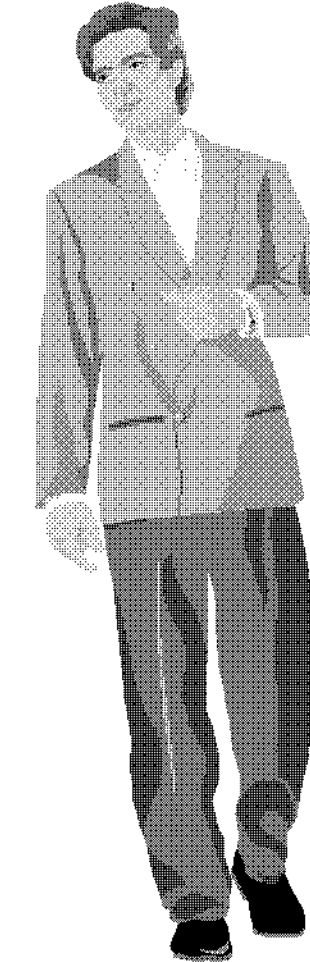
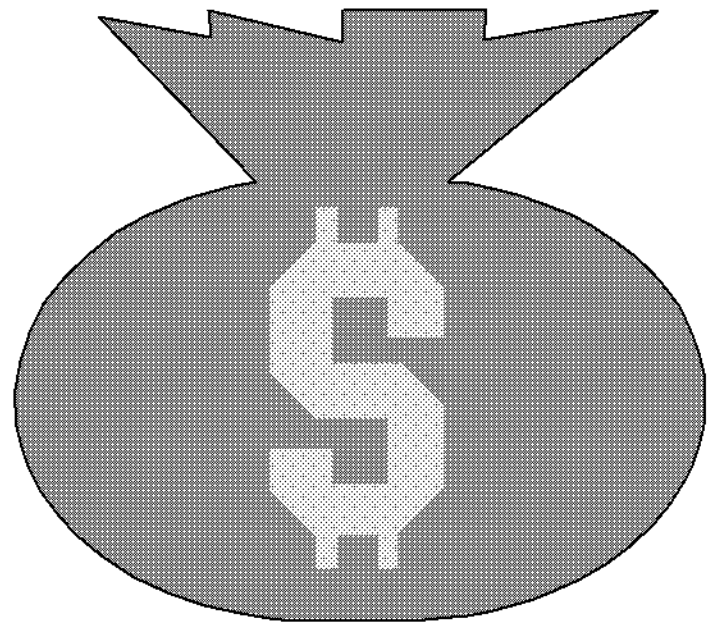


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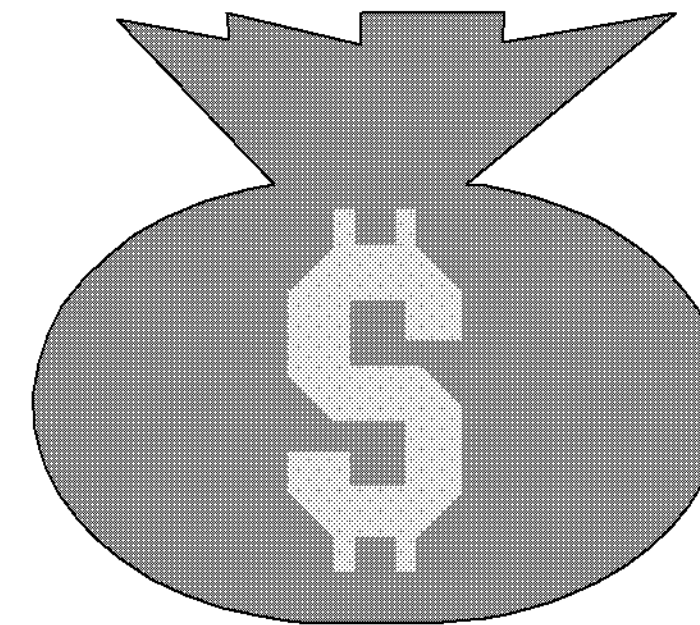
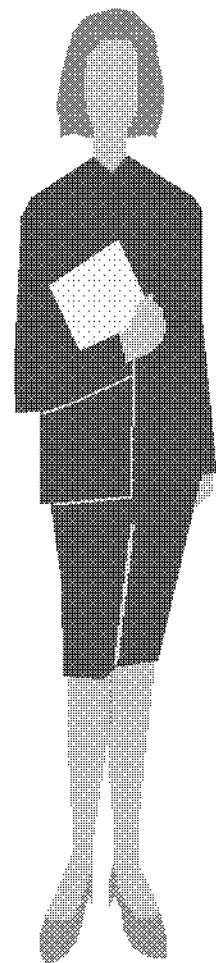
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**ZYPREX**  
*Olanzapine*



# *Resources*



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**“Formation of a heavyweight team does not need to imply heavy resource commitment...**

**It is a process where resource intensity should vary during the development cycle.”**

**W. C. Fields**

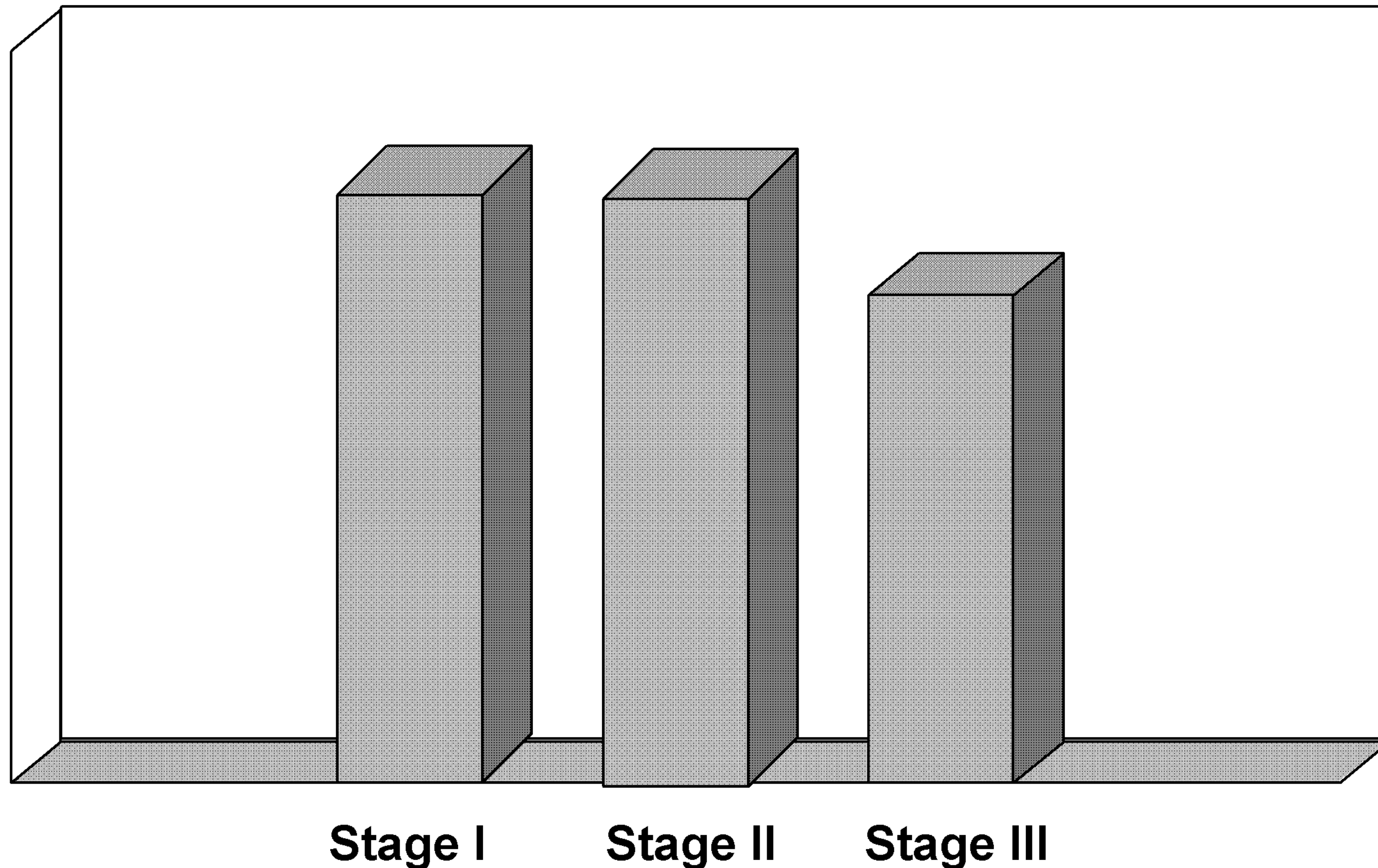
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# HWT Resource Requirements

Resource Intensity



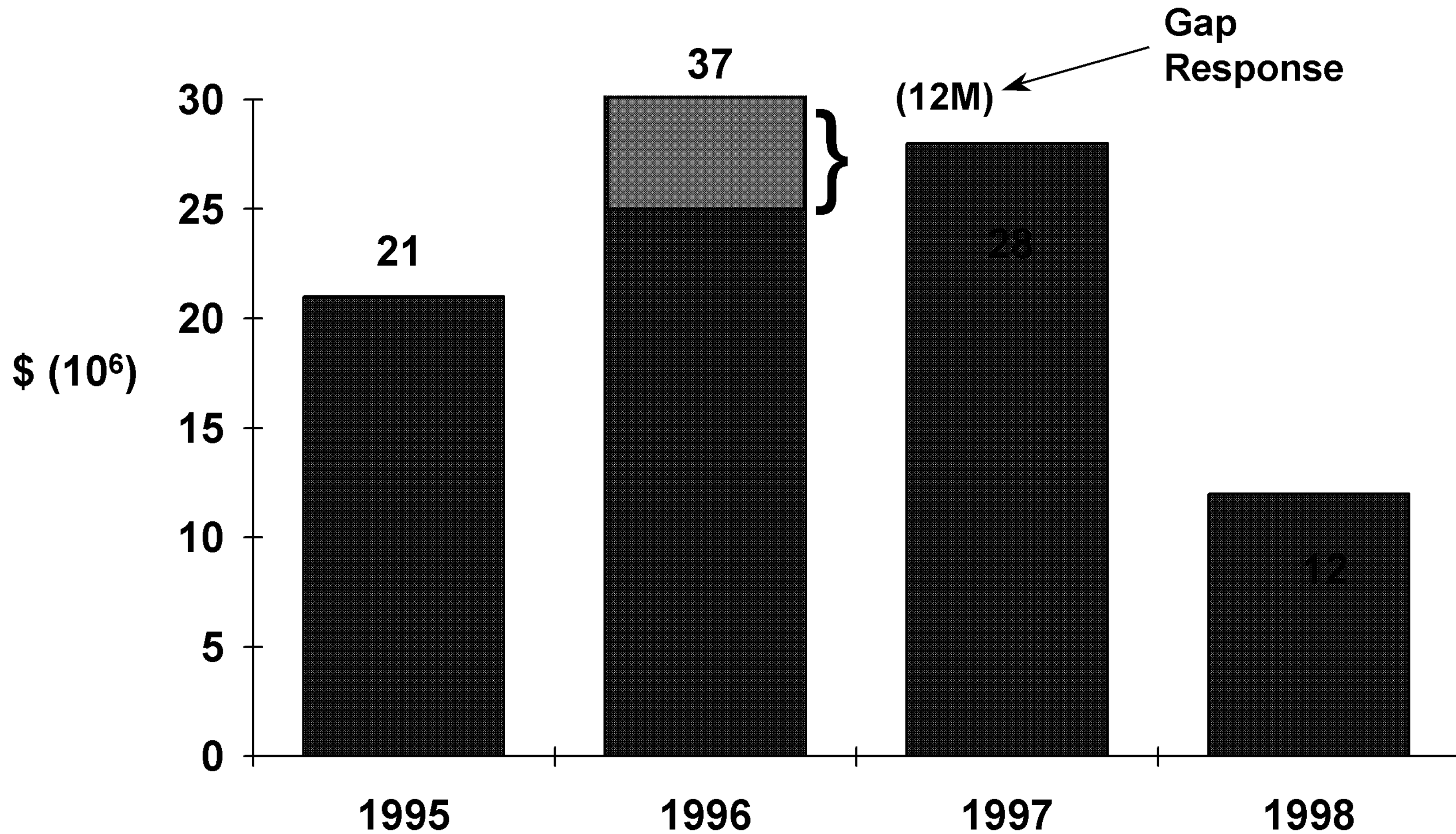
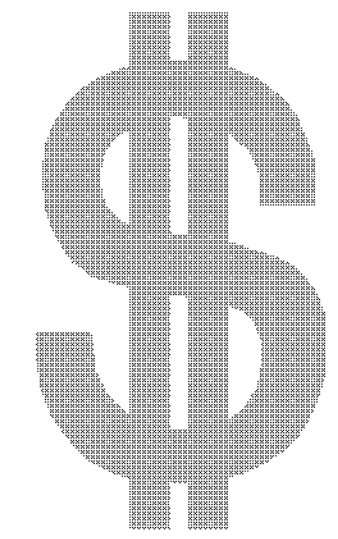
**Key - A nucleus of product core competency (experience) must be maintained through the cycle i.e., succession planning**

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# Resourcing: Medical Clinical Grants - \$



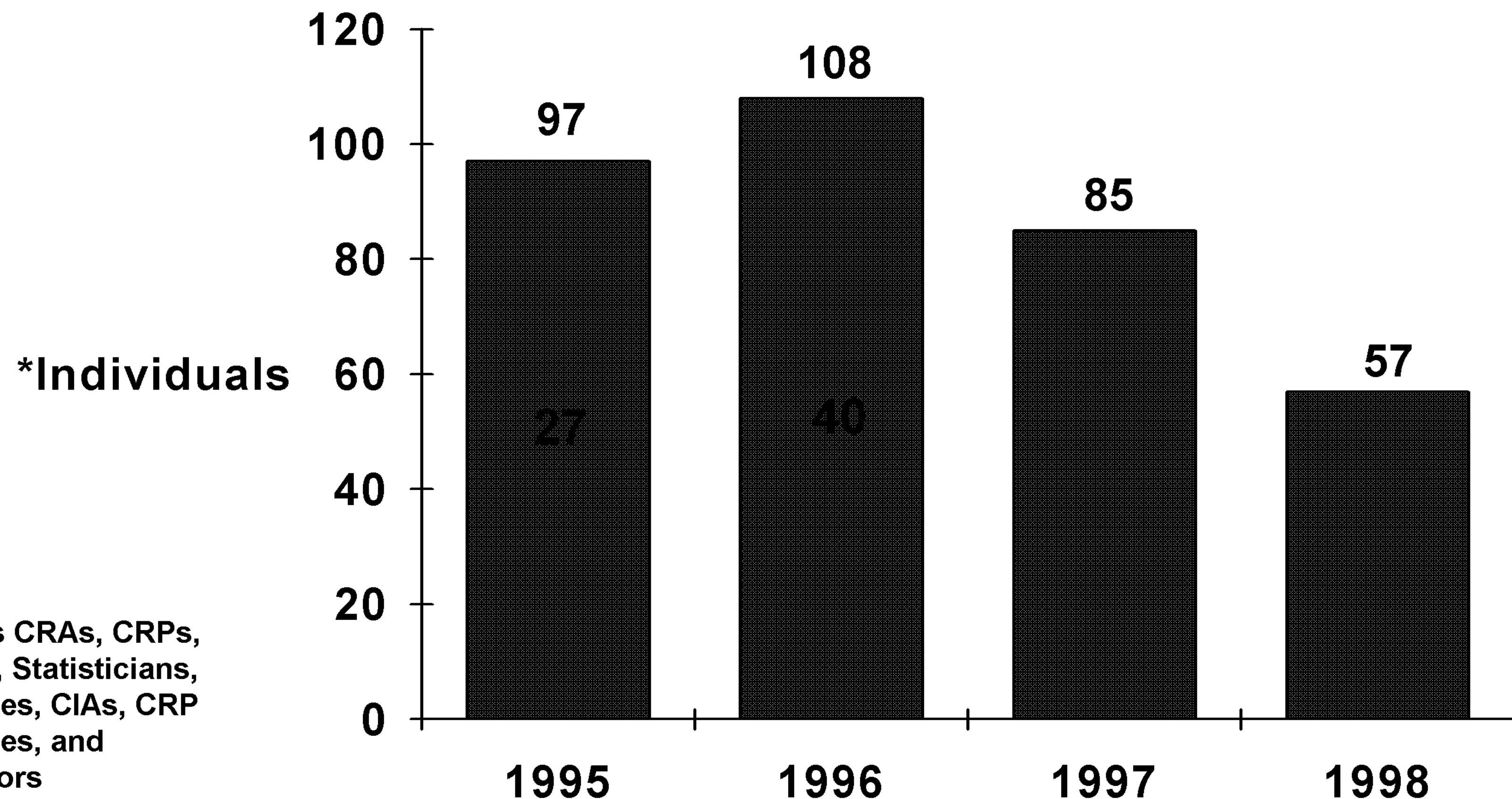
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# Clinical Grants - Medical Plans and Data Management Headcount



\*Individuals

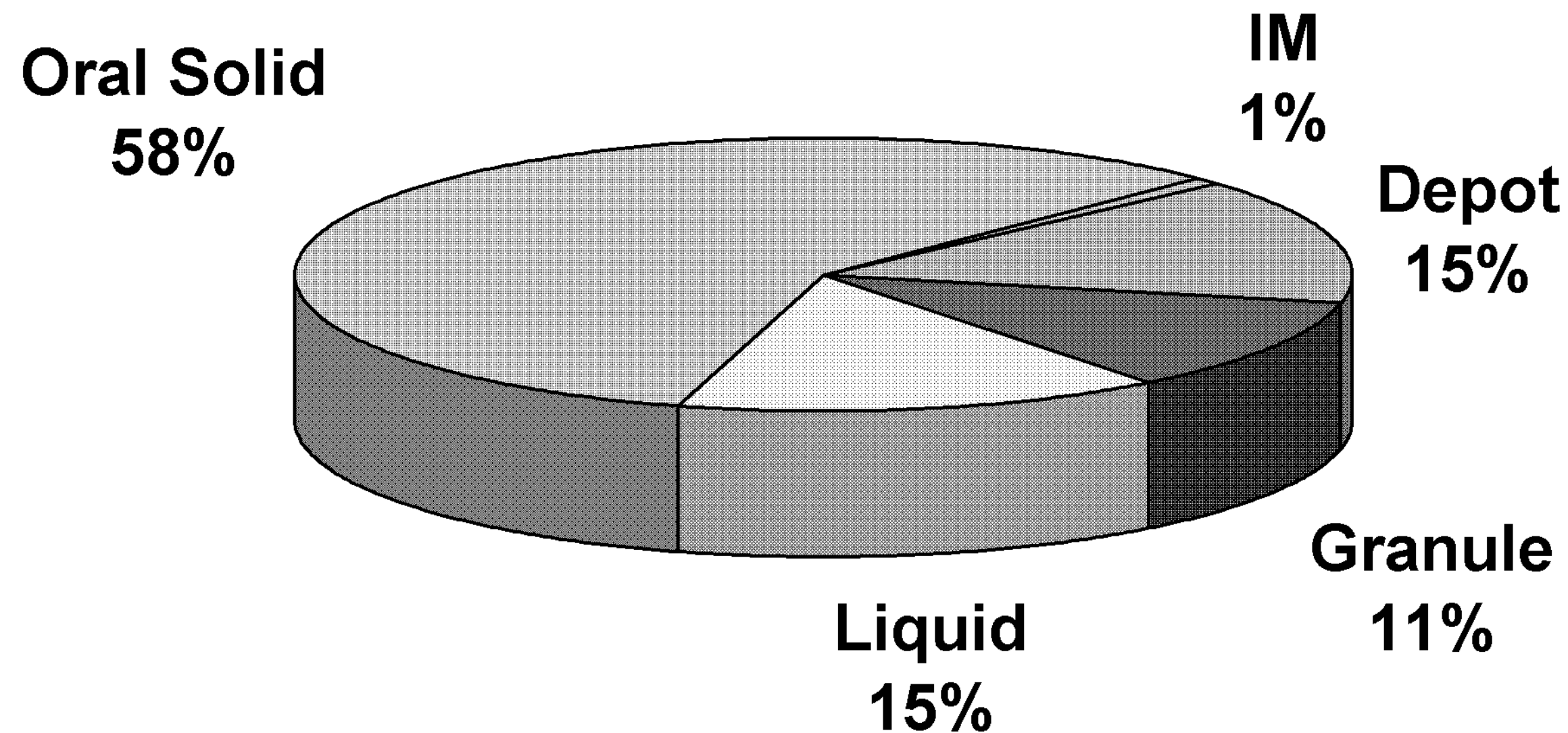
\*Includes CRAs, CRPs, Systems, Statisticians, Secretaries, CIAs, CRP Secretaries, and Contractors

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# Resourcing a Customer-focused Product Development Plan

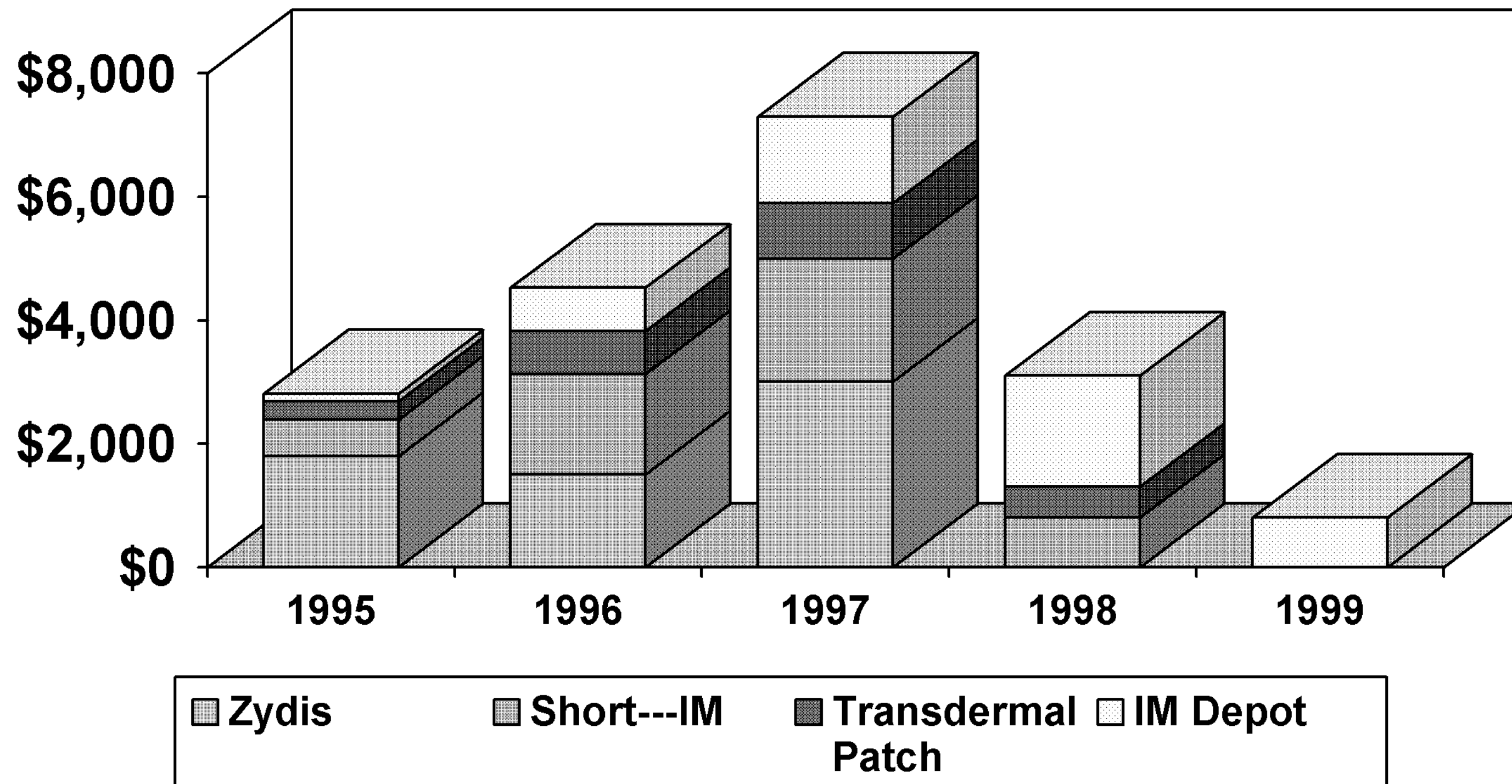


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# Expenses - Dollars (000's)



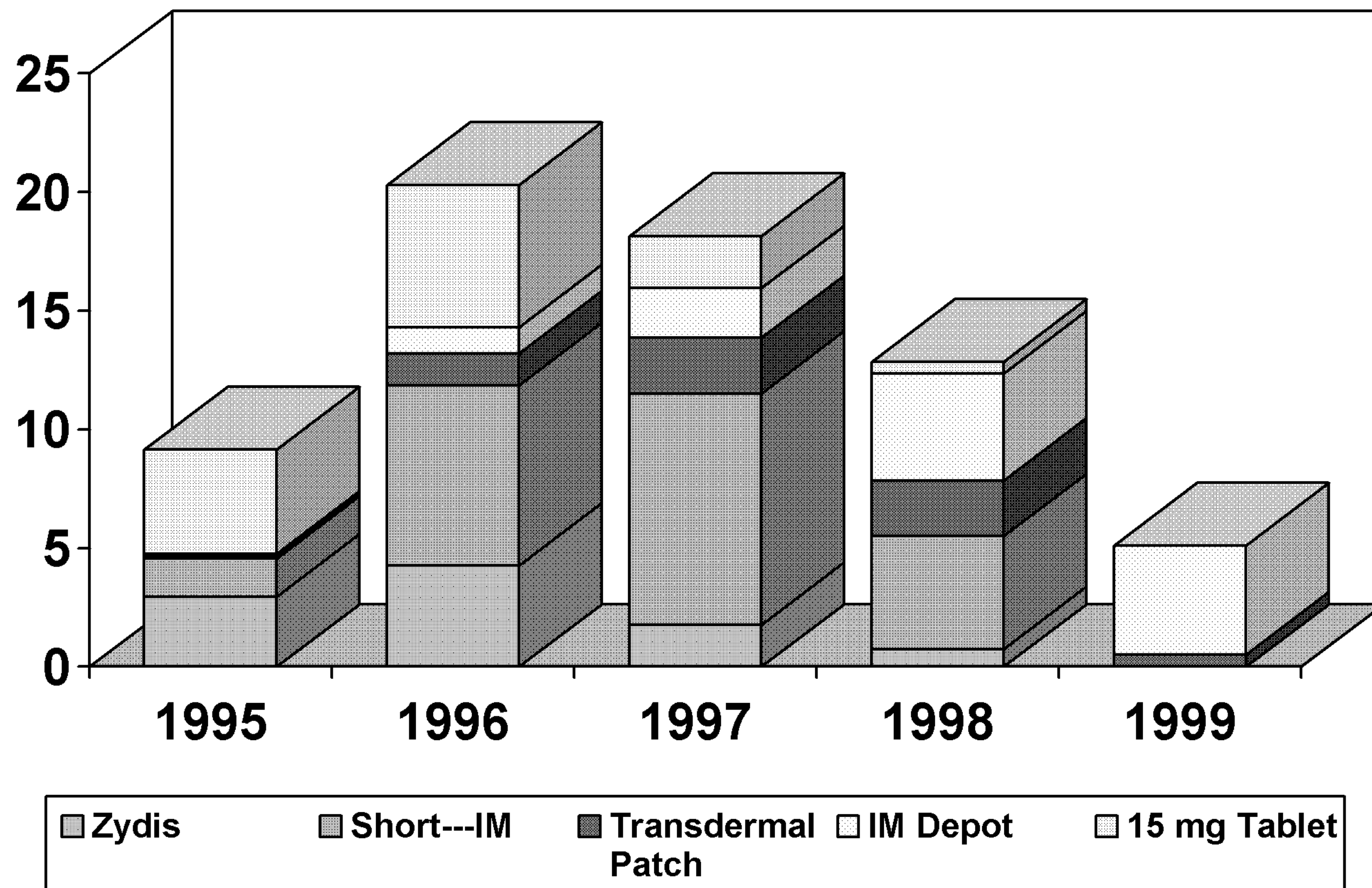
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# Internal Resources (FTE's)



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# GAP Analysis

- **Immediate needs:**
  - RA-CMC for Zydis®
  - Analytical development for 15 mg tablet
- **Yet undefined additional resources anticipated in 96-98 for other line extensions**

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# ***GPAC Issues***

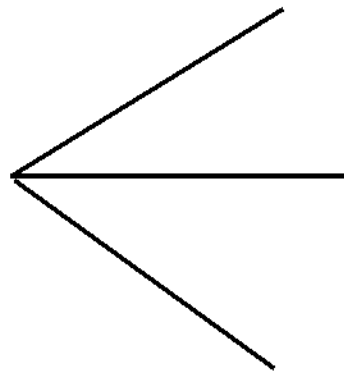
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## Issues

# What the HWT Would Like from GPAC

- **Affiliate accountability/prioritization**  **launch readiness  
opinion leaders  
cultivated  
marketing plan**
- **Development resources - line extensions in GPAC prioritization exercise**
- **Japan - mandate that the HWT is empowered/accountable or role clarification**

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## Issues

# What the HWT Would Like from GPAC - cont'd.

- **Budget**
  - a single cross-functional budget to provide flexibility, control, and accountability
- **Human resources**
  - acknowledgment that registration, commercialization, and speed to launch initiatives are essential/post October 1 the work is not over
  - recognition/protection of current team members' 2-3 year commitment to the project
  - support a planned, orderly succession strategy when opportunities for team members to assume senior roles as other projects emerge

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# Conclusion

**HWT...**

- **Work!**
- **Represent a process improvement < speed efficiency**
- **Create a better work environment**
- **Add economic value**
- **Require adjustments by us all**

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**ZYPREX**  
*Olanzapine*



**If you can't run with the Big Dogs...  
stay on the porch!**

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# Olanzapine HWT 3 Year Plan (Estimate)

	<u>95 F</u>	<u>1996</u>	<u>1997</u>	<u>1998</u>
<b>Subtotal Grants</b>	<b>21,273</b>	<b>36,834</b>	<b>27,863</b>	<b>16,846</b>
<b>Subtotal Med HCT</b>	<b>11,643</b>	<b>13,494</b>	<b>11,091</b>	<b>7,751</b>
<b>CRP/MGMT</b>	<b>750</b>	<b>780</b>	<b>811</b>	<b>844</b>
<b>Project Coord</b>	<b>360</b>	<b>374</b>	<b>389</b>	<b>405</b>
<b>PPD</b>	<b>600</b>	<b>624</b>	<b>649</b>	<b>675</b>
<b>Regulatory</b>	<b>360</b>	<b>374</b>	<b>389</b>	<b>405</b>
<b>Subtotal Marketing</b>	<b><u>1,649</u></b>	<b><u>5,935</u></b>	<b><u>6,707</u></b>	<b><u>6,432</u></b>
<b>Total</b>	<b>38,284</b>	<b>64,351</b>	<b>54,607</b>	<b>39,790</b>

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