

Global Value Committee Review of Zyprexa

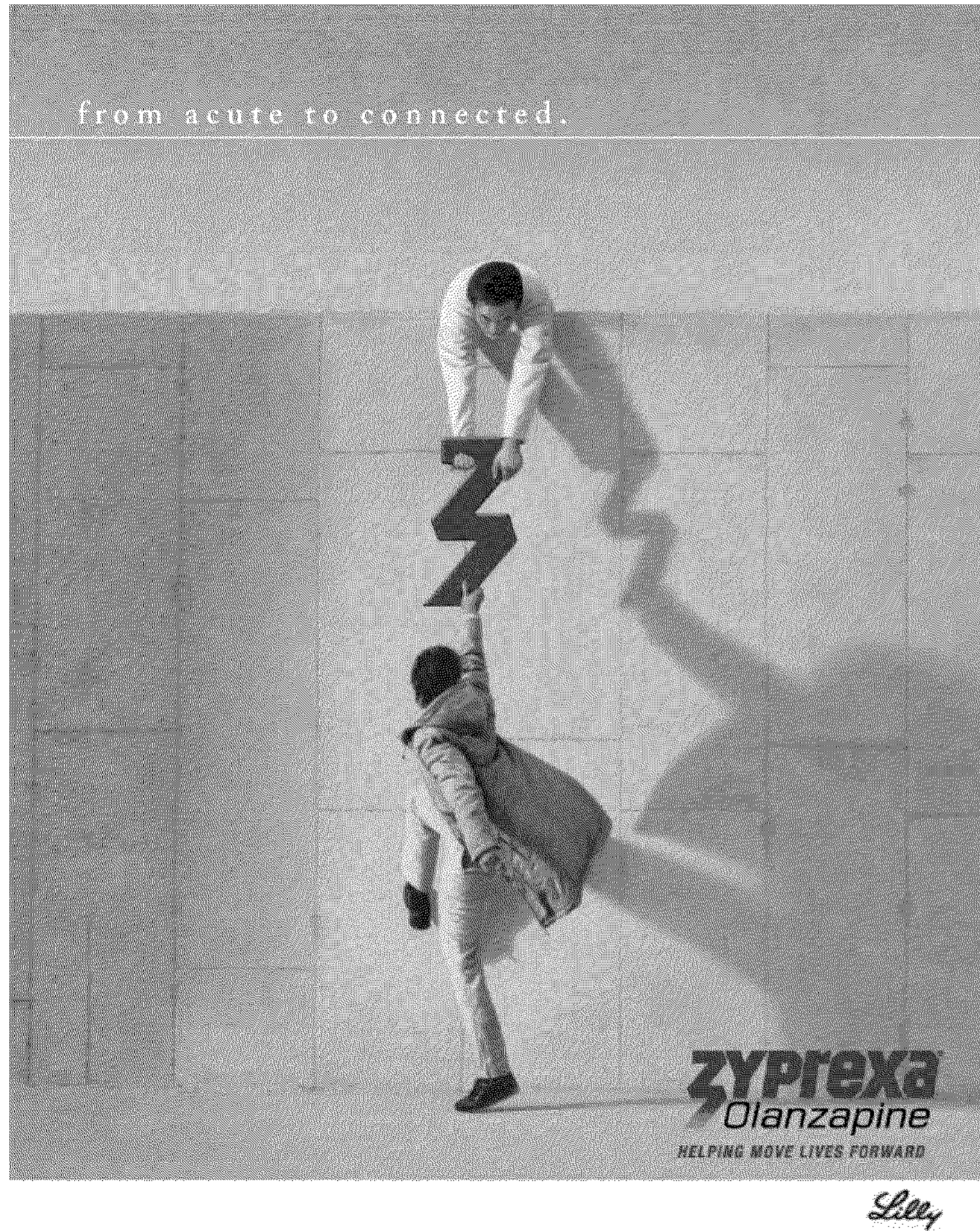
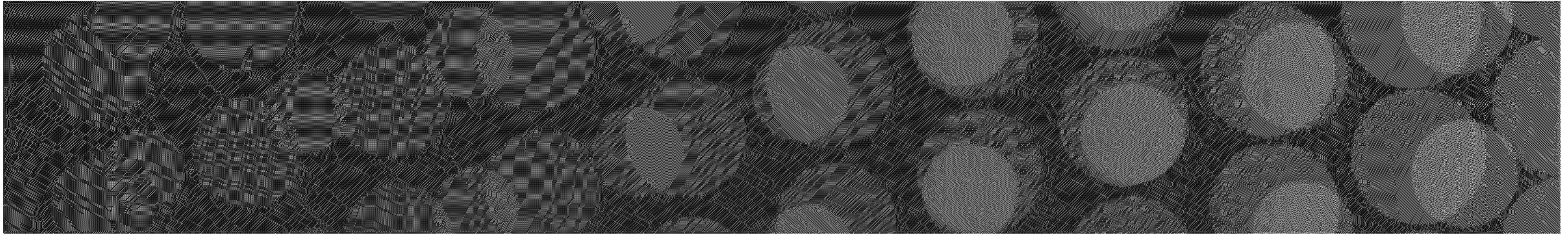
John Bamforth
Marion Enie
Alisa Lask
Madhav Namjoshi

Wednesday, August 28, 2002

Lilly
Answers That Matter.

Objectives

- Provide a brief overview of
 - Brand Strategy
 - Health Outcomes Research Strategy
- Review Health Outcomes Research issues
- Identify information/data gaps
- Outline action plans and assign responsibility

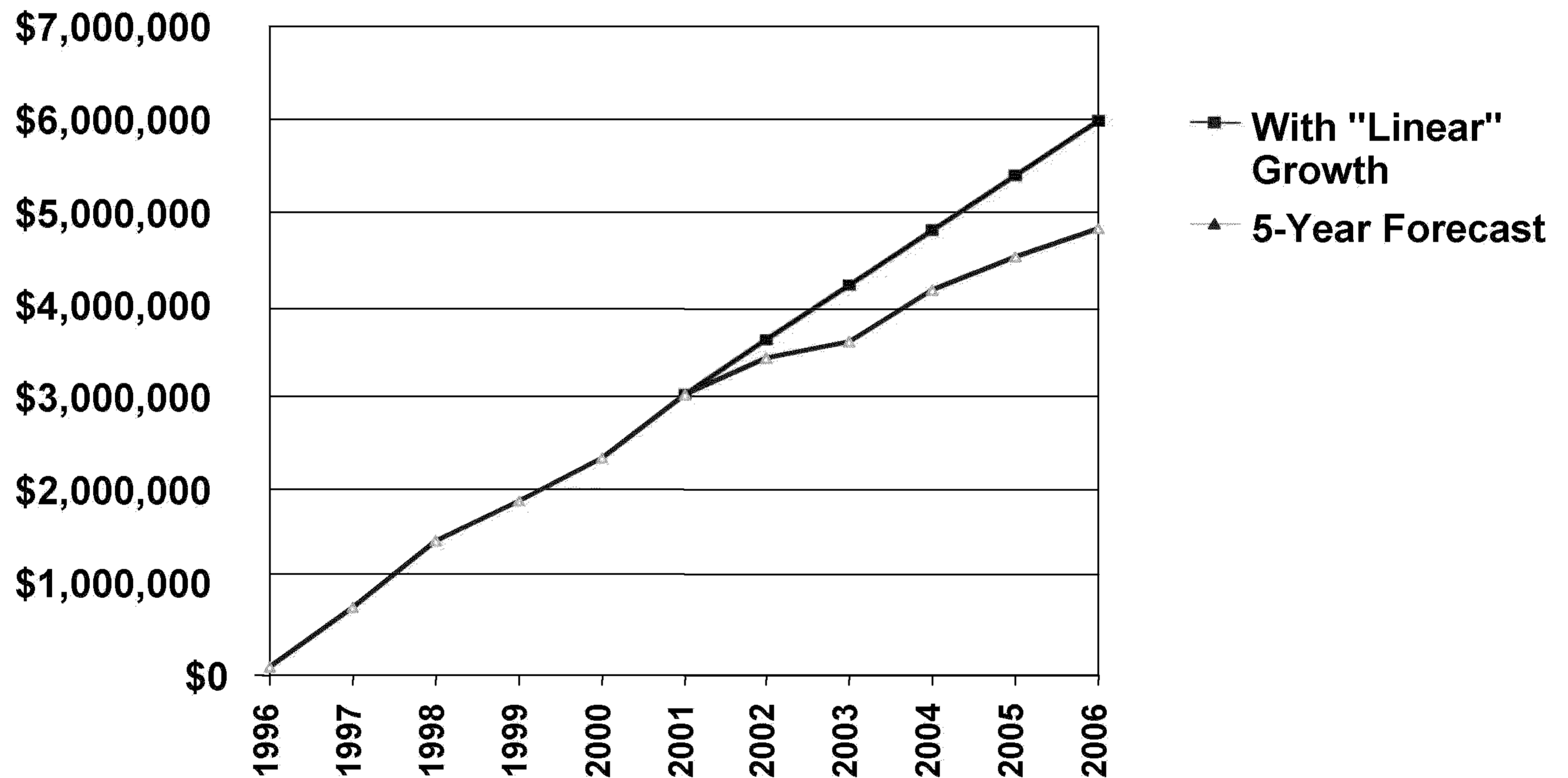


Brand Strategy Overview

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Strategic Intent

\$6 billion by 2006.....delivering linear growth!!



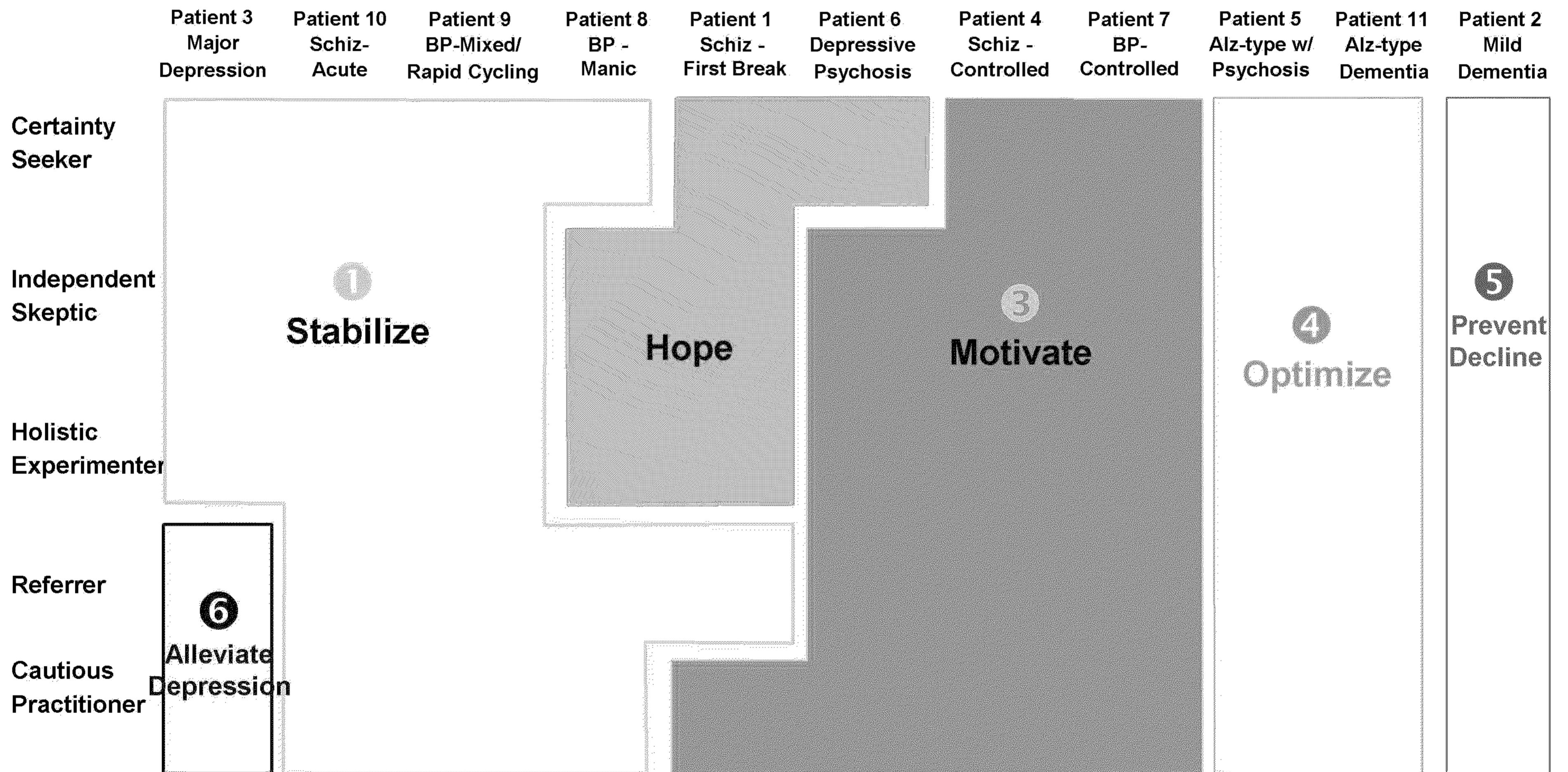
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Average growth per year from 1997-2001 = \$589 million

Zyprexa Strategy

- **What makes Zyprexa special?**
 - ZYPREXA is the Collaborative, Dedicated Leader that offers the **Dependable Control** you need to establish a more effective **Therapeutic Alliance** so you can help your patients begin to **move their lives forward and realize their potential.**
- **What are the Zyprexa core message elements?**
 - Dependable control
 - Therapeutic Alliance
 - Helping to Move Lives Forward

Segment Map (US Example)



The Choices we made!!

Stabilize

Hope

Motivate

Optimize

**Prevent
Decline**

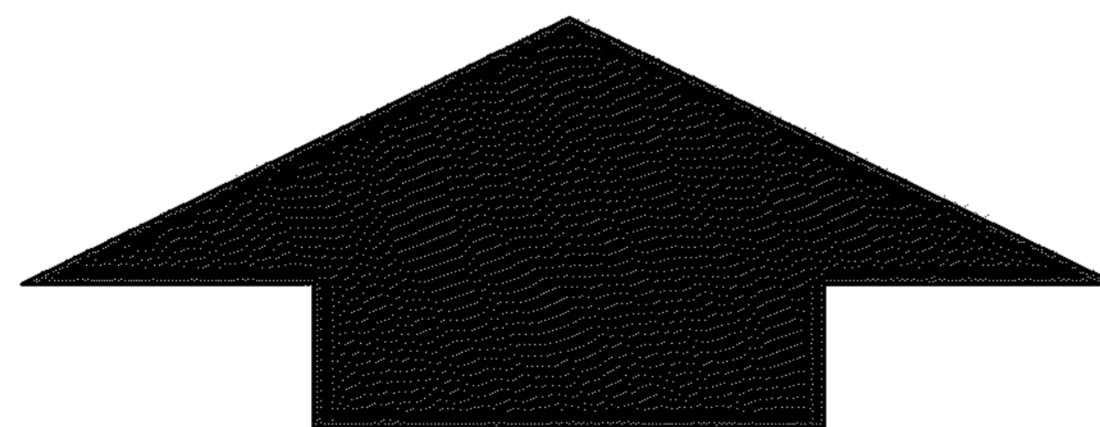
**Alleviate
Depression**

Rationale

- Largest \$ volume segments
- Leverage current Zyprexa brand equity/volume strengths and new indications/forms
- Competitive vulnerabilities to be exploited
- Lower price sensitivity vs segments 5 and 6
- Fits with company core competence as leader in neuroscience

- Small \$ volume opportunity
- Different target audience (PCPs)
- Constrained cost environments
- Lack of brand drivers/potential drivers
- Few competitive vulnerabilities

Redacted



Zyprexa Brand Territory

CSF 1: Realize Zyprexa Brand Promise

Realize the Zyprexa Brand Promise:

ZYPREXA is the Collaborative, Dedicated Leader that offers the Dependable Control you need to establish a more effective Therapeutic Alliance so you can help your patients begin to Move their lives forward and realize their potential.

Marketing Objective #1:

Drive Zyprexa positioning through the superior delivery of the Brand Promise elements.

Metric:

Brand Equity Tracking Tool (consistent improvement in targeted parameters)

CSF 2: Protect the Brand

Anticipate and provide timely, credible and relevant answers to effectively address marketplace issues.

Marketing Objective #2: Achieve positioning goals for targeted issues.

Metric: Improved relative marketplace perceptions as measured by the Brand Equity Tracking Tool:

**Weight gain
Hyperglycemia/diabetes
DKA
Triglycerides
Other emergent issues**

CSF 3: Proactively Position the Competition

Proactively influence the use of competitive products and assertively protect the position of Zyprexa as the market leader.

Marketing

Objective #3: Achieve positioning goals for targeted competitors.

Metric: Improved relative marketplace perceptions as measured by the Brand Equity Tracking Tool and competitive monitoring system relative to:

Risperidone (Depot)

Aripiprazole

Seroquel

Geodon

Depakote

Other

CSF 4: Pursue Unrestricted Access

Pursue / maintain equal and unrestricted access in Top Nine markets by demonstrating the superior value of Zyprexa in target segments

Marketing

Objective #4: In partnership with BC affiliates, establish/maintain the superior Value of Zyprexa with target customers

Metric: Performance on Pricing Architecture Tool: Zyprexa within target price/value quadrant

CSF 5: Fuel the Future/Build the Business

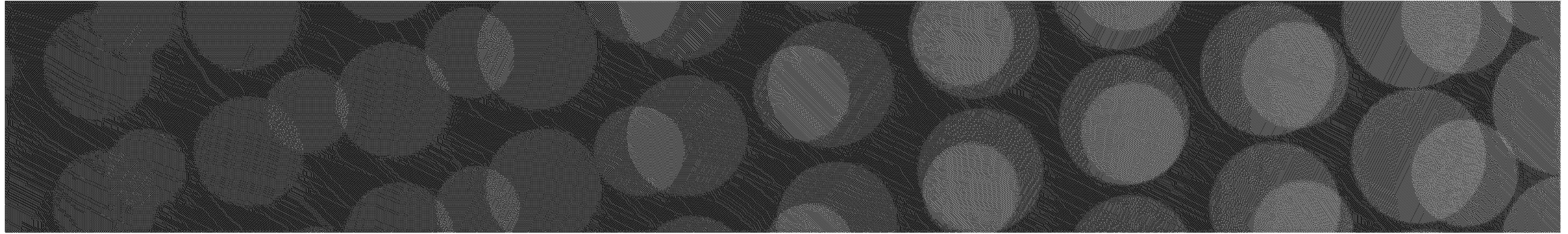
Grow the Zyprexa franchise in schizophrenia and bipolar and realize two significant new opportunities for brand expansion.

Marketing Objective #5: Develop the brand map for new opportunities (Q3 2002) and commercialize two opportunities by 2004.

Metric: Evolve and implement the product life cycle plan to achieve linear growth through '06.

Areas of Focus

- **High Dose**
- **Borderline**
- **Bipolar Depression**
- **Child and adolescent**



Core Message Elements & Core Value Message Element Integration

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Core Message Elements

The SDDS/NRT process will deliver data dissemination events to the 9 message categories detailed here:

Core Message Element

Dependable Control

Therapeutic Alliance

Help Move Lives Forward

Message Category

- ① Wide range effectiveness
- ② Dependability in multiple formulations
- ③ Count on it to control
- ④ Known and manageable side effects
- ⑤ Thinks more clearly
- ⑥ Bond emotionally
- ⑦ Enduring efficacy and relapse less
- ⑧ Realize an individual's potential
- ⑨ Better patient outcomes at equal total cost

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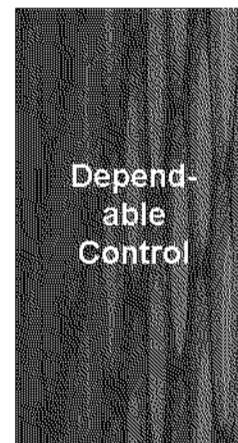
Core Message Elements with Core Value Message Elements

- 1 Wide range effectiveness**
Schizophrenia is a significant burden on families and national economies
Bipolar disorder is a significant burden on families and national economies
- 2 Dependability in multiple formulations**
- 3 Count on it to control**
For symptom control patients prefer Zyprexa
- 4 Known and manageable side effects**
Patients on Zyprexa use equal or fewer side effect medications
- 5 Thinks more clearly**
Patients using Zyprexa demonstrate better social functioning because of their ability to think more clearly
- 6 Bond emotionally**
Patients using Zyprexa are better able to bond emotionally both with physicians, other caregivers and family members
- 7 Enduring efficacy and relapse less**
The symptoms of patients using Zyprexa improve over time resulting in less relapse, rehospitalization, suicide and caregiver burden
- 8 Realize an individual's potential**
Zyprexa is better able to return patients to meaningful, fulfilling and productive lives (QOL)
- 9 Better patient outcomes at equal total cost**
Zyprexa produces better patient outcomes in schizophrenia and bipolar disease with no incremental cost

Prioritized Core Value Message Elements

Demonstrate superiority to Atypicals (Risperdal: oral/depot, Seroquel, Geodon, Abilitat), typicals & mood stabilizers (Depakote & Lithium)

Priority



Depend-
able
Control

- C** Schizophrenia and Bipolar disorder are a significant burden on families and national economies
- C** For symptom control patients prefer Zyprexa
- C** Patients on Zyprexa use equal or fewer side effect medications



Thera-
peutic
Alliance

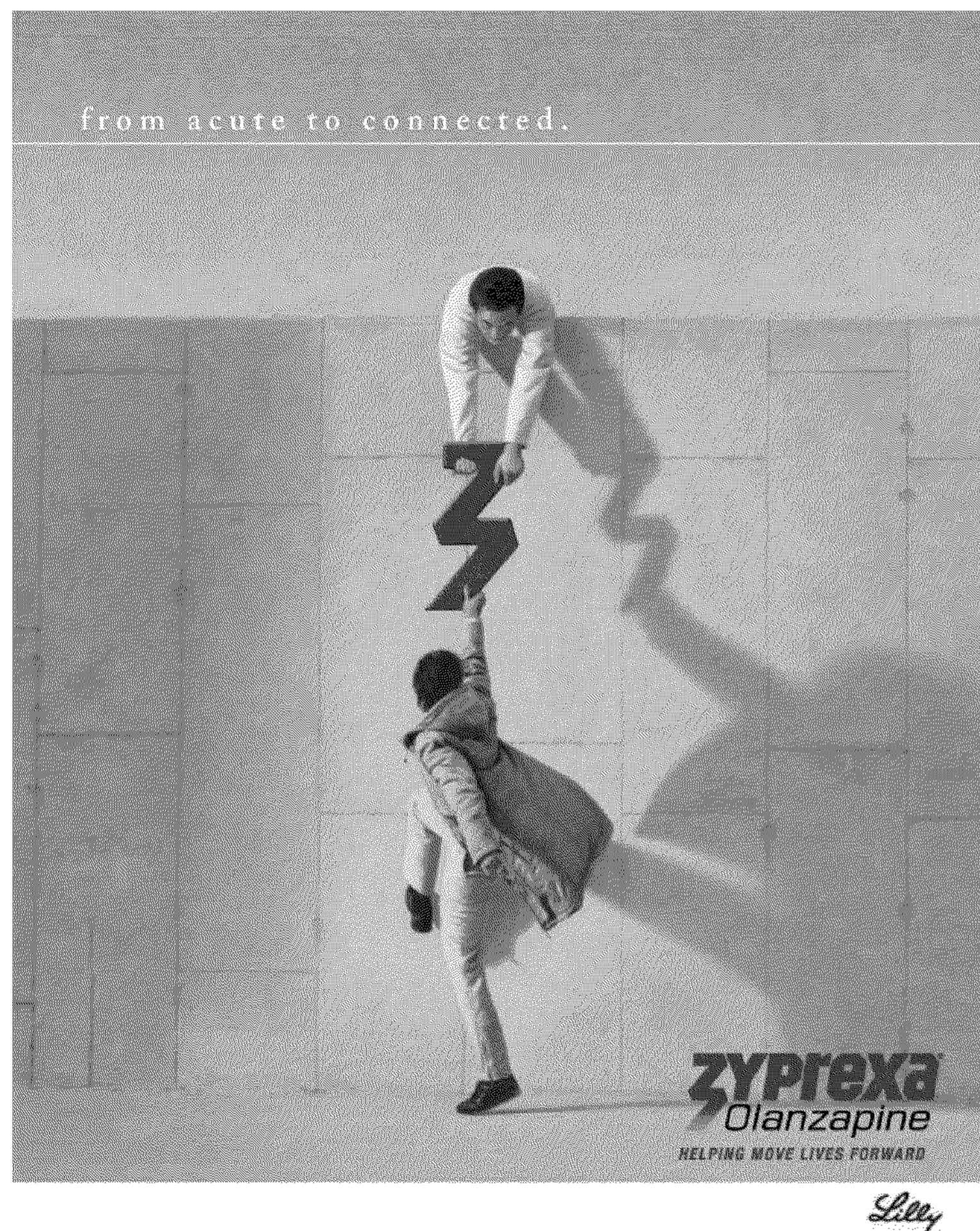
- B** Patients using Zyprexa demonstrate better social functioning because of their ability to think more clearly
- B** Patients using Zyprexa are better able to bond emotionally both with physicians, other caregivers and family members



Help Move
Lives
Forward

- A** Zyprexa is better able to return patients to meaningful, fulfilling and productive lives (QOL)
- A** The symptoms of patients using Zyprexa improve over time resulting in less relapse, rehospitalization, suicide and caregiver burden
- A** Zyprexa produces better patient outcomes in schizophrenia and bipolar disease with no incremental cost

Health Outcomes Research



Strategy and Plans

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Health Outcomes Research Strategy

- Align with Brand Strategy
- Provide data to support the Brand Promise & Core Value Message Elements
- Generate data from pivotal studies to support affiliate reimbursement/access discussions
- Focus on Brand Council affiliates (US, UK, Canada, Australia, France, Spain, Germany, Italy, and Japan)
- Facilitate shared learning between Brand Council affiliates

Health Outcomes Research Action Plan

- **Outline:**
 - review existing health outcomes body-of-evidence
 - review on-going studies with health outcomes endpoints
 - review timelines for analyses and presentation of data from on-going studies
 - review data mining opportunities

Priority 'A' Value Message Elements

- Zyprexa is better able to return patients to meaningful, fulfilling, and productive lives (QOL)
- The symptoms of patients using Zyprexa improve over time resulting in less relapse, rehospitalization, suicide, and caregiver burden
- Zyprexa produces better patient outcomes in schizophrenia and bipolar disease with no incremental cost (Total Costs)

Existing evidence for “Zyprexa is better able to return patients to meaningful, fulfilling, and productive lives”

- **Published Papers:**

- Tran, *J. Clin. Psychopharm.*, 1997
- Tunis, *J. Clin. Psychiatry*, 1999
- Revicki, *Quality of Life Research*, 1999
- Namjoshi, *J. Affective Disorders*, 2002
- Shi, *Int. Clin. Psychopharm.*, 2002
- Hamilton, *Int.Clin. Psychophar.*, 2001
- Hamilton, *Neuropsychopharm.*, 1998

- **Published Abstracts:**

- Badia, *Value in Health*, 1999
- Grainger, *European Neuropsychopharm.*, 1998
- Namjoshi, *Int.J. Neuropsychopharm.*, 2000
- Shi, *Int. J. Neuropsychopharm.*, 2002
- Namjoshi, *Int. J. Neuropsychopharm.*, 2002

On-going studies to support “Zyprexa is better able to return patients to meaningful, fulfilling, and productive lives”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
US-SCAP	US Outcomes Research	Ascher-Svanum	Q4, 2002	APA 2003 (Q2)			
Pan-EU SOHO	EU Health Outcomes	Edgell	6-mth data Q4, 2002	APA 2003 (Q4), Venice Meeting (Q1)			
BIDES	US Outcomes Research	Zhao	3-mth data - Q4, 2003	APA (Q2) 2004			
HGGD	US Outcomes Research	Tunis/Ascher-Svanum	Q1, 2003	IPS (Q3, 2003)			
HGGN	ZPT Health Outcomes	Namjoshi	Q1, 2002	CINP 2002			

On-going studies to support “Zyprexa is better able to return patients to meaningful, fulfilling, and productive lives”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
HGHJ	ZPT Health Outcomes	Namjoshi	Q1, 2003	ECNP (Q3, 2003)			
SCAP Pooling	ZPT Health Outcomes	Kody	Q4, 2002	APA (Q2, 2003)			
GEO	German Affiliate	Clouth	6-mth data Q1, 2003	ECNP (Q3, 2003)			
HGGY	ZPT Health Outcomes	Shi	Q1, 2002	CINP 2002, WPA 2002			
NONA	US Outcomes Research	Ascher-Svanum	Q1, 2003	IPS (Q3, 2003)			

Existing evidence for “*The symptoms of patients using Zyprexa improve over time resulting in less relapse, rehospitalization, suicide, and caregiver burden*”

- **Published Papers:**

- Hamilton, *Pharmacoeconomics*, 1999
- Tunis, *J.Clin. Psychiatry*, 1999
- Tran, *J.Clin. Psychopharmacology*, 1997
- Sanger, *J. Clin. Psychiatry*, 2000
- Namjoshi, *J. Affective Disorders*, 2002
- Edgell, *Pharmacoeconomics*, 2000

- **Published Abstracts:**

- Grainger, *European Neuropsychopharmacology*, 1998
- Edgell, *J. Psychopharmacology*, 2002

On-going studies to support “The symptoms of patients using Zyprexa improve over time resulting in less relapse, rehospitalization, suicide, and caregiver burden”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
US-SCAP	US Outcomes Research	Ascher-Svanum	Suicide data – Q4, 2002; Relapse data – Q1, 2003	APA(Q2)/ ECNP (Q3) 2003			
Pan-EU SOHO	EU Health Outcomes	Edgell	6-mth analyses – Q4, 2002	APA (Q2) 2003; Venice Meeting (Q1) 2003			
BIDES	US Outcomes Research	Zhao	3-mth data – Q4, 2003	APA (Q2) 2004			
HGHJ	ZPT Health Outcomes	Namjoshi	Q1, 2003	ECNP (Q3) 2003			
HGGN	ZPT Health Outcomes	Namjoshi	Q1, 2002	ECNP (Q3) 2002			

On-going studies to support *“The symptoms of patients using Zyprexa improve over time resulting in less relapse, rehospitalization, suicide, and caregiver burden”*

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
GEO	German Affiliate	Clouth	6-mth data - Q1, 2003	ECNP (Q3) 2003			
HGGD	US Outcomes Research	Tunis/Ascher-Svanum	Q1, 2003	IPS (Q3) 2003			
NONA	US Outcomes Research	Ascher-Svanum	Q1, 2003	IPS (Q3) 2003			

Existing evidence for “Zyprexa produces better patient outcomes in schizophrenia and bipolar disease with no incremental cost”

- **Published Papers:**

- Hamilton, *Pharmacoeconomics*, 1999
- Tunis, *J.Clin. Psychiatry*, 1999
- Le Pen, *Encephale*, 1999
- Palmer, *Am. J. Managed Care*, 1998
- Edgell, *Pharmacoeconomics*, 2000
- Namjoshi, *J. Affective Disorders*, 2002
- Almond, *Pharmacoeconomics*, 1998
- Obenchain, *Drug Information Journal*, 1999
- Glazer, *Journal of Clinical Psychiatry*, 1998
- Zhao, *Managed Care Interface*, 2002
- Rascati, *Pharmacoeconomics*, 2002

- **Published abstracts:**

- LeLorier, *European Neuropsychopharm.*, 2000
- Rascati, *Value in Health*, 2001
- Zhao, *Value in Health*, 2001
- Russo, *Int. J. Neuropsychopharm.*, 2002
- Zhu, *Value in Health*, 2002
- Zhao, *Schizophrenia Research*, 2002
- Spannheimer, *Value in Health*, 1999
- Spannheimer, *Schizophrenia Research*, 2002

On-going studies to support “Zyprexa produces better outcomes in schizophrenia and bipolar disease with no incremental cost”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
US-SCAP	US Outcomes Research	Ascher-Svanum	Q2, 2003	Davos (Q1) 2004			
Pan-EU SOHO	EU Health Outcomes	Edgell	12-mth data - Q1, 2003	ECNP (Q3) 2003			
GEO	German Affiliate	Clouth	6-mth data – Q1, 2003	ECNP (Q3) 2003			
BIDES	US Outcomes Research	Zhao	3-mth data – Q4, 2003	APA (Q2) 2004			
HGGN	ZPT Health Outcomes	Namjoshi	Q3, 2002	ICSR (Q2) 2003; APA (Q2) 2003			

On-going studies to support “Zyprexa produces better patient outcomes in schizophrenia and bipolar disease with no incremental cost”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
HGGD	US Outcomes Research	Tunis/Ascher-Svanum	Q1, 2003	IPS (Q3) 2003; ECNP (Q3) 2003			
HGHD	ZPT Health Outcomes	Shi	Q4, 2002	APA (Q2) 2003			

Priority 'B' Value Message Elements

- Patients using Zyprexa demonstrate better social functioning because of their ability to think more clearly
- Patients using Zyprexa are better able to bond emotionally with physicians, caregivers, and family members

Existing evidence for “*Patients using Zyprexa demonstrate better social functioning because of their ability to think more clearly*”

- **Papers/Reports:**

- Jerrell, *study report*, 1999
- Hamilton, *Int. Clin. Psychopharm.*, 2001

- **Published abstracts:**

- Gregor, *European Neuropsychopharmacology*, 1999
- Badia, *Value in Health*, 1999
- Edgell, *J. Psychopharm.*, 2002

On-going studies to support “Patients using Zyprexa demonstrate better social functioning because of their ability to think more clearly”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
US-SCAP	US Outcomes Research	Ascher-Svanum	Q4, 2002	APA (Q2) 2003			
Pan-EU SOHO	EU Health Outcomes	Edgell	6 mth data – Q4, 2002	APA (Q2) 2003, Venice Meeting (Q1) 2003			
BIDES	US Outcomes Research	Zhao	3-mth data – Q4, 2003	APA (Q2) 2004			
GEO	German Affiliate	Clouth	Q1, 2003	ECNP (Q3) 2003			

Existing evidence for *“Patients using Zyprexa are better able to bond emotionally with physicians, caregivers, and family members”*

- Not aware of any data that **directly** supports *“Patients using Zyprexa are better able to bond emotionally with physicians, caregivers, and family members”*
- However, all the data on social functioning and social well-being discussed earlier **indirectly** supports *“bonding emotionally with caregivers and family members”*
- There however currently is no data to support *“bonding emotionally with the physician”*
- An on-going randomized patient study at UCLA comparing olanzapine and risperidone includes a *“Therapeutic Alliance Scale”*. Data from this study will be analyzed in 2004

Priority 'C' Value Message Elements

- Schizophrenia and Bipolar Disorder are a significant burden on families and national economies
- For symptom control patients prefer Zyprexa
- Patients on Zyprexa use equal or fewer side-effect medications

Existing evidence for “*Schizophrenia and Bipolar Disorder are a significant burden on families and national economies*”

- **Published Papers:**
 - Begley, *Pharmacoeconomics*, 2001
 - Wyatt, *Soc.Psych.*, 1995
 - Armond, *Occup Med.*, 1998
 - Gunderson, *Am. J. Psychiatry*, 1975
 - Rice, *Br. J. Psychiatry*, 1998
 - Davies, *Psych. Bull.*, 1990
 - Knapp, *Br. J. Psych.*, 1997
 - Rouillon, *Pharmacoeconomics*, 1997
 - Goeree, *Can. J. Psychiatry*, 1999
 - Andrews, *Arch. Gen. Psych.*, 1985
 - Moscarelli, *Schiz. Bull.*, 1991
- **NO ADDITIONAL STUDIES PLANNED**

Existing evidence for “*For symptom control patients prefer Zyprexa*”

- Not aware of any available data that **directly** supports “*For symptom control patients prefer Zyprexa*”
- However, an on-going initiative in Australia assesses patients’ preferences for Zyprexa using the Time Trade-Off technique
- In addition, data on “length of therapy for Zyprexa versus competitors” from the following studies serve as an excellent proxy for “preference”
 - US SCAP
 - Pan-EU SOHO
 - The National VA Study
 - Texas Medicaid
 - MEDSTAT MarketScan Study
 - IMS initiatives
- Do we need a “preference” study that directly addresses this value message element?

Existing evidence for “Patients on Zyprexa use equal or fewer side-effect medications”

- **Published Abstracts:**
 - Kody, *Int. J. Neuropsychopharm.*, 2002
 - Edgell, *J. Psychopharm.*, 2002
 - Russo, *Int. J. Neuropsychopharm.*, 2002

On-going studies to support “Patients on Zyprexa use equal or fewer side-effect medications”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
US-SCAP	US Outcomes Research	Ascher-Svanum	Diabetes data from 75 patients – Q4, 2002	APA (Q2) 2003			
Pan-EU SOHO	EU Health Outcomes	Edgell	6-mth EPS data – Q4, 2002	APA (Q2) 2003, Venice Meeting (Q1) 2003			
VA Study	US Outcomes Research	Ascher-Svanum	EPS data - Q3, 2002	IPS (Q4) 2002			
MEDSTAT MarketScan Study	ZPT Health Outcomes	Namjoshi	EPS data – Q1, 2002	CINP (Q2) 2002			

On-going studies to support “Patients on Zyprexa use equal or fewer side-effect medications”

Study Name	Study Management	Study Owner	Timeline for data analyses	Timeline for first presentation	Working title for first presentation	Working title for journal article	Timeline for paper publication
MEDSTAT MarketScan Study	ZPT Health Outcomes	Namjoshi	Diabetes data - Q3, 2002	ICSR (Q2) 2003			
IMS Study	US Outcomes Research	Zhao	Diabetes data – Q2, 2002	IPS (Q4) 2002			
Protocare Study	US Outcomes Research	Ascher-Svanum	EPS & Diabetes data – Q2, 2002	APNA Meeting – Q4, 2002			
Pharmetrics Study	US Outcomes Research	Ascher-Svanum	Diabetes data – Q3, 2002	APA (Q2) 2003			

Summary and Gaps

- **For Priority 'A' Value Message Elements (quality-of-life, hospitalizations, total costs) –** there is a significant amount of published evidence for Zyprexa, and a number of on-going initiatives to build on this body-of-evidence
- Gap in our data for Priority 'A' Value Message Elements include data on caregiver burden
- **For Priority 'B' Value Message Elements (social functioning, bonding emotionally) –** there is a lesser amount of published evidence for Zyprexa, but there are on-going initiatives to get data on social functioning/well-being
- Gap in our data for Priority 'B' Value Message Elements include data to support “bonding emotionally with the physician”
- **For Priority 'C' Value Message Elements (burden-of-illness, patient preference, side-effects) –** there is a significant amount of published evidence on burden-of-illness, and a large number of on-going initiatives to address the issues related to side-effect medication use
- Gap in our data for Priority 'C' Value Message Elements include data to directly support patient preference, but proxy data is available

New studies planned for a 2002/2003 start

- EMBLEM (European Mania in Bipolar Disorder Evaluation of Medicines) Study
- HGHZ (US registration study for depot formulation)
- HGKA (EU registration study for depot formulation)
- National VA Diabetic Ketoacidosis Study
- Australian Bipolar Mania Prospective Observational Study

Data Mining Recommendations...

Helping to move lives forward

Priority	Message Category	Overview	Sources	Comparators	Owner
A	Realize an individual's potential	Olz vs Ris QoL improvements using multiple scales	HGBG, HGGN, EFESO	Risperidone	
A	Realize an individual's potential	Olz treated pts able to pursue meaningful productive activity	Comparator studies 6 mos or longer with HO scales	Haldol, Risperidone	
A	Realize an individual's potential	Olz improves QoL in bipolar disorder	HGHD, HGHQ, HGEH	Depakote, Haldol	
A	Realize an individual's potential	Pts treated with Olz have superior work status	Work status captured in trials HGAJ, HGBG, HGGN	Haldol, Risperidone	
A	Realize an individual's potential	Stabilized pts continue to improve their QoL with long term use of Olz	HGGI	Placebo	

Data Mining Recommendations...

Therapeutic Alliance

Priority	Message Category	Overview	Sources	Comparators	Owner
B	Bonds emotionally	Olz helps patients bond with family/caregivers	HGHD, HGEH, HGAJ, HGBG	Haldol, Risperidone	
B	Bonds emotionally	Olz improves social functioning	Longer term studies with social functioning scales	Haldol, Depakote, Ris.	
B	Bond emotionally	Superior compliance enables a more productive therapeutic alliance	Comparator studies with compliance measurement scales	Depakote	
B	Bonds emotionally	Improvement of social well being with olz treatment in bipolar pts	HGHD, HGHQ	Depakote, Haldol	

Data Mining Recommendations...

Dependable Control

Priority	Message Category	Overview	Sources	Comparators	Owner
C	Known and manageable side effects	What drives weight gain?	SOHO longitudinal look at wt gain	Risperidone, Quetiapine	