

United States Senate

COMMITTEE ON FINANCE
WASHINGTON, DC 20510-6200

August 12, 2009

Via Electronic Transmission

The Honorable Herb Kohl
Chairman
United States Senate Special Committee on Aging
Washington, DC 20510

Dear Chairman Kohl:

The United States Senate Committee on Finance (Finance) has jurisdiction over the Medicare and Medicaid programs and, accordingly, a responsibility to the more than 100 million Americans who receive coverage under these programs. As Chairman and Ranking Member of the Finance Committee we have a duty to protect the health of all Americans and safeguard taxpayer dollars authorized and appropriated by Congress for health programs.

On August 5, 2009, you sent us a letter requesting documents related to continuing medical education (CME) and other issues regarding the relationship between industry and academia. We are attaching several documents to this letter that are responsive to this request with the understanding that these documents are now public.

Thank you for your attention to this matter and dedication to transparency. If you have any questions, please do not hesitate to contact Christopher Law with Senator Baucus or Paul Thacker with Senator Grassley at (202) 224-4515.

Sincerely,



Max Baucus
Chairman



Charles E. Grassley
Ranking Member

Lexapro Documents

CME Payments
Payments to Professional Societies
Payments for Studies
Payments to Physicians

**Lexapro
FY04 Marketing Plan**

 FOREST LABORATORIES, INC.

Lexapro
escitalopram oxalate ™

FISCAL YEAR 2004 MARKETING PLAN

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Developed April 1, 2003

EXECUTIVE SUMMARY

Fiscal Year 2004 (FY04) still marks the launch phase for Lexapro™, escitalopram oxalate. This document outlines Forest Laboratories, Inc.'s marketing plan for the continued launch of Lexapro in the U.S. market. This plan covers all aspects of the launch period including a market analysis, objectives, SWOT analysis, critical issues, a detailed description of FY04 strategies and tactics, including the launch of the generalized anxiety disorder (GAD) indication in Q4 FY04.

LEXAPRO DEVELOPMENT

On August 12, 2002 Lexapro received approval from the FDA for the treatment of major depressive disorder. After stocking the trade and training the sales representatives, sales force promotion of Lexapro commenced on September 5, 2002. As of April 1, 2003, Lexapro has 10.4% of the new prescription market share and 7.7% of the total prescription market share. This market share demonstrates the initial success of Lexapro's launch. Lexapro is currently tracking as the sixth best launch in pharmaceutical history with a high likelihood of surpassing Viagra® (sildenafil citrate)¹ and Clarinex® (desloratadine)², which began declining after initial spikes in the first 4 months of launch. Although Lexapro has encountered initial success, the aggressive launch phase continues as current and upcoming SRI competitors are increasing their efforts.

Further motivation for the competitive response can be gleaned from the fact that Lexapro's gains in new prescription market share have come at the expense of all competitors, not just Celexa. As of April 1, 2003, 50% of Lexapro's growth has come from Celexa and 50% from the other competitors, primarily the Paxil®³ (paroxetine hydrochloride) franchise. Since the launch of Lexapro, every SSRI has lost market share and the growth for Effexor® XR (venlafaxine hydrochloride)⁴ has slowed down. However, since January of 2003, the competitors are beginning to rebound as Effexor XR has slowly continued its growth, Zoloft® (sertraline hydrochloride)⁵ has steadied its declines and even the fluoxetine franchise has stabilized. Furthermore, another Eli Lilly compound, Cymbalta™ (duloxetine hydrochloride)⁶, an SNRI used in the treatment of MDD with a potential focus on pain and other somatic symptoms is due to launch in FY04. For all of these reasons, in FY04, Lexapro will need to increase its competitive efforts in order to combat the competitive responses and new competitor entries.

¹ Viagra is a registered trademark of Pfizer Inc.

² Clarinex is a registered trademark of Schering Corporation.

³ Paxil is a registered trademark of GlaxoSmithKline

⁴ Effexor XR is a registered trademark of Wyeth-Ayerst Laboratories.

⁵ Zoloft is a registered trademark of Pfizer Inc.

⁶ Cymbalta is a trademark of Eli Lilly and Company.

EXECUTIVE SUMMARY

COMMUNICATION OBJECTIVES

- Communicate the positioning of Lexapro across all promotional venues: "Lexapro, the single isomer of Celexa, is an effective first-line SSRI for all adult depressed patients, which offers superior efficacy and tolerability over all SRIs."
- Incorporate the seven key selling points in every program

PROMOTIONAL OBJECTIVES

- Achieve first place in detail dollar share of voice in the SRI market
- Maintain SRI category leadership in number of journal ad inserts
- Maintain SRI category leadership in total number of medical education events (including CME symposia, speaker programs, teleconferences, and peer selling programs)
- Generate significant Lexapro specific news coverage to both consumers and healthcare professionals
- Have Lexapro included in all depression/anxiety related round up articles/stories that discuss treatment

MANAGED CARE OBJECTIVES

- Gain unrestricted formulary access for Lexapro
- Improve the formulary position of Lexapro in the SSRI class by:
 - 1) Continue to establish favorable tiered co-pay position for Lexapro versus competitors
 - 2) Pre launch GAD data initiatives to improve formulary status
 - 3) Improve existing Lexapro formulary status to more favorable position
 - 4) Non formulary to formulary
 - 5) 3rd to 2nd tier
 - 6) 2nd tier to 1 of 2 preferred
- Exceed individual MCO market share and net sales goals as defined in account manager business plans through enhanced, targeted pull-through efforts.
- Target pull-through efforts and resources
 - 1) 60% for top tier accounts at or below national market share
 - 2) 40% to maximize potential and reinforce positive relationships in high performing top tier MCOs

EXECUTIVE SUMMARY

- Increase Lexapro promotional noise level through improved communication to external customers regarding the value of Lexapro in managed care
- Establish baseline managed care training for field force beginning with Phase I training.
 - 1) Develop ongoing coaching tools for District Manager's to implement on a continuous basis with field representatives
- Integrate communication between Managed Healthcare Operations, Lexapro Brand Team, and Field Sales Force

CRITICAL ISSUES

SHARE OF VOICE LEADERSHIP

The antidepressant market is the most heavily detailed category in the pharmaceutical industry. It is therefore imperative that Lexapro maintain SOV leadership in FY04 by:

- **Continue to competitively sell:** Leverage strong comparative and clinical data including head-to-head venlafaxine and sertraline data in MDD and head-to-head paroxetine data in GAD.
- **Maintain/increase field support:** Continue leadership in Lunch & Learns and detailing, and increase samples
- **Increase Med Ed efforts:** More sponsorships of CME, increased level of speaker programs, maintain level of teleconferences and peer selling
- **Expansion contingencies:** Prepare for internal disruptions in the field due to the promotion of other products and potential launches

"OUT PERFORM" IN ALL MARKET SEGMENTS

In order to achieve market dominance, Lexapro cannot lag in any market segments. In FY04, Lexapro will out perform in the following market segments:

- **Disorder (anxiety):** Maximize pre-launch and launch efforts in GAD
- **Provider (psych):** Accelerate psychiatry penetration and make Lexapro the standard of care. Be proactive with selectivity message to address competitors head on
- **Patient Segment (age):** Generate more geriatric and pediatric data and pursue indications as necessary
- **3rd Party Access:** Secure access (formularies and VAs) and pull through (LTC)

EXECUTIVE SUMMARY

INNOCULATION

In an effort to be prepared for the expected and unexpected attacks from competitors and competitive entry, it is necessary to predict and provide responses for such situations. A number of issues effecting Lexapro have been identified. They are:

- **SSRIs versus non-selective reuptake inhibitors (SNRIs, others)**

There has been a trend in the SRI category of promoting reuptake inhibition at more than one receptor site as a benefit to patients in terms of efficacy. Products such as Effexor XR and duloxetine have reuptake inhibition at multiple sites (5HT and NE). Even SSRIs such as Zoloft and Paxil have promoted their more modest effects at the Dopamine and NE receptor sites respectively. The promotional message from these findings has focused on enhanced efficacy versus products that have their primary effects mediated by reuptake blockade at only the serotonin receptor site. Since Lexapro is the most selective SSRI, it could be the subject of criticism relating to this issue.

- **Pending Launch of Cymbalta**

Lilly is poised to launch Cymbalta (duloxetine HCL) an SNRI that will be positioned as a dual action agent from its starting dose and as the "new standard of depression therapy." Lilly is putting focus on the somatic symptoms of pain in their depression trials and may pursue this indication in the future. Currently, Lilly has some manufacturing issues at its Indianapolis plant that has delayed the launch. However, when approved, Cymbalta could be a major threat as Lilly has tremendous resource potential.

- **Generic Paroxetine**

GlaxoSmithKline is currently in litigation with Apotex regarding the patent of Paxil and the availability of a generic paroxetine. There is a strong likelihood that this will not occur until late 2004 or 2005; however, Lexapro must be prepared especially in managed care arenas with the introduction of a second generic to the class.

- **European News**

Although a completely different regulatory environment exists in Europe, news and events there may have an adverse affect on the U.S. market. Labeling language and potential non-approval in certain countries may have a negative effect on Lexapro in the U.S. market.

SUMMARY/CONCLUSION

The FY04 tactical plan contains many field and non-field based programs to continue the successful launch of Lexapro. All tactics are designed to increase promotional share of voice and help Lexapro outperform in all market segments of indications (anxiety), providers (psychiatrists), third-party payers (managed care) and age groups (pediatric and geriatric development programs). The launch of the GAD indication will also assist Lexapro achieve market dominance in years to come. With more data and indications on the way, Lexapro promotion will remain strong throughout the immediate future.

EXECUTIVE SUMMARY

Market Sales¹³

A. TOTAL SALES

Zoloft dominated the SRI market in terms of dollar sales in 2002, while Prozac sales were more than cut in half. Paxil sales were above \$2 billion, with Celexa and Effexor close behind at \$1.587 billion and \$1.524 billion respectively. Being a late entrant into the market in 2002, Lexapro's sales were just shy of \$1 million. While the overall market remained constant, all of the SRIs, with the exception of Prozac, Effexor, Remeron, Luvox, Fluvoxamine, and Serzone exhibited double-digit sales growth in 2002.

Table 3.0: SRI Dollar Sales

| Product | 2001 Total Sales [†] (billions) | 2002 Total Sales [†] (billions) | Change (%) | Share (%) |
|-------------------------------|---|---|------------|-----------|
| SRI Market | \$10.695 | \$10.690 | 0.0 | 100 |
| Zoloft | \$2.271 | \$2.545 | 12.1 | 23.8 |
| Paxil | \$2.154 | \$2.341 | 8.7 | 21.9 |
| Paxil CR | \$0 | \$0.205 | N/A | 1.9 |
| Celexa | \$1.156 | \$1.587 | 37.2 | 14.8 |
| Effexor XR | \$1.106 | \$1.524 | 37.7 | 14.3 |
| Fluoxetine | \$0.631 | \$0.749 | 18.7 | 7.0 |
| Prozac | \$2.074 | \$0.428 | (79.4) | 4.0 |
| Remeron | \$0.399 | \$0.388 | (2.9) | 3.6 |
| Serzone | \$0.385 | \$0.272 | (29.4) | 2.5 |
| Paxil CR | -0- | \$0.205 | N/A | 1.9 |
| Effexor | \$0.137 | \$0.135 | (1.6) | 1.3 |
| Remeron Soltab | \$0.045 | \$0.127 | 182.8 | 1.2 |
| Prozac Weekly | \$0.061 | \$0.105 | 72.3 | 1.0 |
| Sarafem | \$0.093 | \$0.103 | 10.3 | 1.0 |
| Lexapro | -0- | \$0.099 | N/A | 0.9 |
| Fluvoxamine | \$0.080 | \$0.062 | (22.3) | 0.6 |
| Luvox | \$0.103 | \$0.022 | (78.4) | 0.2 |
| Wellbutrin+SR +generic | \$1.201 | \$1.541 | 28.4 | |

[†] Includes chain store pharmacies, independent pharmacies, food stores, LTC facilities, mail order houses, federal facilities, non-federal hospitals, clinics, and direct purchasing staff HMOs, home health care, misc. channels

¹³ Retail and Provider Perspectives ©2002 IMS Health

B. TOTAL PRESCRIPTIONS

Although the overall trends are the same Paxil and Zoloft continue to fare better when it comes to total prescriptions as a result of continuing refills. For the year 2002, Zoloft was the market leader (22.3%), followed by Paxil (20.06%). Celexa demonstrated the second to largest growth amongst all SRIs (33.29%) and secured 15.81% of total prescriptions. While Effexor XR continues to grow, it increased growth at a slower rate of 31% [Table 3.2]. Lexapro's total share of prescriptions for 2002 was .9% and growing.

Table 3.2: SRI Total Prescriptions

| Product | 2001 TRx (thousands) | 2002 TRx (thousands) | Change (%) | Share (%) |
|----------------|-------------------------|-------------------------|---------------|--------------|
| Market | 121,910 | 140,072 | 14.90 | 100 |
| Zoloft | 27,974 | 31,229 | 11.64 | 22.30 |
| Paxil | 26,058 | 28,103 | 7.85 | 20.06 |
| Celexa | 16,612 | 22,142 | 33.29 | 15.81 |
| Fluoxetine | 7,287 | 21,227 | +++ | 15.15 |
| Effexor XR | 11,321 | 14,885 | 31.48 | 10.63 |
| Remeron | 5,330 | 4,877 | (8.50) | 3.48 |
| Serzone | 4,671 | 3,065 | (34.40) | 2.19 |
| Prozac | 16,875 | 2,908 | (82.77) | 2.08 |
| Paxil CR | -0- | 2,386 | N/A | 1.70 |
| Remeron Soltab | 634 | 2,298 | +++ | 1.64 |
| Effexor | 1,836 | 1,778 | (3.17) | 1.27 |
| Prozac Weekly | 705 | 1,312 | 86.07 | .094 |
| Lexapro | -0- | 1,256 | N/A | 0.90 |
| Sarafem | 1,135 | 1,232 | 8.53 | 0.88 |
| Fluvoxamine | 916 | 1,212 | 32.35 | 0.87 |
| Luvox | 556 | 162 | (70.90) | 0.12 |

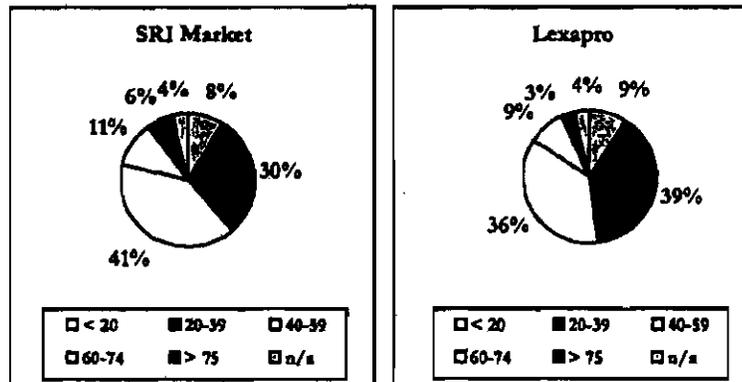
1. REFILL RATES

Increases in the number of new prescriptions, average prescription sizes, and refill rates have fueled growth of the SRI prescription market. Each product in the market posted equal or higher refill rates and prescription sizes in 2002 than 2001 [Figure 3.7]. The average ratio of TRx to NRx was 2.26.

E. USES BY AGE

Depression is an illness that affects all ages and SRIs are used for patients ranging from the very young to the very old. Eight percent of total SRI usage is for patients under the age of 20 (this age group represents 29% of the U.S. population.) SRI usage is most prevalent in the adult population. Patients between the ages of 20-39 and 40-59 represent the majority of the market at 30% and 41% of usage, respectively. Usage of SRIs in older patients (over 60 years of age) mirrors the general population at 16% [Figure 3.10].

Figure 3.10: CY 2002 Usage by Age: SRIs vs. Lexapro



Product market shares vary by age group, with Lexapro under performing in the under 20 age segment (9%). This is expected since it is a relatively new product with which physicians are not as comfortable with the SSRIs in treating children.

Despite their product profile, which makes them an ideal product for the elderly, Celexa and Lexapro do not significantly over perform in this segment. Zoloft and Paxil/CR both have a higher percentage of reported uses in the elderly population, both in patients 60-74 and >75.[Table 3.5].

Table 3.5 CY 2002 SRI Usage by Age (Columns Total to 100%)

| Product | All Ages (%) | <20 (%) | 20-39 (%) | 40-59 (%) | 60-74 (%) | >75 (%) | Unspecified (%) |
|------------------------|--------------|---------|-----------|-----------|-----------|---------|-----------------|
| Market | 100.0 | 8.5 | 30.1 | 40.2 | 11.2 | 6.4 | 3.6 |
| Lexapro | 3.1 | 3.4 | 4.0 | 2.8 | 2.5 | 1.6 | 3.2 |
| Celexa | 17.4 | 16.0 | 17.9 | 16.4 | 17.7 | 21.5 | 18.0 |
| Effexor+XR | 13.8 | 11.3 | 13.8 | 16.2 | 9.4 | 9.2 | 13.8 |
| Luvox | 1.2 | 2.7 | 1.1 | 1.2 | 1.2 | .07 | 0.4 |
| Paxil+CR | 21.0 | 22.3 | 22.1 | 18.8 | 22.7 | 24.4 | 20.9 |
| Prozac (brand+generic) | 15.8 | 14.3 | 15.8 | 17.7 | 15.0 | 7.2 | 16.5 |
| Remeron Line | 4.5 | 3.0 | 2.9 | 4.8 | 6.2 | 10.5 | 3.1 |
| Sarafem | 0.8 | 0.3 | 1.4 | 0.6 | 0.1 | 0.0 | 1.5 |
| Serzone | 2.4 | 1.0 | 1.8 | 3.4 | 2.4 | 0.8 | 2.9 |
| Zoloft | 20.0 | 25.6 | 19.1 | 18.0 | 22.9 | 24.1 | 19.7 |

Paxil maintained the positions it achieved in 2001 showing movement only in the 20-39 age group (+3%) and the 40-59 (-2%) age groups. Zoloft showed significant movement only in the 40-59 group (+1%) and maintained (moving only $\pm 1\%$) in the other age groups. Lexapro's data cannot be compared to 2001, but it has the majority of its patient population rooted in the 20-39 and 40-59 age group, while Celexa's share remained constant across all age groups ($\pm 2\%$). Effexor XR was relatively constant in all age groups showing significant movement in the 60-74 age group (-3%).

F. PRESCRIPTIONS BY SPECIALTY

Primary care physicians (PCPs) write 30.3% of all SRI NRx and psychiatrists account for another 31.1%. Together, these two specialties prescribe almost eight out of ten SRI NRx with PCPs steadily becoming a large portion. OBGs (3.6%) and neurologists (1.5%) fall well behind in terms of prescribing potential.

Celexa still has good penetration with the specialist although the gap is narrowing and although Lexapro's numbers were not huge for the end of 2002 they are steadily growing [Table 3.6]. Paxil/CR, Zoloft, and Effexor/XR also all over performs with psychiatrists – having a greater share than Celexa and Lexapro – and slightly under performs with PCPs and OBGs. Prozac and generic fluoxetine both have a higher than average share in the OBG office especially since the launch of Sarafem and its PMDD indication.

It should be noted that NRx market share for Celexa (Table 3.6a) indicates that Celexa has an even distribution among all specialties and hovers around 14% in all categories.

e) *Lexapro Oral Solution*

Lexapro oral liquid was launched in late 2002. The Lexapro oral liquid is peppermint-flavored and is concentrated as a 5 mg/5mL solution. It is currently packaged in 240 mL (8 oz) bottles which deliver approximately twenty-four 10mg doses per bottle.

Lexapro oral liquid has not been aggressively promoted to physicians and has never been sampled.

Table 3.17: SSRI Oral Liquid New Prescriptions

| Product | 2001 NRx (thousands) | 2002 NRx (thousands) | Change (%) | Share (%) |
|------------|-------------------------|-------------------------|---------------|--------------|
| Market | 166 | 172 | 3.6 | 100.0 |
| Fluoxetine | 16 | 56 | +++ | 32.6 |
| Paxil | 53 | 46 | (13.2) | 26.7 |
| Celexa | 19 | 31 | 63.2 | 18.0 |
| Zoloft | 12 | 20 | 66.7 | 11.6 |
| Prozac | 66 | 19 | (71.2) | 11.0 |

VI. SRI MARKET PROMOTION^{18, 19, 20, 21, 22, 23}

A. DETAILING

The SRI market is a highly competitive one, with 4.5 million physician contacts recorded in calendar year 2002. This was achieved through several of the largest sales forces in the pharmaceutical industry [Figure 3.18]. Both Paxil and Prozac Weekly increased their sales forces, 18% and 15%, respectively. Remeron *decreased* their sales force by 53%.

¹⁸ Integrated Promotional Services Audit ©2002 IMS Health.

¹⁹ National Journal Audit ©2002 IMS Health.

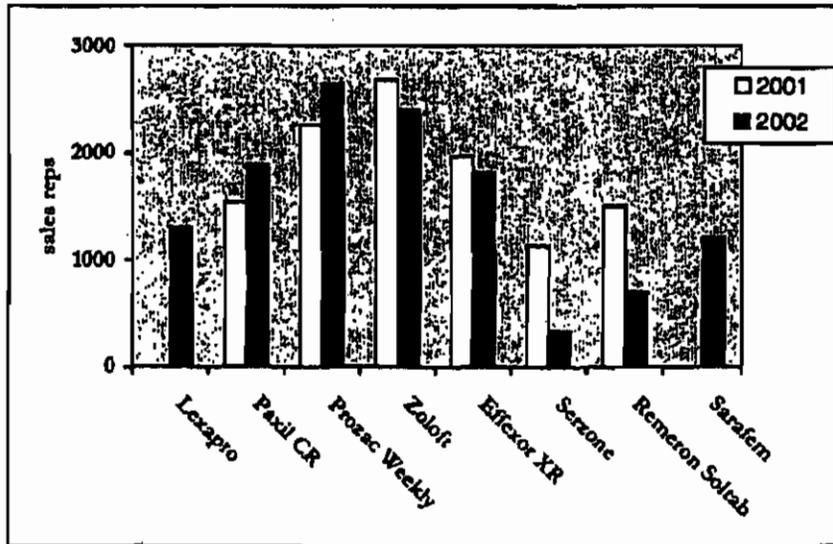
²⁰ Promotional Meeting and Event Audit ©2002 Scott-Levin Associates.

²¹ NPA Plus ©2002 IMS Health.

²² Drug Topics® Red Book® ©2002 Medical Economics Company, Inc.

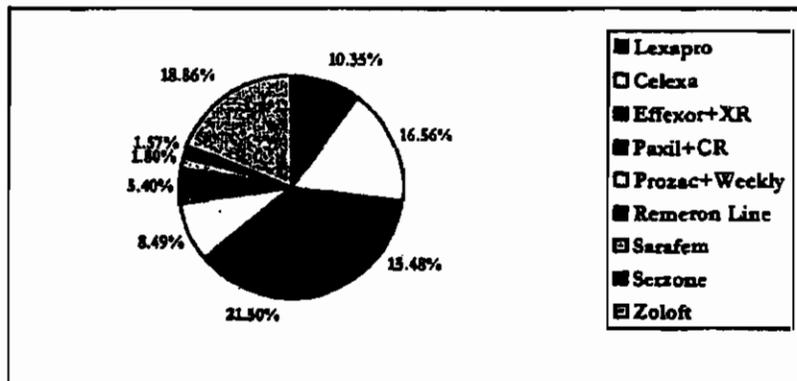
²³ Spring 2002 LTC Promotional Audit ©2002 Scott-Levin Associates.

Figure 3.18: SRI Sales Force Size



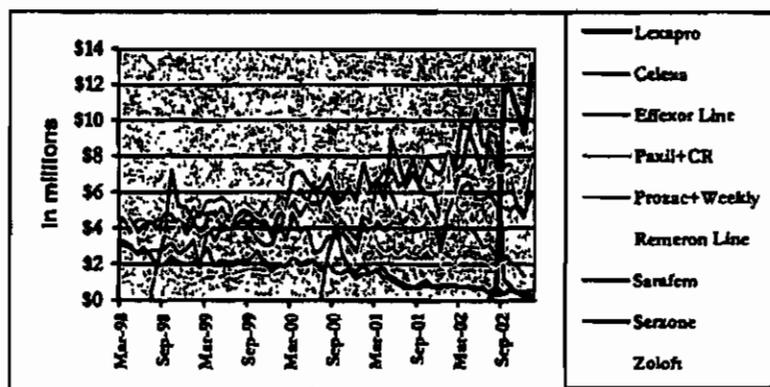
IMS audits reported Lexapro to have 374,000 detailing contacts in 2002 while Celexa had 611,000. Zoloft was the market leader in this category with a little over 1 million detailing contacts. Paxil/CR and Effexor XR and were second and third behind Zoloft with 983,000 and 653,000 detailing contacts, respectively.

Figure 3.19: CY 2002 SRI Detailing Dollars



Detailing expenditures have increased steadily and significantly for Paxil, Celexa and Effexor XR while Serzone, Sarafem, Prozac and Prozac Weekly, and Zoloft have all reduced their spending during 2002. [Figure 3.20].

Figure 3.20: SRI Detailing Dollars Over Time



1. DETAILING BY SPECIALTY

All of the SRIs spend more detailing time overall in PCP offices, given the large size of this audience. The bulk of SRI detailing time is spent on PCPs (50.9%) and PSYCHs (34.1%), with OBGs (6.9%) and Neurologists (1.8%) falling far behind in detailing emphasis [Table 3.8]. This distribution of promotional effort is proportional to the contribution each specialty makes to total SRI volume.

Table 3.8: CY 2002 SRI Detailing Dollars by Specialty (Columns Total to 100%)

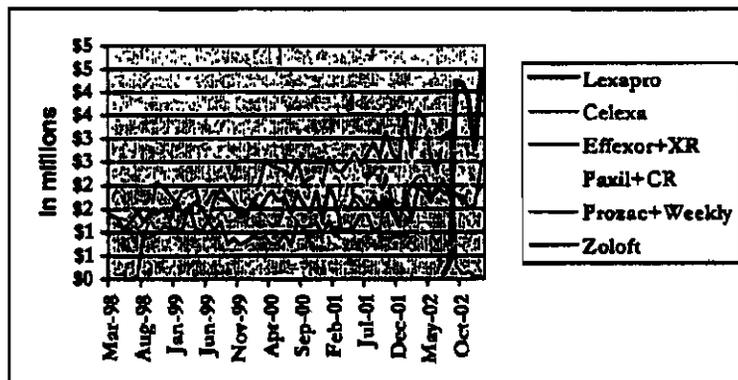
| Product | All Specialties (%) | PCP (%) | PSY (%) | OBG (%) | N (%) | All Others (%) |
|---------------|---------------------|---------|---------|---------|-------|----------------|
| Lexapro | 10.4 | 10.5 | 10.6 | 8.3 | 9.9 | 10.2 |
| Celexa | 16.6 | 16.9 | 17.0 | 12.6 | 15.2 | 15.7 |
| Effexor+XR | 15.5 | 16.4 | 15.5 | 11.1 | 9.4 | 13.9 |
| Paxil+CR | 21.5 | 22.3 | 22.0 | 11.5 | 25.3 | 22.1 |
| Prozac+Weekly | 8.5 | 10.1 | 6.6 | 6.8 | 5.1 | 8.6 |
| Remeron Line | 5.4 | 3.7 | 9.8 | 0.1 | 1.2 | 2.7 |
| Sarafem | 1.8 | 1.1 | 0.1 | 16.5 | 0.0 | 0.8 |
| Serzone | 1.6 | 0.4 | 3.8 | 0.0 | 1.9 | 0.3 |
| Zoloft | 18.9 | 18.6 | 14.3 | 33.2 | 32.0 | 25.6 |

Table 3.8 (a): CY 2002 SRI Detailing Dollars by Specialty (Rows total 100%)

| Product | PCP (%) | PSY (%) | OBG (%) | N (%) | All Others (%) |
|---------------|---------|---------|---------|-------|----------------|
| SRI Market | 50.9 | 34.1 | 6.9 | 1.8 | 6.4 |
| Lexapro | 51.5 | 35.0 | 5.6 | 1.7 | 6.2 |
| Celexa | 52.0 | 35.1 | 5.3 | 1.6 | 6.0 |
| Effexor+XR | 54.0 | 34.2 | 5.0 | 1.1 | 5.7 |
| Paxil+CR | 52.8 | 35.0 | 3.7 | 2.1 | 6.5 |
| Prozac+Weekly | 60.3 | 26.7 | 5.6 | 1.1 | 6.5 |
| Remeron Line | 34.5 | 61.8 | 0.1 | 0.4 | 3.1 |
| Sarafem | 31.5 | 1.9 | 63.7 | 0.0 | 2.9 |
| Serzone | 13.0 | 83.6 | 0.0 | 2.1 | 1.3 |
| Zoloft | 50.3 | 25.9 | 12.2 | 3.0 | 8.6 |

In many ways, SRI performance with each specialty mirrors the promotional effort devoted to that segment. In the OBG offices, Zoloft and Prozac have a greater share of voice and a correspondingly higher market share. Effexor XR appears to have broadened its promotion to hit PCPs more. Its share of voice with PCPs is now significantly higher than its share of voice with psychiatrists. Lexapro and Celexa detailing by specialty is relatively similar with slightly higher share of voice with psychiatrists and PCPs and slightly lower with OBGs. Meanwhile Paxil has its highest share of voice with neurologists and it's lowest with OBGs.

Figure 3.21: SRI Detailing Dollars by Specialty (Psych)



COMPETITIVE ENVIRONMENT ■

B. SAMPLING

Total extended unit samples were 408.1 million as of MAT August, 2002 which is down 1.9% from 2001. [Table 3.9]. The sampling trend is a bit different than it was in 2001 when the majority of products increased their sampling. In fact, in 2002, Paxil and Paxil CR, Prozac and Prozac Weekly, Celexa, the Remeron line, Serzone and Luvox all decreased their sampling efforts. The share of Celexa samples in 2002 was 12.7%, up only slightly from 2001, and Lexapro was at 7.9% at the end of 2002. A total of 51.7 million Celexa tablets were distributed in 2002 compared to 58.9 million in 2001 (down 12%) and a total of 34 million Lexapro tablets were distributed in 2002. Celexa and Lexapro's sampling efforts were surpassed by Paxil/CR (88.1 million tablets) and Zoloft (118.5 million tablets) which showed the most growth in 2002 (up 19%). Celexa and Lexapro were also surpassed by Effexor/XR (72.8 million tablets) which was up 10% from 2001. (Note that the tablet/capsule figures are audited and therefore may be understated by as much as 50%. However, audits are useful in determining relative levels of sampling.)

Table 3.9: CY 2002 SRI Sampling

| Product | Tabs/Caps Sampled 2001 (millions) | Tabs/Caps Sampled 2002 (millions) | Change (%) | Share (%) |
|---------------|---|---|---------------|--------------|
| SRI Market | 416.2 | 408.1 | (2.0) | 100.0 |
| Zoloft | 95.9 | 118.5 | 23.5 | 29.0 |
| Paxil+CR | 94.5 | 88.1 | (6.8) | 21.6 |
| Effexor+XR | 65.5 | 72.8 | 11.1 | 17.8 |
| Celexa | 58.9 | 51.7 | (12.2) | 12.7 |
| Lexapro | -0- | 32.4 | NC | 7.9 |
| Prozac+Weekly | 42.2 | 14.1 | (66.5) | 3.5 |
| Remeron Line | 15.5 | 13.3 | (14.1) | 3.3 |
| Sarafem | 14.0 | 9.0 | (35.7) | 2.2 |
| Serzone | 27.6 | 8.1 | (70.8) | 2.0 |
| Luvox | 2.2 | 0.1 | (95.4) | 0.0 |

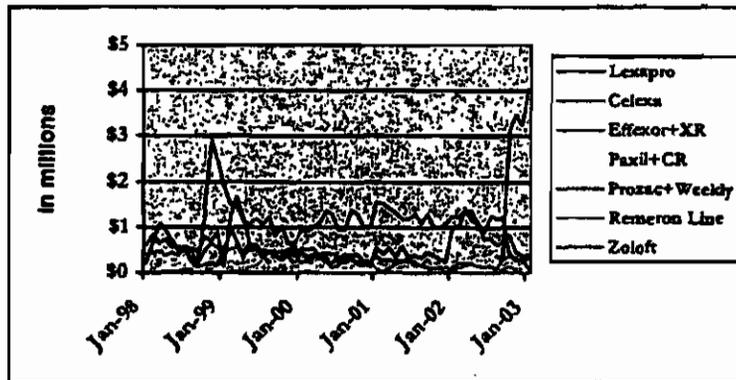
COMPETITIVE ENVIRONMENT ■

Table 3.10: CY 2002 SRI Journal Spend

| Product | 2001 Journal Spend (millions) | 2002 Journal Spend (millions) | Change (%) | Share (%) |
|---------------|-------------------------------|-------------------------------|------------|-----------|
| SRI Market | \$28.59 | \$39.25 | 37.3 | 100.00 |
| Celexa | \$14.92 | \$11.87 | (20.5) | 30.2 |
| Lexapro | \$0- | \$10.45 | N/A | 26.6 |
| Effexor+XR | \$4.84 | \$10.25 | 111.8 | 26.1 |
| Paxil+CR | \$2.01 | \$2.63 | 31.3 | 6.7 |
| Zoloft | \$2.59 | \$2.39 | (7.7) | 6.1 |
| Remeron Line | \$2.46 | \$1.61 | (34.5) | 4.1 |
| Prozac+Weekly | \$1.75 | \$0.05 | (97.1) | 0.1 |
| Sarafem | \$0.02 | \$0.00 | (100.0) | 0.0 |

Through the twelve months ending December 2002, Celexa was the SRI market leader in journal advertising spend, with a total of \$15.237 million [Table 3.10]. This placed Celexa third in the entire pharmaceutical market in terms of journal advertising. In the SRI Market, Lexapro was second in journal advertising with \$10.45 million [Table 3.10].

Figure 3.29: SRI Journal Spend

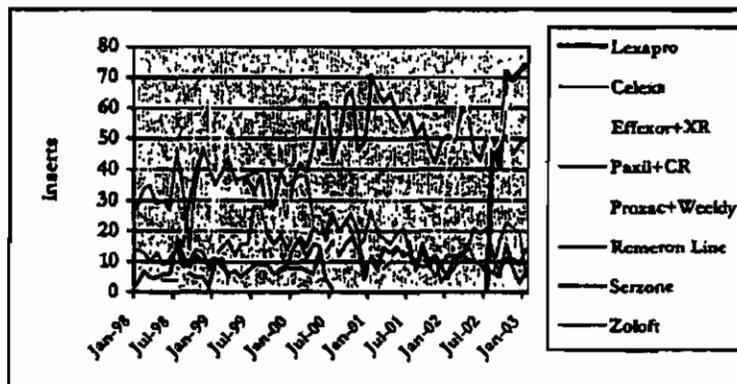


The dollars spent by Celexa remained relatively constant for most of 2002, with a dip in the latter portion of the year [Figure 3.29], and as well, the number of inserts decreased (11%) [Table 3.11]. Lexapro was third amongst SRIs in journal ad inserts with 303 for 2002 [Table 3.11] and their dollars spent was the highest at year end 2002 [Figure 3.29].

Table 3.11: SRI Journal Inserts

| Product | 2001 Journal Inserts | 2002 Journal Inserts | Change (%) | Share (%) |
|---------------|----------------------|----------------------|------------|-----------|
| SRI Market | 1,539 | 1,930 | 25.4 | 100.0 |
| Effexor+XR | 310 | 602 | 94.2 | 21.2 |
| Celexa | 676 | 599 | (11.4) | 31.0 |
| Lexapro | -0- | 303 | NA | 15.7 |
| Paxil+CR | 133 | 160 | 20.3 | 8.3 |
| Zoloft | 175 | 157 | (10.3) | 8.1 |
| Remeron Line | 135 | 106 | (21.5) | 5.5 |
| Prozac+Weekly | 108 | 3 | (97.2) | 0.2 |

Figure 3.30: SRI Journal Inserts



D. PHYSICIAN MEETINGS AND EVENTS

Physician meetings and events are a crucial element of the marketing mix for any SRI. During 2002, Celexa dominated the market with 9,069 events that reached approximately 60,000 physicians. Lexapro was a close second with 7,700 events in 2002 reaching approximately 47,000 physicians [Table 3.12] [Figure 3.31]. The audited cost for these events was \$39.5 million for Celexa which was a 9% decrease from 2001 whereas Lexapro spent \$31.4 million and was third in the category [Table 3.13]. While Effexor increased their spend significantly in this category (32%), making them second amongst SRIs. While Prozac and Prozac Weekly significantly reduced their spend (-49%), the number of events diminished at almost the same rate (-35%). In terms of physician meetings and events in 2002, Celexa was the leader followed by Lexapro, Effexor/XR and Zoloft.

Table 3.12: SRI Physician Meetings and Events

| Product | 2001 Events | 2002 Events | Change (%) | Share (%) |
|----------------|----------------|----------------|---------------|--------------|
| SRI Market | 26,695 | 33164 | 24.2 | 100.00 |
| Celexa | 7,996 | 9,069 | 13.4 | 27.3 |
| Lexapro | 113 | 7,700 | +++ | 23.2 |
| Effexor+XR | 4,484 | 6,391 | 42.5 | 19.3 |
| Zoloft | 2,699 | 3,411 | 26.4 | 10.3 |
| Paxil+CR | 4,237 | 2,895 | (31.7) | 8.7 |
| Prozac+Weekly | 3,602 | 2,321 | (35.6) | 7.0 |
| Remeron+Soltab | 1,366 | 618 | (54.8) | 1.9 |
| Serzone | 837 | 270 | (67.7) | 0.8 |
| Sarafem | 1,349 | 224 | (83.4) | 0.7 |
| Duloxetine | 12 | 136 | +++ | 0.4 |
| Cymbalta | -0- | 124 | NC | 0.4 |
| Luvox | -0- | 5 | NC | 0.0 |

COMPETITIVE ENVIRONMENT ■

CRITICAL ISSUES

I. SHARE OF VOICE LEADERSHIP

The antidepressant market is the most heavily detailed category in the pharmaceutical industry. It is therefore imperative that Lexapro maintain SOV leadership in FY04 by:

- **Continue to competitively sell:** Leverage strong comparative and switch clinical data including venlafaxine and sertraline (comparative data) and fluoxetine (switch data)
- **Maintain/increase field support:** Continue leadership in Lunch & Learns and detailing, and increase samples
- **Increase Med Ed efforts:** More sponsorships of CME, increased level of speaker programs, maintain level of teleconferences and peer selling
- **Expansion contingencies:** Prepare for internal disruptions in the field due to the promotion of other products and potential launches

II. "OUT PERFORM" IN ALL MARKET SEGMENTS

In order to achieve market dominance, Lexapro cannot lag in any market segments. In FY04, Lexapro will out perform index in the following market segments:

- **Disorder (anxiety):** Maximize pre-launch and launch efforts in GAD
- **Provider (psych):** Accelerate psychiatry penetration and make Lexapro the standard of care. Be proactive with selectivity message to address competitors head on
- **Patient Segment (age):** Generate more geriatric and pediatric data and pursue indications as necessary
- **3rd Party Access:** Secure access (formularies and VAs) and pull through (LTC)

III. INNOCULATION

In an effort to be prepared for the expected and unexpected attacks from competitors and competitive entry, it is necessary to predict and provide responses for such situations. A number of issues effecting Lexapro have been identified. They are:

CRITICAL ISSUES

- 3) significantly improves depression for many patients beginning at week 1 or 2 (effect may take 4 to 6 weeks)
- 4) effectively treats anxiety symptoms associated with depression
- 5) at 10 mg, overall incidence of side effects and drop out rates due to AEs no different than placebo
- 6) favorable drug interaction profile
- 7) simple 10 mg starting dose for all patients

IV. PROMOTIONAL OBJECTIVES

- Achieve first or second place in detail dollar share of voice in the SRI market
- Maintain SRI category leadership in number of journal ad inserts
- Maintain SRI category leadership in total number of medical education events (including CME symposia, speaker programs, teleconferences, and peer selling programs)
- Generate significant Lexapro specific news coverage to both consumers and healthcare professionals
- Have Lexapro included in all depression/anxiety related round up articles/stories that discuss treatment

V. MANAGED CARE OBJECTIVES

- 1) Gain unrestricted formulary access for Lexapro
- 2) Improve the formulary position of Lexapro in the SSRI class by:
 - Continue to establish favorable tiered co-pay position for Lexapro versus competitors
 - Pre launch GAD data initiatives to improve formulary status
 - Improve existing Lexapro formulary status to more favorable position
 - Non formulary to formulary
 - 3rd to 2nd tier
 - 2nd tier to 1 of 2 preferred

OBJECTIVES

MARKETING TACTICS

1. FIELD SAMPLES

Samples will be packaged in two forms: field samples and patient starter kits. A total of 300 MM 10 mg sample tablets will be produced in FY04. Representatives will not receive samples of the Lexapro 20 mg tablet.

A. FIELD SAMPLES

Lexapro field samples will be provided in individual boxes holding one blister card of seven 10 mg tablets (1x7) in a gravity-feed dispenser holding eight of the 1 x 7 boxes.

60% of all samples or 180 MM tablets produced will be distributed as field samples in FY04.

Timing: Q1 – Q4
Quantity: 180 MM tablets, 25.7 MM starters (1x7 boxes)

B. PATIENT STARTER KITS

Patient Starter Kits (PSKs) which contain two weeks of Lexapro samples along with an educational, branded Lexapro brochure will be sampled to physicians during FY04. The rationale for providing PSKs is twofold. First, many physicians and Managed Care Organizations (MCOs) have been asking for patient education, which is incorporated in a sample. In fact, many physicians have stated that they prescribe Paxil, Zoloft, or Effexor XR because of the PSKs available for those brands. Because physicians are requesting PSKs, their availability will help representatives gain selling time and increase rapport with key physicians.

Second, providing patient education to patients could increase the likelihood that a patient will fill a prescription for Lexapro and become a loyal user. A patient who understands what to expect from Lexapro treatment will be more likely to stay on Lexapro over the long term. The educational brochure in the PSK will be updated to reflect GAD information when appropriate

NOTE: Each PSK will contain fourteen 10 mg tablets of Lexapro along with an educational brochure. Each PSK is in a tri-fold design with six PSKs comprising a sample unit. 40% of samples will be in the form of PSKs equaling over 120 MM tablets or 1.4 MM sample units.

Timing: Q1 – Q4
Quantity: 120 MM tablets, 8.6 MM starters (14 tablets)

Total Estimated Cost: \$15,741,464

TACTICAL PLAN

Bylined Articles

Bylined articles will allow us to fold Lexapro messages into articles on depression, anxiety and co-morbidity developed by (or ghostwritten for) thought leaders. We will identify a Lexapro thoughtleader to place 2-3 bylined articles in trade journals, consumer publications and on the Internet. Estimated costs include article development, revisions and honoraria for the authors. Examples of topics include co-morbidity of depression and anxiety and selectivity.

Timing: Q1-Q4
Estimated Cost: \$100,000

Paid Media Outreach

In addition to the traditional editorial media outreach, there are also opportunities in which we can increase control over the final product by paying for the placement. These opportunities, which will supplement our core activities, may include Lexapro message placement in radio programs (e.g., American Health Radio) or other "advertorial" venues. Expenses may include spokesperson honoraria, production costs, logistics and script writing.

Timing: Q1-Q4
Estimated Cost: \$200,000

VII. ADVERTISING AGENCY FEES

The advertising agency of record will work on a variety of projects supporting Lexapro during FY04. Most of the projects captured in this tactical plan are listed below. Advertising agency account time is captured in General and Administrative (G&A) fees. All creative and Out of Pockets (OOPs) are captured in individual projects. The list of projects the agency will work on include (more projects may be initiated once identified and finalized):

| | | |
|-----------------------------|--------------------------------|---------------------------------|
| Annotated Package Insert | Annotated Master Visual Aid | Dosing Card |
| Annotated Reprints | Clinical Series and Letterhead | Rep Triggered Mail |
| Patient Education Brochures | Starter Kit Brochure | GAD announcement Mailer |
| Market Research | Convention Panels | Sales Resource Binder/POA Guide |
| 8 Page Ad | 4 Page Ad | 2 Page Ad |
| Hospital Panels | File Card | Master Visual Aid |
| File Card | | |

TACTICAL PLAN

B. VA/DOD SPONSORSHIP FUNDS

Funds have been allocated to the Government Sales Group to increase VA/DoD formulary penetration, enhance formulary position by moving to preferred status, and facilitate pull-through at all VA/DoD hospitals through individualized programs including, but not limited to:

- Local Special Events
- Local Educational Programs
- Pull-Through Programs designed to drive Lexapro NRx and enhance compliance/length of therapy

Funding allocations will be dependent upon submission/approval of well-developed business rationale. A committee composed of members of the Lexapro Brand Team, and Managed Health Care Operations will review all requests.

Timing: Q1 – Q4
Estimated Cost: \$250,000 Sponsorship Funds

XI. CONTINUING MEDICAL EDUCATION

The general goal and purpose of the CME program is to: Sponsor the development of continuing medical education activities that will educate physicians and other healthcare providers and assist them in acquiring the most current knowledge in the diagnosis and treatment of depression and other related disorders.

A. ENDURING CME

In order to amortize the content from Forest sponsored symposia at academic conventions and regional programs, Forest will sponsor the development of several enduring CME pieces.

Forest will sponsor "special reports" and "brief communicators" in publications like *CNS News*, *Psych Times*, and the *Journal of Clinical Psychiatry*, as well as university-affiliated newsletters such as Duke University. Four of these 6-8 page CME accredited reports will summarize symposia at ADAA, APA, AAFP, and AAGP. Others will be created to educate physicians on the latest information available on antidepressant treatment.

Timing: Q1 – Q4
Quantity: 6
Cost Per Unit: \$100,000
Estimated Cost: \$600,000

A reporter from publications like *CNS News*, *Psych Times*, and the *Journal of Clinical Psychiatry* will be sent to cover key Lexapro data presented at important medical meetings. Data from ADAA, APA, ACNP, and WCP will be reported in the journal as a CME supplement.

Timing: Q1 – Q4

TACTICAL PLAN

Quantity: 4
Cost Per Unit: \$75,000
Estimated Cost: \$300,000

A videotaped satellite program will be sponsored to extend the reach of our medical education activities into the larger psychiatric community. The content will consist of a videotaped satellite CME broadcast of thought leaders discussing new treatments for depression, anxiety and related disorders.

Timing: Q3
Quantity: 12,000
Cost Per Unit: \$8.30
Estimated Cost: \$100,000

Total Estimated Cost: \$1,000,000

B. INTERNET/ELECTRONIC CME

Online CME

Many physicians now use the Internet as a way to gain CME credits. Sponsoring online enduring CME programs is an effective way of amortizing the high cost of a live program and extending the reach of the program. Symposia sponsored at APA, ADAA, AAFP and AAGP will be placed on the Internet in FY04. Avenue-E/IntraMed will create an online webcast that will reach the audience from the two largest internet sites, E-medicine and MedScape. These CME webcasts will be available within 4-6 weeks of the live program.

Some physicians prefer the interactive format of CD ROMs as their vehicle to gain CME credits. In FY04, Forest will sponsor a CME CD ROM for this audience.

Timing: Q1 - Q4
Quantity: 5
Cost Per Unit: \$120,000. - Online CME, \$200,000ea. - CD ROM
Estimated Cost: \$800,000

C. NATIONAL CME SYMPOSIA

Sponsoring symposia at major meetings will allow thought leaders to present new data as it becomes available as well as address questions from their peers and attending media. Symposia will be sponsored to address key topics of interest for the medical field. The audience at the majority of the meetings will be psychiatrists and PCPs; however, there will also be meetings with OB/GYNs, managed care and others.

The detailed Lexapro symposia plan is provided as part of the Professional Meeting and Symposia appendix to this marketing plan (see *Appendix IV*).

Timing: Q1 - Q4
Quantity: 18
Cost Per Unit: ~\$167,000 each
Estimated Cost: \$3,000,000

TACTICAL PLAN

D. REGIONAL CME SYMPOSIA

Forest will continue to sponsor the central development and regional implementation of a series of educational programs to serve multiple medical subspecialties, including primary care and psychiatry. In conjunction with medical education agencies, academic health centers, medical associations and professional societies, Forest will address educational needs that are relevant, problem-based and timely. Approximately 100-200 physicians will be in attendance at each CME regional program.

A series of 80 regional programs will be run by CME Inc. CME Inc. asked Forest for an unrestricted educational grant to sponsor a series regarding anxiety. Dr. Murray Stein, Dr. Mark Pollack and others will serve as the Chairmen for this series. There are also potential opportunities with Duke University and Stephen Stahl to conduct regional series on selectivity and preclinical items for psychiatrists.

| | |
|------------------------|---------------------------------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Quantity:</i> | 145 programs. 110 Psych, 35 PCP |
| <i>Cost Per Unit:</i> | ~\$42,000 each |
| <i>Estimated Cost:</i> | \$6,000,000 |

E. SPONSORSHIP OF SCIENTIFIC SESSIONS

Some of the smaller, more prestigious meetings do not accept industry-supported symposia. In such cases, sponsorship of a study group or plenary session is recommended. Marketing will work with the professional relations group regarding potential opportunities. SOBP, NCDEU, ACNP and AAFP are the four meetings that will be targeted in FY04.

| | |
|------------------|-----------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Quantity:</i> | 4 events |
| <i>Cost:</i> | \$200,000 |

XII. ADVISOR RELATIONS

A. ADVISOR COMMUNIQUÉS

Forest will communicate regularly with thought leaders, advisors, and Lexapro investigators throughout FY04 to keep them abreast of all pertinent information with Lexapro. Monthly mailings will be developed to transmit information that will include topics like the approval of Lexapro for GAD, the filing of Panic Disorder, posters presented at important medical meetings like ADA, APA, and ACNP, and recently published data.

The detailed Advisor Communiqués plan is provided as an appendix to this marketing plan (see *Appendix XI*).

| | |
|----------------|----------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Cost:</i> | \$50,000 |

TACTICAL PLAN

B. CONSULTANTS

During FY04, Forest will employ the consultant services of several thought leaders as advisors to Lexapro in order to obtain critical feedback and recommendations on educational and promotional strategies and tactics. Advisors will be selected based upon their specific area of expertise and the marketing and/or medical need(s) at the time.

Timing: Q1 - Q4
Cost/ Hour: \$250
Estimated Cost: \$180,000

C. CONSULTANTS MEETING

A two-day meeting for key escitalopram consultants and thought leaders will be held one year after launch. The purpose of this meeting will be to provide an update to our consultants on the progress of Lexapro and seek advice on the upcoming GAD launch. Half was paid in FY03 for space reservation, recruitment, etc. The remainder will be paid in FY04.

Timing: Q2
Cost: \$200,000

D. EXECUTIVE ADVISORY BOARDS

The primary purpose of the Lexapro Executive Advisory Board is to gain the counsel of the key opinion leaders from around the country. Ancillary to gaining advice and guidance, the executive advisory board keeps our advisors apprised of the commercial development and potential benefits of escitalopram. Market issues and their potential impact on escitalopram, emerging clinical and preclinical Lexapro data are also discussed. Two one-day meetings in San Francisco & New York are proposed for FY04.

Timing: Q1-Q4
Quantity: 2
Cost per meeting: \$105,000
Cost: \$210,000

E. PRIMARY CARE ADVISORY BOARDS

The objective of the primary care executive advisory board meetings is to obtain critical feedback and recommendations on educational and promotional strategies and tactics, as well as cultivate, build, and maintain professional alliances with key internists and primary care thought-leaders. The primary care advisory board will consist of nationally recognized internists and PCPs.

The agenda of these meetings will cover an update on the status of Lexapro clinical trials and clinical development plan, and a discussion of marketing strategies to primary care physicians based on the outcomes to date.

Timing: Q2-Q3
Quantity: 1
Cost per meeting: \$100,000
Cost: \$100,000

discussion on marketing related topics they deem important to their markets. A total of 200 local advisory boards will be conducted in FY04.

Approximately 40 speakers participate as moderators/presenters for the Lexapro local advisory board program. These speakers will be brought together for a training and feedback session on the program. This would allow us to train them on the most current data, including GAD, and address any issues with the program.

Timing: Q1 – Q4
Quantity: 200
Cost Per Unit: \$28,000
Estimated Cost: \$5,600,000

B. REP PROMOTIONAL PROGRAMS

Through the approximately 2,000 psychiatrists and PCPs that have been recruited and trained to serve as faculty for the Lexapro Speakers' Bureau Program, reps will organize speaker events. These meetings may be large-scale dinner programs with a slide presentation, small roundtable discussions or one on one advocate lunches. The trained psychiatrists and PCPs include national and local thought leaders.

These meetings are necessary to maintain the strong presence and share of voice of Lexapro. In addition, dinner programs provide an opportunity for the rep to interact and build relationships with a number of physicians in their territory.

Timing: Q1 – Q4
Quantity: 15,000 (1,942 reps, avg. 7.7 per rep)
Cost Per Unit: \$2,300
Estimated Cost: \$34,700,000

C. SPEAKERS' BUREAU ADMIN FEE

The agency will provide all logistical support for the Lexapro Speakers' Bureau. Activities covered may include processing of speaker honorarium, travel and expenses, RSVP management, invitations/posters, and setting up a venue for the program.

The agency's fee is based on the level of their involvement in the planning of the program. The different levels are summarized below:

Allocation 1 - Agency involvement includes securing a speaker and processing honorarium/expenses for the speaker and providing invitations and posters to the rep for distribution.

Allocation 2 - Agency involvement includes securing a speaker, and processing honorarium/expenses for the speaker and coordinating all travel arrangements. Agency will also provide invitations and posters to the rep for distribution.

Allocation 3 - Agency involvement includes full event planning – securing a speaker, developing invitations and posters, managing RSVPs, all logistical arrangements (venue and menu selection, AV needs) and processing honorarium/expenses.

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Timing: Q1 – Q4
Quantity: 15,000
Cost Per Unit: \$300, 650 or 1,500
Estimated Cost: \$4,280,000

D. SPEAKERS' BUREAU SLIDE KIT

A speaker's slide kit containing a comprehensive review of Lexapro data has been developed. The slide kit will be updated as new data, including GAD when approved, becomes available. Speakers at promotional events such as dinner programs, roundtables, grand rounds and other events will use the slide kit.

Timing: Q1 – Q4
Quantity: 2000
Estimated Cost: \$400,000

E. SPEAKER TRAINING

Three speaker training meetings will take place during October – December 2003. The meetings will be located in New York, Florida and Los Angeles. 1,000 existing speakers from the speaker's bureau will be recruited and trained on new Lexapro data including GAD. The trained psychiatrists include national and local thought leaders.

Webcast/CD based speaker training will be rolled out in FY04 as well. Divisional Managers will have the opportunity to train additional Lexapro speakers. This program or one similar may be used to update existing speakers who cannot attend a live speaker training meeting on new data.

Timing: Q1-Q4
Quantity: 3
Cost Per Meeting: \$800,000
Estimated Cost: \$3,300,000

F. SPEAKERS BUREAU ON-LINE COMPONENT

Communication and training of thought leaders and speakers can be optimized by offering them an online resource to alleviate the burden of:

- Disseminating new data
- Training
- Provide current materials

A small secure site will be built for these physicians. Potential site features will include:

- Promotional guidelines
- Slide decks and slide deck updates
- Relevant literature and literature updates
- Press releases
- Travel expenses
- Contact list for Forest

Timing: Q1 – Q4
Estimated Cost: \$300,000

TACTICAL PLAN

XV. LUNCH AND LEARNS

Providing lunch for a physician creates an extended amount of selling time for representatives. It also gives them the opportunity to utilize other selling tools like the lunch and learn video, teleconferences, etc.

Timing: Q1 - Q4
Quantity: 1,942 sales reps
Cost Per Rep: \$18,500/rep/year
Estimated Cost: \$36,000,000

XVI. FIELD AIDS

Field aids provide support to the field force to help drive Lexapro prescriptions. In FY04, the sales force will be armed with strong clinical and promotional support for Lexapro. These materials will provide vehicles for rep utilization that will generate interest and help the rep engage the physician in a consultative discussion.

The Lexapro marketing team will provide new selling materials each POA to prevent rep fatigue. In addition, product and category updates will be delivered for reps to keep physician calls relevant and engaging.

A. CLINICAL REPRINTS/POSTERS

The following reprints will be made available in FY04:

1. Gotman J. et al. Efficacy comparison of escitalopram and citalopram in the treatment of Major Depressive Disorder: Pooled Analysis of Placebo-Controlled Trials. *CNS Spectrums*. 2002;

Purpose: To compare the efficacy of escitalopram 10-20 mg vs citalopram 20-40 mg.

2. Burke, W. et al. Fixed dose trial of the single isomer SSRI escitalopram in depressed outpatients. *Journal of Clinical Psychiatry*. 2002;

Purpose: Compare the efficacy and tolerability of escitalopram and citalopram in the treatment of Major Depressive Disorder.

3. Wade, A. et al. Escitalopram 10 mg/day is effective and well tolerated in the treatment of depression in primary care. *International Clinical Psychopharmacology*. 2002

Purpose: Demonstrate the efficacy and tolerability of escitalopram at a dose of 10 mg/day.

Additional reprints will be made available during FY04.

The following posters will be made available during FY04:

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designed to include clinicians that may not be able to attend a dinner meeting due to scheduling conflicts or geographic challenges. Ten physicians from around the United States are convened by teleconference to discuss their experience with Lexapro and to hear specific clinical messages about Lexapro prescribing. Lexapro Peer Group moderators host each 90-minute TeleMAP session.

Both MAPs and TeleMAPs give Forest a way to reach healthcare professionals with strong, consistent product messages and to provide peer-to-peer dialogue. The Peer Group will dialogue with product management to facilitate ongoing training and provide new data to the moderators in order to create synergistic programs that leverage sales efforts as well. The participants of each program will receive a pre-meeting and post-meeting survey along with relevant literature provided by Lexapro Product Management at each event. Each participant will also receive an AMA approved honorarium valued at \$100 for his or her participation.

Timing: Q1 - Q4
Quantity: MAPS - 480 TeleMAPS - 720
Cost Per Unit: MAPS - \$4,800 TeleMaps - \$3,300
Estimated Cost: \$4,800,000

XXI. SPONSORSHIPS

A. ASSOCIATION SPONSORSHIPS

Funds have been allocated to aid the Professional Relations Group in their mission of establishing mutually beneficial long-term relationships with appropriate professionals and associations. These relationships will further best medical practices and policies in the treatment of depression and will optimize commercial opportunities for Lexapro. These relationships will also provide the basis for advocacy development and issues management, and will establish an appropriate environment for commercial and policy activities.

Additional information on associations of priority is provided as an appendix to this marketing plan (see *Appendix VII*).

Timing: Q1 - Q4
Estimated Cost: \$1,900,000

B. EMORY UNIVERSITY UNRESTRICTED EDUCATIONAL GRANT

The CNS marketing team has committed to Emory University to provide funds to the Department of Psychiatry and Behavioral Sciences (Department) at Emory for a period of three years; FY04 is the final year. The annual grant will create a fund for scientific discovery to support activity and programs related to junior faculty advancements within the Department and recognition of outstanding commitments in the field. Public relations activities surrounding this initiative to raise the awareness of Forest's support in the field of psychiatry will be explored.

Timing: Q4
Estimated Cost: \$100,000

TACTICAL PLAN

MEDICAL SCIENCE LIAISONS

The Medical Science Liaison (MSL) group for Forest Laboratories, Inc. is dedicated to providing thought leaders with the most current scientific and clinical information. Critical areas of contribution are developing and identifying strategic opportunities through phase IV research initiatives, publications, and establishing a close rapport with key members of the medical community important to Forest's therapeutic areas of interest.

Comprised of, but not limited to, professional industry Medical Liaisons, PharmDs, and MDs, these positions form the outreach network emanating from the Medical and Marketing departments assuring continued interaction with local, national, and international opinion and thought leaders within the global medical community.

The 19 CNS MSLs are charged with establishing, developing, and maintaining long term sustainable working partnerships with members of the medical community whom may have regional, national, and/or international impact. Through these collaborative relationships, 19 MSLs promote awareness of medical knowledge and issues relating to the company's ongoing development efforts, and marketed products essential to the organization. This group also serves as a front line, advanced medical/technical force to be tapped into by regional/local opinion leaders. In addition, these individuals serve as a medical information resource to managed care efforts, and facilitate various company educational programs, most notably the speaker's bureau, regional advisory boards, and regional scientific programs and symposia.

A. MSL INVESTIGATOR GRANTS

MSL Investigator Grants cover the cost of Thought Leader Initiated Phase IV studies with Lexapro. In each of these cases, the investigator approaches an MSL with his/her concept and protocol for the study.

The detailed Lexapro Phase IV program is provided as an appendix to this marketing plan (see *Appendix V*).

| | |
|------------------------|-------------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Quantity:</i> | 45 |
| <i>Cost per study:</i> | ~\$87,400 |
| <i>Estimated Cost:</i> | \$3,934,000 |

B. MSL REGIONAL CME SYMPOSIA

The MSLs will fund regionally developed and O/TL initiated CME symposia. Symposia will be funded based on the specific educational needs of the region. The symposia will be conducted in conjunction with academic health centers, medical associations and professional societies. Approximately 100-150 physicians, mostly psychiatrists, will be in attendance at each regional CME program. Cost for co-sponsorships is based on 2 co-sponsorships of established CME symposia per MSL in a year at a cost of \$20,000 per co-sponsorship for a total cost of \$40,000 per MSL per year. Since we have 19 MSLs, 2 co-sponsorships/MSL x \$20,000/co-sponsorship x 19 MSLs = approximately \$750,000.

| | |
|------------------------|-------------------------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Quantity:</i> | 38 (2 per MSL; 19 MSLs) |
| <i>Cost per grant:</i> | \$20,000 |
| <i>Estimated Cost:</i> | \$750,000 |

TACTICAL PLAN

C. MSL UNRESTRICTED GRANTS

MSL unrestricted grants cover non-symposium educational programs, publication grants, travel grants to enable O/TLs to present Lexapro posters or presentations, support of local chapters of the APA at the request of an O/TL etc.

Timing: Q1 - Q4
Budget per MSL: ~\$40,000 (about \$2,100 per O/TL)
Estimated Cost: \$750,000

D. REGIONAL GRANTS

Regional grant funds can be used to support local or regional symposia. RDs can provide up to \$20,000 in the form of unrestricted educational grants.

Timing: Q1 - Q4
Cost: \$20,000/RD (26)
Estimated Cost: \$520,000

XXII. SEMINARS AND TRAINING

A. ANNOTATED MASTER VISUAL AID

The annotated sales aid provides helpful hints and ideas so that representatives can better understand the content of the Master Visual Aid. Each bullet point in the MVA is explained and helps to provide a consistent message to the field force. The annotated sales aid will be updated once for each POA. This piece is for training purposes only and will not be used in promotion.

Timing: Q1-Q4
Quantity: 11,000 (1,942 reps, 5/rep)
Cost Per Unit: \$8.75
Estimated Cost: \$90,000

B. ANNOTATED PACKAGE INSERT

The annotated package insert allows representatives the opportunity to review the key points of the package insert and the selling messages that the points reference. The annotated package inserts will be used train representatives on the revised package insert which will include GAD information when appropriate. This piece is for training purposes only and will not be used in promotion.

Timing: Q1-Q4
Quantity: 2,000
Cost Per Unit: \$9.00
Estimated Cost: \$15,000

C. ANNOTATED REPRINTS

As new reprints are selected for promotional use the representatives need to be trained on them. The annotated reprints allow representatives the opportunity to review the key points of the clinical study and the selling messages that the points reference. These pieces are for training purposes only and will not be used in promotion.

TACTICAL PLAN

Timing: Q1-Q4
Quantity: 40,000
Cost Per Unit: \$3.15
Estimated Cost: \$120,000

D. MEETING WORKSHOPS

POA workshops will include PI and MVA reviews, clinical reprint and objection handling workshops, and role-plays. A vendor will be responsible for designing the workshops and will create all necessary leader's and participant's guides. Three POA meetings are scheduled for FY04.

Timing: Q1-Q4
Estimated Cost: \$1,300,000

E. LEARNING SYSTEM- DEPRESSION

The Lexapro Depression Learning System has been developed in FY03 and each contains six written modules, five audiotapes, two videotapes, and a complete glossary. In FY04, we expect to reproduce approximately 1000 due to expansion and other training needs. The contents of each module are:

- Module 1: *Fundamentals of Neuroanatomy and Neurotransmission*
- Module 2: *Basics of Depression and Other Disorders*
- Module 3: *Therapeutic Options for the Treatment of Depression*
- Module 4: *The Competitors and the Marketplace*
- Module 5: *Understanding Lexapro*
- Module 6: *Celexa Overview*

Timing: Q1-Q3
Quantity: 1,000
Cost Per Unit: \$100
Estimated Cost: \$100,000

F. LEARNING SYSTEM - ANXIETY

The Lexapro Anxiety Learning System will contain 4 modules with audiotapes/videotapes. The GAD training will most likely begin in September 2003 and the Panic Disorder training in January 2004. The suggested contents of each module are:

- Module 1: *Anxiety States*
- Module 2: *Lexapro and GAD*
- Module 3: *Competitors and the GAD Marketplace*
- Module 4: *Competitors and the Panic Disorder Marketplace*

Timing: Q2-Q4
Quantity: 2,000
Cost Per Unit: \$100
Estimated Cost: \$200,000

TACTICAL PLAN

XXIII. CONTESTS

A. CONTESTS

The Lexapro 20% market share club will be introduced to the field during the June 2003 National Sales Meeting. Each representative will receive an individually chosen high value gift item when they reach 20% new market share for Lexapro. Gift items are still under development but will likely be a small selection of carefully chosen items ranging from watches, wallets to candle stick holders. The ongoing Lexapro fast start contest will also be funded during FY04.

Timing: Q1-Q4
Estimated Cost: \$350,000

XXIV. CONVENTIONS

The presence of a Lexapro booth display and promotional activities at medical conventions serves to increase awareness of Lexapro and its benefits for the treatment of depression with target audiences.

The detailed Lexapro convention schedule is provided as an appendix to this marketing plan (see *Appendix I*).

A. ABSTRACTS-ON-DISK

Forest will continue to sponsor the Abstracts-on-Disk program at the national meeting of the APA and ACNP. The Abstracts-on-Disk program makes all of the abstracts and new data submissions at the meeting available to meeting participants.

Timing: Q1-Q4
Quantity: 2
Estimated Cost: \$45,000

B. ADVERTISEMENTS

A Lexapro advertisement will be placed in convention meeting booklets which are handed out to meeting participants. The advertisement is designed to be a reminder ad to physicians.

Timing: Q1-Q4
Estimated Cost: \$190,000

C. BOOTH AND PANELS

The Lexapro convention booth panels will be updated in FY04 to reflect new Lexapro data. The purpose of the panels is to attract and retain booth traffic with captivating graphics and a powerful product message. Also included are panels for tabletop and in-line displays.

Timing: Q1-Q4
Estimated Cost: \$100,000

TACTICAL PLAN

D. DRAWS/GIVEAWAYS

Every professional association meeting has its own character. Appropriate booth activities for each major meeting will be developed in order to encourage booth traffic and complement the meeting's overall tone. Forest will take advantage of many meeting sponsored "door drops" by inserting a Lexapro promotional piece that is meeting-specific (symposia invitations, etc.), booth draw (giveaways, coupons, etc.) or brand message. The Lexapro Interactive Challenge will continue to be offered at various meetings. This activity is designed to engage meeting participants in a fun, learning activity where they learn about Lexapro's promotional messages.

Timing: Q1 - Q4
Quantity: 26 conventions
Cost Per Unit: \$30,000
Estimated Cost: \$755,000

E. MEETING RECEPTIONS

Opportunities for Forest medical and marketing staff, as well as MSLs, to interact with opinion leaders (in both small and larger groups) will be scheduled at a number of major medical meetings during FY04. The purpose of these events is to develop personal relationships and provide intimate settings for scientific discussion. Programs may include dessert receptions with association members and other special events. Invitations will be issued via the MSLs. Among the meetings targeted in FY04 are the following:

- * College of Psychiatric and Neurological Pharmacists (CPNP) - May 2003
- * American Society of Health System Pharmacists (ASHP) - May 2003
- * New Clinical Development Evaluation Unit (NCDEU) - May 2003
- * American College of Neuropsychopharmacology (ACNP) - December 2003
- * Anxiety Disorders Association of America (ADAA) - March 2004

Timing: Q1 - Q4
Quantity: 5 receptions @ \$24,000
Estimated Cost: \$120,000

XXV. PUBLICATIONS

Publications will be geared toward psychiatrists, PCPs, pharmacists, osteopaths, nurses, managed care organizations, LTC and others. Articles will appear in several formats, including original reports, review articles, and journal supplements. It is the brand team's intention to aggressively disseminate all new clinical data analyses when available.

A. ABSTRACTS AND POSTERS

Emerging preclinical and clinical data, as well as pooled analyses of Lexapro data, will be disseminated in poster (or occasionally oral/slide) format at all appropriate medical meetings. During FY04, approximately 70 abstracts/posters (both original and reread) will be presented at

TACTICAL PLAN

U.S. meetings with a similar number of abstracts/posters presented at European meetings. The focus of the presentations in FY04 will be comparative and switch data in both depression and anxiety, clinical data in depression, GAD, panic disorder, SAD, and safety data. There will also be ample preclinical data and data from investigator initiated studies.

See *Appendix II* for the detailed publication plan

| | |
|------------------------|----------------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Quantity:</i> | 50 |
| <i>Cost Per Unit:</i> | \$6,000/poster |
| <i>Estimated Cost:</i> | \$300,000 |

B. MANUSCRIPTS

As detailed in the Forest/Lundbeck Escitalopram Poster and Manuscript Preparation Plan (*Appendix II*), publications will be generated based on preclinical and clinical data, as it becomes available. Articles will appear in several formats, including original reports, review articles, and journal supplements. Approximately 10-12 manuscripts based on original data (generated by Forest) will be developed and submitted for publication during FY04, supporting the usefulness of Lexapro in the acute and long-term treatment of depression, and in the treatment of anxiety disorders (GAD, panic disorder, and SAD). There will also be publications on the comparative trials with venlafaxine, paroxetine, and sertraline, as well as the switch study with fluoxetine. Additionally, up to 10-12 review articles will be developed and submitted for publication during FY04. Articles will include reviews of Lexapro-specific pharmacology, efficacy in depression, efficacy in anxiety disorders, and safety including geriatric and pediatric patients (e.g., targeted to psychiatry, primary care, psychopharmacology, and pharmacy/formulary journals), as well as articles that include Lexapro data within the context of a broader review (e.g., safety in the geriatric population, current approaches to treating anxiety disorders, and selectivity of action).

See *Appendix II* for the detailed publication plan

| | |
|------------------|----------------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Quantity:</i> | 24 manuscripts |
| <i>Cost:</i> | \$700,000 |

C. PUBLICATION PLANNING AND STRATEGIC COUNSEL

Publication planning includes all agency time spent managing the publication grid, researching potential publication topics and attending all publication related activities and meetings. Strategic counsel and input to marketing activities as well as the development of strategic and tactical plans for the FY05 marketing plan.

| | |
|----------------|-----------|
| <i>Timing:</i> | Q1 - Q4 |
| <i>Cost:</i> | \$350,000 |

D. ROUNDTABLES

Closed roundtables provide opportunities for a small group of experts to discuss topics especially relevant to the positioning and marketing of Lexapro. The deliverable from a roundtable is a journal supplement that is disseminated to a much larger audience. Closed roundtables can be held in conjunction with major medical meetings, or as stand-alone events. It is recommended that four

TACTICAL PLAN

closed roundtables be held during FY04. Suggested topics include: 1) Panic Disorder; 2) SAD; 3) Geriatric; 4) Pediatric; and 5) Somatic symptoms associated with depression and anxiety.

Timing: Q2 - Q4
Quantity: 4 events
Cost: \$500,000 (Includes event only)

E. SUPPLEMENTS

As part of a comprehensive publication plan, journal articles and supplements will be developed based on important content of particular Forest-sponsored symposia and roundtables. These published manuscripts will help disseminate relevant Lexapro data and messages to key target audiences, including psychiatrists, primary care physicians, managed care organizations, long-term care medical directors, and others. This amount assumes submission and publication of four supplements, and includes editorial support and page charges and does not include costs for reprints.

Timing: Q2 - Q4
Quantity: 4
Cost Per Unit: \$162,500
Estimated Cost: \$630,000

TACTICAL PLAN

APPENDIX I

CONVENTION SCHEDULE

| APRIL | | MIK = Medical Information Kiosk | |
|---------|---|---------------------------------|--------------|
| 1 - 3 | AAN - American Academy of Neurology Honolulu, HI | 8,000 | 10x10 |
| 3 - 5 | PRI-MED WEST Long Beach, CA | 7,000 | 20x30 |
| 3 - 5 | ACP/ASIM - American College of Physicians American Society of Internal Medicine San Diego, CA | 6,000 | 20x30 |
| 9 - 12 | AMCP - American Managed Care Pharmacy Minneapolis, MN | 3,000 | 30x30 MIK |
| 28 - 30 | ACOG - American College of Obstetricians & Gynecologists New Orleans, LA | 5,000 | 20x30 |
| MAY | | | |
| 14 - 16 | ASCP - American Society of Consultant Pharmacists Midyear Geriatrics '03 - Tampa, FL | 1,500 | 20x40 |
| 15 - 16 | AGS - American Geriatrics Society Baltimore, MD | 2,500 | 20x30 |
| 18 - 21 | APA - American Psychiatric Association San Francisco, CA | 16,000 | 60x80 MIK |
| JUNE | | | |
| 9 - 10 | NADONA/LTC Cincinnati, OH | 400 | 10x20 |
| 19 - 21 | PRI-MED MIDWEST Rosemont, IL | 7,000 | 30x30 |
| 19 - 21 | US GERI - US Geriatrics & Long-Term Care Congress San Francisco, CA | 2,000 | 30x30 |

| JULY | | | |
|------------------|---|--|--------------|
| | | MIK = Medical Information Kiosk | |
| 10 - 12 | Nurse Practitioner Symposium Keystone, CO | 1,500 | 10x30 |
| AUGUST | | | |
| 23 - 27 | NACDS - National Association of Chain Drug Store Pharmacists Philadelphia, PA | 2,600 | 10x30 |
| SEPTEMBER | | | |
| | | | |
| OCTOBER | | | |
| 2 - 4 | AAFP - Am. Acad. of Family Physicians New Orleans, LA | 6,500 | 30x50 MIK |
| 2 - 4 | APNA - American Psychiatric Nurse Assoc. Atlanta, GA | 2,000 | 10x20 |
| 12 - 15 | AOA - American Osteopathic Association New Orleans, LA | 3,500 | 20x30 |
| 16 - 18 | PRI-MED MID-ATLANTIC Washington, DC | 5,000 | 20x30 |
| 19 - 22 | ANA - American Neurological Association San Francisco, CA | 1,300 | 10x20 |
| 10/30 - 11/1 | APA-I - Am. Psychiatric Association - Institute of Psych. Services Boston, MA | 2,200 | 20x30 |
| ?? | NAVY ACP Location? | 200 | Table Top |
| NOVEMBER | | | |
| 6 - 9 | US PSYCH & MHC - US Psych & Mental Health Congress Orlando, FL | 3,000 | 30x30 |
| 7 - 9 | PRI-MED EAST Boston, MA | 7,000 | 30x40 |
| 12 - 14 | ASCP Annual - American Society of Consultant Pharmacists San Antonio, TX | 2,000 | 30x30 |
| ?? | ARMY ACP Location? | 200 | Table Top |
| DECEMBER | | | |
| 8 - 11 | ASHP - American Society of Health System Pharmacists New Orleans, LA | 18,000 | 30x30 |

| JANUARY | | | |
|--|---|--------------|----------------------|
| MIK = Medical Information Kiosk | | | |
| FEBRUARY | | | |
| 13 - 15 | PRIMED WEST Long Beach, CA | 8,000 | 30X40 |
| MARCH | | | |
| 1 - 4 | NMHCC - National Managed Health Care Congress Washington, DC | 3,000 | 10x30 |
| 4 - 6 | AMDA - American Medical Directors Association Phoenix, AZ | 1,200 | 20x20 |
| 12 - 15 | AAGP - American Academy of Geriatric Psychiatry Atlanta, GA | 1,250 | 30x30 MIK |
| ?? | ADAA - Anxiety Disorders of America Location?? | 350 | 10x20 |
| 28 - 30 | APhA - American Pharmaceutical Association Seattle, WA | 5,000 | 20x20 |

APPENDIX II

PUBLICATION PLAN

APPENDIX II PUBLICATION PLAN

APPENDIX II

Publication Plan

| Forest/Lundbeck Escitalopram Studies | | | | | | | | | | |
|--|------|---|----------------|--|--------------|-------------------|-----------------------------------|----------------------------|---------------------|---|
| Poster and Manuscript Preparation Plan | | | | | | | | | | |
| Study | Type | Description | Study Director | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Comments |
| PK-01 | PK | Desipramine/Fluoxetine in vivo 2D6 pathway | FRX | Escitalopram has the lowest potential for drug interactions | Nov-00 | | | | | Data insufficient to support publication To be included in PK review article |
| PK-02 | PK | Ritonavir/lo control in vivo 3A4 pathway | FRX | Escitalopram has the lowest potential for drug interactions | Jan-01 | | SOBP May-01 NCDEU May-01 | Sep-02 | Apr-03 | Clinical Therapeutics, in press |
| PK-03 | PK | Metoprolol/Paroxetine in vivo 2D6 pathway | FRX | Escitalopram has the lowest potential for drug interactions | Dec-00 | | | | | Data insufficient to support publication To be included in PK review article |
| PK-04 | PK | BE tablet marketing vs clinical | FRX | NA | Jan-01 | NA | NA | NA | NA | NA |
| PK-05 | PK | Pharmacokinetics in healthy elderly vs healthy young adult volunteers | FRX | Escitalopram has an excellent dosing profile | Sep-00 | | | | | To be included in PK review article |
| PK-06 | PK | BE oral solution vs tablet (food effect) | FRX | Escitalopram has an excellent dosing profile | Mar-01 | NA | NA | | | To be included in PK review article |
| PK-07 | PK | Drug interaction with warfarin | FRX | Escitalopram has the lowest potential for drug interactions | Apr-01 | | | | | |
| PK-13 | PK | Pharmacokinetics in pediatric patients | FRX | Escitalopram has an excellent dosing profile | Planned | | | | | |
| 98106 | PK | Single dose study to compare the pharmacokinetics and tolerability of escitalopram and citalopram | HLU | Escitalopram has an excellent dosing profile | Available | | NCDEU May-01 | | | To be included in PK review article |
| 98107 | PK | Double-blind, multi-dose, bio-way crossover comparing the pharmacokinetics and tolerability of escitalopram and citalopram | HLU | Escitalopram has an excellent dosing profile | Available | NA | NA | NA | NA | Data insufficient to support publication To be included in PK review article |
| 98113 | PK | Bridging study of FRX and HLU clinical formulations and dosage form equivalence | HLU | NA | Sep-00 | NA | NA | NA | NA | NA |
| 98186 | PK | Dose-proportionality at 10, 20 and 30 mg. also assesses effect of age | HLU | Escitalopram pharmacokinetics is linear and only modestly altered by age or gender | Oct-00 | | | | | |
| In vitro P450 isoenzymes | PK | R-Ct, S-Ct, R-OCT, and S-OCT are weak or negligible inhibitors of human cytochromes P450. This is unlikely to be of clinical importance | | Escitalopram has the lowest potential for drug interactions | Available | | | Nov-00 | Published Aug-01 | vol Motile et al., Drug Metab Dispos 2001,29 1102-9 |

Clinical Data

| Study | Time | Description | Study Disease | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Conference | |
|-------|------|---|---------------|---|--------------|-------------------|----------------|----------------------------|---------------------|---|--|
| MD-01 | 0 | Head to Head Comparison of the Safety and Efficacy of Escitalopram, Citalopram, and Placebo in the Treatment of Major Depressive Disorder | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Dec-00 | | | | Submitted Mar-01 | Published Apr-02 | Burks et al., J Clin Psychiatry 2002, 63:331-338 |
| | | | | | | | ACAP Dec-00 | | | primary results poster | |
| | | | | | | | APA May-01 | | | results poster with additional posters that pool data from MD-01, MD-02 and 99003 (efficacy comparison of S-CT with CT) MD-01, MD-02 and 99003 (comparison of effects of S-CT and CT on anxiety Sx) | |
| | | | | | | | NCEU May-01 | | | primary results poster | |
| | | | | | | | WCP Jul-01 | | | results poster with additional posters that pool data from MD-01, MD-02 and 99003 (efficacy comparison of S-CT with CT) MD-01, MD-02 (comparison of effects of S-CT and CT on anxiety Sx) | |
| | | | | | | | APA Oct-01 | | | Poster pools data from MD-01, MD-02 (comparison of effects of S-CT and CT on anxiety Sx) | |
| | | | | | | | SNP Apr-02 | | | Poster based on MADRS single item subscale | |
| | | | | | | | ACP May-02 | | | Poster pools data from MD-01, MD-02, 99003 (efficacy comparison w/ CT) | |
| | | | | | | | APA May-02 | | | Poster pools data from MD-01, MD-02, 99003 (efficacy comparison w/ CT) | |
| | | | | | | | NCEU Jun-02 | | | Poster pools data from MD-01, MD-02, 99001, 99003 (safety database) w/ SCT vs CT comparison | |
| | | | | | | | CNP Jun-02 | | | Poster pools data from MD-01, MD-02, 99003 (efficacy in severity # patients) | |
| | | | | | | | WCP Aug-02 | | | Poster pools data from MD-01, 99001 for MADRS single item subscale Poster pools data from MD-01, MD-02, 99001, 99003 (efficacy in severity # patients) | |
| MD-01 | cont | | | | | | | | | | |

| Block | Drug | Description | Study Director | Key Messages | Final Report | Abstract Due Date | Manuscript Submission Date | Publication Date | Journal/Comments |
|-------|------|--|----------------|--|--------------|-------------------|--|---|--|
| MD-03 | D | Phase-III Controlled Evaluation of the Safety and Efficacy of Escitalopram in the Prevention of Depression Relapse | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Oct-01 | Feb-03 | ACNP Dec-01 AEP May-02 NDEU Jun-02 CNP Jun-02 WCP (WPA) Aug-02 APA1 Dec-02 ECP Oct-02 CPNP Apr-03 | Poster pools data from MD-01, MD-02, 99001, 99002 (efficacy in severity of relapse) Poster pools data from MD-01, MD-02, 99001, 99002 (safety in geriatric patients) Poster pools data from MD-01, MD-02, 99001, 99002, 99004 (safety in geriatric patients) Poster pools data from MD-01, MD-02, 99001, 99002 (efficacy in severity of relapse) | Journal/Comments |
| MD-04 | A | Phase Dose Comparison of the Safety and Efficacy of Escitalopram, Citalopram, and Placebo in the Treatment of Panic Disorder | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram has improved side effect, drug interaction and safety profile resulting from the removal of the inactive isomer, the R-enantiomer | Feb-02 | Feb-03 | ADAA Mar-02 APA May-02 NDEU Jun-02 CNP Jun-02 WCP (WPA) Aug-02 | Poster pools data from MD-03, 99002, 99002a (long-term tolerability) Primary results poster and 2nd poster with switch data Primary results poster and 2nd poster with switch data Poster pools data from MD-03, 99002, 99002a (long-term tolerability) | J Clin Psychiatry, submitted Primary results poster 2nd poster pools data from MD-04, MD-03, 99012, placebo (analogy effects predicted by animal models) |

| Study | Track | Description | Study Director | Key Message | Final Report | Abstract Due Date | Meeting Date | Minisession Date | Publication Date | Journal Comments |
|-------|-------|---|----------------|--|--------------|-------------------|--|---|------------------|---|
| MD-05 | A | Flexible Dose Comparison of Safety & Efficacy of S-CT vs Placebo in the Treatment of Generalized Anxiety Disorder | FFOX | Escitalopram represents a new more selective and/or potent generation of SSRNs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Dec-01 | Nov-02 | ADAA Mar-03 ACNP Oct-02 ECNP Oct-02 ADAA Mar-03 | ADAA Mar-03 ACNP Oct-02 ECNP Oct-02 | Dec-01 | Primary results poster 2nd poster pools data from MD-04, MD-05, 99012, preclinical (anxiolytic effects predicted by animal models) Poster pools data from MD-04, MD-05, 99012, preclinical (anxiolytic effects predicted by animal models) Poster pools data from MD-04, MD-05, 99012, preclinical (anxiolytic effects predicted by animal models) Publish as part of pooled analyses of GAD trials? |
| MD-06 | A | Flexible Dose Comparison of Safety & Efficacy of S-CT vs Placebo in the Treatment of Generalized Anxiety Disorder | FFOX | Escitalopram represents a new more selective and/or potent generation of SSRNs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram has a favorable side effect profile | Oct-02 | Nov-02 | ACNP Dec-02 ADAA Mar-03 | ACNP Dec-02 ADAA Mar-03 | Oct-02 | Primary results poster 2nd poster pools data from MD-04, MD-05, 99012, preclinical (anxiolytic effects predicted by animal models) Poster pools data from MD-04, MD-05, 99012, preclinical (anxiolytic effects predicted by animal models) Poster pools data from MD-04, MD-05, 99012, preclinical (anxiolytic effects predicted by animal models) Poster pools data from MD-05, MD-06, MD-07 Additional poster pools data from MD-05, MD-06, MD-07 Poster pools data from MD-05, MD-06, MD-07 Publish as part of pooled analyses of GAD trials? Poster pools data from MD-05, MD-06, MD-07 Poster pools data from MD-05, MD-06, MD-07 |

| Study | Topic | Description | Study Design | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Comments |
|-------|-------|---|--------------|--|--------------------------------------|-------------------|--|----------------------------|------------------|---|
| MD-07 | A | Flexible Dose Comparison of Safety & Efficacy of S-CT vs Placebo in the Treatment of Generalized Anxiety Disorder | PRX | Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of anxiolytic effect Escitalopram represents a new more selective anxiolytic potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile | Oct-02 | Feb-03 Jan-03 | CHMP Apr-03 APA May-03 | Dist Jan-03 | | Poster pools data from MD-05, MD-06, MD-07 Poster pools data from MD-05, MD-06, MD-07 Depression and Anxiety, submitted Also publish as part of pooled analysis of SSAD trials? Primary efficacy poster Additional poster pools data from MD-05, MD-06, MD-07 Primary efficacy poster Additional poster pools data from MD-05, MD-06, MD-07 Primary efficacy poster Additional poster pools data from MD-05, MD-06, MD-07 Primary efficacy poster |
| MD-08 | D | Drug Combination in S-CT Nonresponders from Placebo Study | PRX | Escitalopram represents a new more selective anxiolytic potent generation of SSRIs | Nov-02 | | | | | |
| MD-09 | D | Prevalence Sleep, Fluid dose comparison of escitalopram and placebo in patients with MDD, double blind, randomized, parallel group | PRX | Escitalopram represents a new more selective anxiolytic potent generation of SSRIs Escitalopram has a favorable side effect profile Escitalopram is an effective first line treatment for depression Escitalopram has a favorable side effect profile | Oct-02 | | | | | |
| MD-10 | D | Psychomotor / Alcohol Interaction, Motor volume levels of escitalopram and alcohol in healthy volunteers | PRX | Escitalopram does not potentiate effects of alcohol Escitalopram has a favorable side effect profile | Oct-02 | Oct-02 Jan-03 | BoGP May-03 NCDEU May-03 | | | |
| MD-11 | D | Depression Recurrence/Switch Cyan-Label recurrence in responders after switch from other SSRIs to S-CT Response to S-CT in previous non-responders to other SSRIs Response to S-CT in previous AE drops with other SSRIs Double-blind recurrence in S-CT responders | PRX | Escitalopram represents a new more selective anxiolytic potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram has a favorable side effect profile Escitalopram is the active isomer of citalopram in terms of antidepressant effect | Feb-02 Apr-02 Apr-02 Aug-02 | | CHMP Jan-02 WCP (WPA) Aug-02 ECMP Oct-02 APA-I Oct-02 | | | Response to S-CT in previous AE drops with other SSRIs Response to S-CT in previous AE drops with other SSRIs Response to S-CT in previous AE drops with other SSRIs Response to S-CT in previous AE drops with other SSRIs |

| Study | Treat | Description | Study Director | Key Messages | Final Report Due Date | Abstract Due Date | Meeting Date | Abstract Submission Date | Publication Date | Journal/Comments |
|-------|-------|--|----------------|---|-----------------------|-------------------|--------------|--------------------------|------------------|---|
| MD-12 | D | Variable comparative | FRX | | Aug-03 | | | | | |
| MD-13 | D | Prophylactic | FRX | | Jan-04 | | | | | |
| MD-16 | D | 9-week double blind comparison of escitalopram and fluoxetine in MDD | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first-line treatment for depression Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive isomer, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Jan-02 | | | | | |
| MD-17 | A | Open Label Extension of Safety & Efficacy of S-CT in the Treatment of Generalized Anxiety Disorder | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first-line treatment for anxiety disorders Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Nov-02 | | | | | |
| MD-18 | D | Variable comparative | FRX | | Aug-03 | | | | | |
| MD-19 | D | Open Label Extension of Safety & Efficacy of S-CT in Depression | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs | Oct-03 | | | | | |
| MD-20 | A | Comparison of Safety & Efficacy of S-CT vs Paroxetine in the Treatment of Generalized Anxiety Disorder | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs | Apr-03 | | | | | |
| MD-21 | D | Fluoxetine Switch | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs | Jun-03 | | | | | |
| MD-26 | D | In-patient depression | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs | Feb-04 | Jan-03 | APA May-03 | | | |
| | | | | | | Jan-03 | NCOEU May-03 | | | |
| 99001 | D | 10 mg fixed dose for MDD | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first-line treatment for depression | Available | | | Dec-01 | May-02 | Woods et al., International Clinical Psychopharmacology 2002;17 86-102 S-CT 10 mg vs placebo |

| Study | Phase | Study Arm(s) | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manufacture Submission Date | Publication Date | Journal/Comment | | | | |
|------------|-------|--|--|--------------|-------------------|---|-----------------------------|------------------|--|--|--|--|--|
| 99001 cont | | | - 10 mg dose - primary care setting - no difference in AE drop outs vs placebo Escitalopram has a favorable side effect profile Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | WOSP Jul-01 | | | S-CT 10 mg vs placebo additional poster pools data from MD-01, MD-02, 99001, 99003 (safety) (safety comparison of S-CT and CT) S-CT 10 mg vs placebo | | | | |
| | | | | | | Forum on Mood & Anxiety Disorders Nov-01 | | | | Poster pools data from MD-01, MD-02, 99001, 99003 (safety database) S-CT 10 mg vs placebo 2nd poster pools data from MD-01, MD-02, 99001, 99003 (safety database) w/ S-CT vs CT comparison Poster pools data from MD-01, MD-02, 99001, 99003 (efficacy in anxiety disorders) Poster pools data from MD-01, 99001 for MOCs single item analysis | | | |
| 99002 | D | Open long-term treatment from 99001 or 99003 | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of antidepressant/analgetic effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Feb-02 | | | | | | TBD Primary results, long-term efficacy Poster pools data from MD-03, 99002, 99022 (long-term tolerability) Poster present long-term efficacy of escitalopram Second poster presents data on switch from citalopram | | | |
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| Study | Year | Description | Study Director | Key Messages | Final Report | Abstract Date | Meeting Date | Abstract Submission Date | Publication Date | Journal/Comments |
|------------|------|--|----------------|--|--------------|---------------|----------------|--------------------------|------------------|--|
| 99003 | 0 | Flexible-dose comparative of citalopram and Escitalopram | HU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram has an excellent dosing profile Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profile resulting from the removal of the inactive isomer, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Available | Jan-03 | SCMP Apr-03 | TBD | TBD | Long-term efficacy of escitalopram TBD 4-week data combined with PCL-104 Montgomery et al "Pharmacol Ther" 2001, 68: 295-305 pooled 4-week "low" dose, 8-week flexible dose pooled 4-week "high" dose additional pooled data from MD-01, MD-02 and 99003 (efficacy comparison of S-CT with CT) MD-01, MD-02 and 99003 (comparison of effects of S-CT and CT) Pooled data from MD-01, MD-02, 99003 (comparison of effects of S-CT and CT on anxiety S4) pooled 4-week "high" dose additional pooled data from MD-01, MD-02 and 99003 (efficacy comparison of S-CT with CT) and MD-01, MD-02, 99001, 99003 (safety comparison of S-CT and CT) Pooled data from MD-01, MD-02, 99003 (comparison of effects of S-CT and CT on anxiety S5) Pooled data from MD-02, 99003 (efficacy comparison of CT in flexible dose studies) Pooled data from MD-01, MD-02, 99003 (efficacy comparison of CT) |
| 99003 cont | | | | | | | APA May-02 | | | Pooled data from MD-01, MD-02, 99001, 99003 (safety database) Pooled data from MD-01, MD-02, 99001, 99003 (safety database) w/ SCT vs CT comparison Pooled data from MD-01, MD-02, 99001, 99003 (efficacy in anxiety & patients) Pooled data from MD-01, MD-02, 99003 (efficacy in anxiety & patients) Primary results pooled 2nd pooled data from MD-01, MD-02, 99003 (efficacy in anxiety & patients) Pooled data from MD-01, MD-02, 99001, 99003 (safety in genetic patients) Pooled data from MD-01, MD-02, 99001, 99003 (safety in genetic patients) Primary results pooled |

Revised March 5, 2003

| Study | Type | Description | Study Design | Key Messages | Final Report | Abstract Date/Event | Meeting/Event | Minimally Substantiated Date | Publication Date | Journal/Comments |
|-------|-------------|---|--------------|---|--------------|---------------------|------------------|--|------------------|--|
| 99072 | D | <p>Phase 3 comparative treatment of citalopram and escitalopram</p> <p>... will include PE assessment</p> | HLU | <p>Escitalopram represents a new more selective and/or potent generation of SSRIs</p> <p>Escitalopram is an effective first line treatment for depression</p> <p>Escitalopram has a favorable side effect profile</p> <p>Escitalopram has an excellent dosing profile</p> <p>Escitalopram is the active isomer of citalopram in terms of antidepressant effect</p> <p>Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the racemic moiety, the R-enantiomer</p> <p>Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability</p> <p>Escitalopram represents a new more selective and/or potent generation of SSRIs</p> | Sep-01 | Jan-03 | AAOP Mar-03 | | | Poster pools data from MD-01, MD-02, 99001, 99003, 99024 (safety in geriatric patients) |
| | | | | | | Feb-03 | SCMP Apr-03 | | | Primary results poster |
| | | | | | | | CPMP Apr-03 | | | Poster pools data from MD-01, MD-02, 99001, 99003, 99024 (safety in geriatric patients) |
| | | | | | | | CHMP Jun-02 | | | Poster pools data from MD-03, 99002, 99022, (long-term tolerability) |
| | | | | | | | WCP (WPA) Aug-02 | | | Poster pools data from MD-03, 99002, 99022, (long-term tolerability) |
| | | | | | | | ECMP Oct-02 | | | Poster pools data from MD-03, 99002, 99022, (long-term tolerability) |
| | | | | | | | IFMAD Nov-02 | | | |
| | | | | | | | SCMP Apr-03 | | | |
| | | | | | | | ECMP Sep-03 | | | |
| | | | | | | 99074 | D | <p>Fixed dose comparison of SCT or fluoxetine vs paroxetine in elderly patients with MDD</p> | HLU | <p>Escitalopram is an effective first line treatment for depression</p> <p>Escitalopram has a favorable side effect profile</p> <p>Escitalopram has an excellent dosing profile</p> <p>Escitalopram is the active isomer of citalopram in terms of antidepressant effect</p> |
| | AAOP Mar-03 | | | Poster pools data from MD-01, MD-02, 99001, 99003, 99024 (safety in geriatric patients) | | | | | | |
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| 99112 | A | <p>Phase 3 Controlled Evaluation of the Safety and Efficacy of Escitalopram in Social Anxiety Disorder. Flex doses 10-20 mg escitalopram vs placebo</p> | HLU | <p>Escitalopram represents a new more selective and/or potent generation of SSRIs</p> <p>Escitalopram is an effective first line treatment for anxiety disorders</p> <p>Escitalopram has a favorable side effect profile</p> <p>Escitalopram has an excellent dosing profile</p> <p>Escitalopram is the active isomer of citalopram in terms of anxiolytic effect</p> | Nov-01 | | | Dec-01 | TBD | TBD |
| | | | | | | | ADAA Mar-02 | | | |
| | | | | | | | SCMP Apr-02 | | | |
| | | | | | | | ACP May-02 | | | |
| | | | | | | | APA May-02 | | | |
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| Study | Year | Description | Study Director | Key Messages | Final Report | Abstract Due Date | Meeting Date | Abstract Submission Date | Publication Date | Journal/Comments |
|-------|------|---|----------------|--|--------------|-------------------|--|--------------------------|------------------|--|
| 99007 | | Venlafaxine | HLU | | | Jun-02 | ECNP Oct-02 FMAD Mar-02 SCHP Apr-03 SPOR May-03 | ECNP Oct-02 | | Primary results poster 2nd poster pools data from MD-04, MD-05, 99012, preclinical (anxiety) effects predicted by animal models Poster pools data from MD-04, MD-05, 99012, preclinical (anxiety) effects predicted by animal models Primary results poster 2nd poster pools data from MD-04, MD-05, 99012, preclinical (anxiety) effects predicted by animal models Poster pools data from MD-04, MD-05, 99012, preclinical (anxiety) effects predicted by animal models |
| 99187 | | Pragmatic | HLU | | Nov-01 | Nov-01 | | | | |
| 99238 | | Elderly, 10mg-30mg | HLU | | Sep-02 | Sep-02 | | | | |
| 99289 | A | Phase-Controlled Evaluation of the Safety and Efficacy of Escitalopram in Social Anxiety Disorder. Four doses 10-30 mg escitalopram vs placebo, release prevention | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active moiety of citalopram in terms of anxiolytic effect | Feb-03 | Nov-02 | ADAA Mar-03 APA May-03 NDDUE May-03 SPOR May-03 | ADAA Mar-03 | | Primary results poster and P/E poster Primary results poster and P/E poster Primary results poster P/E evaluation of response vs non-response Primary results poster and two P/E posters |
| 99270 | A | Phase-Controlled Evaluation of the Safety and Efficacy of Escitalopram in Social Anxiety Disorder. Dose-titration 5 mg, 10 mg, 15 mg escitalopram, placebo and paroxetine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram has a favorable side effect profile Escitalopram has an excellent dosing profile Escitalopram is the active moiety of citalopram in terms of anxiolytic effect | Mar-03 | Jan-03 | Apr-03 ECNP Sep-03 | Apr-03 | | |

| Index | Doc# | Description | Study Director | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Conference |
|---------|------|--|----------------|--|--------------|-------------------|--|----------------------------|------------------|--|
| 9555 | D | Paroxetine | HLU | | Mar-95 | | | | | |
| 9578 | A | GLAD release prevention | HLU | | GI-5005 | | | | | |
| 9915 | A | GLAD release prevention | HLU | | CS-2004 | | | | | |
| 9949 | D | PMDD | HLU | | Mar-01 | | | | | |
| 9950 | A | Paroxetine for SSRI | HLU | | GI-5005 | | | | | |
| PCL-001 | A | Paroxetine Anxolytic, feedback induced ultramicro encapsulation. CT and S-CT potency induced feedback induced ultramicro encapsulation The maximum inhibition was 60-70% for CT and S-CT inhibited completely RCT inhibited encapsulation with an approximately 15 times lower potency than S-CT Comparisons SSRIa, RCT & S-HTP encapsulation | HLU | Escitalopram represents a new more selective anxiolytic potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Available | | ACNP Dec-00 APA May-01 NDDU Jan-01 WCSP Jul-01 SCNP Apr-02 CNP Jun-02 ECNP Oct-02 | Jul-01 | | Journal TBD manuscript combines data from PCL-001, PCL-002, PCL-003, PCL-101, PCL-103, PCL-107, PCL-302, and in vitro uptake inhibition poster combines data from PCL-001, PCL-002, PCL-303 |
| PCL-002 | A | GLAD (black and white box) set and mica, Comparisons SSRIa, RCT, S-HTP encapsulation | HLU | Escitalopram represents a new more selective anxiolytic potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Available | | ACNP Dec-00 APA May-01 NDDU Jan-01 WCSP Jul-01 ECNP Oct-02 | Jul-01 | | manuscript combines data from PCL-001, PCL-002, PCL-003, PCL-101, PCL-103, PCL-107, PCL-302, and in vitro uptake inhibition poster combines data from PCL-001, PCL-002, PCL-303 |
| PCL-003 | A | Paroxetine Anxolytic, feedback induced ultramicro encapsulation. Comparisons R-Reserpine, venlafaxine, reboxetine | HLU | Escitalopram represents a new more selective anxiolytic potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders | Available | | SCNP Apr-02 CNP Jan-02 | Jul-01 | | Journal TBD manuscript combines data from PCL-001, PCL-002, PCL-003, PCL-101, PCL-103, PCL-107, PCL-302, and in vitro uptake inhibition poster combines data from PCL-001, PCL-003 poster combines data from PCL-001, PCL-002, PCL-003, PCL-101, PCL-103, PCL-107, PCL-302, and in vitro uptake inhibition poster combines data from PCL-001, PCL-002, PCL-303 |

| Study | Topic | Description | Study Design | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manufacture Submission Date | Publication Date | Journal/Comments |
|---------|-------|---|--------------|---|--------------|-------------------|--|-----------------------------|------------------|--|
| PCL-004 | A | Prone to Anxiety, Isotonic Induced Vibrotactile vocalization Comparisons RCT & S-CT | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Available | | ESNP Oct-08 | | | Poster combines data from PCL-001, 002, 101, 102, SSRIs in anxiety, Bibliography, Bibliography |
| PCL-005 | A | Prone to Anxiety, Dorsal Periosteal Oxy Stimulation (DPAS), where panic like attacks are induced by electric stimulation in the periauricular gray area in the brain Acute effect of SSRIs. This model is under development and should be available for assessments in Q3 00 Plans include three responses S-, R-, R,S-CT, combination S- and R-rates 1,2 and 1,4 | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Available | | SNRP May-02 CNP Jan-02 WCP (MPA) Aug-02 | | | Poster combines data from PCL-002, PCL-004, PCL-005, PCL-006 |
| PCL-006 | A | OOD, Polyphasic, rat Abnormal drinking behavior is induced by restricted and scheduled availability of food Applicable as model onset of action Comparisons R-R, R-R, RCT, presentation, Sensitization, variability | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect Escitalopram has a faster onset of action Escitalopram represents a new more effective and/or potent generation of SSRIs | Available | | | | | |
| PCL-007 | A | GAO, GABA α 2-receptor deficient mice, conditioned fear stress model New investigator needed | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders | Planned | | | | | |
| PCL-008 | A | OAD, Conditioned fear stress, rat, Frazzetta, UCLA | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | | | ESNP Oct-02 | | | May be stand-alone |
| PCL-009 | A | S-HIT1A receptor knockout New investigator needed | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for anxiety disorders Escitalopram is the active isomer of citalopram in terms of anxiolytic effect | Planned | | | | | |
| PCL-010 | A | PMOD, Progesterone metabolism in vivo, Comparisons RCT, Benzodiazepine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs | Available | | | | | Possibility for ACCOG May-02 |

| Study | Treat | Description | Study Details | Key Messages | Final Report | Abstract Date | Meeting Date | Meeting Submission Date | Publication Date | Journal/Comments |
|---------|-------|---|---------------|--|------------------------------|---------------|--|-------------------------|------------------|---|
| PCL-102 | D | Depression/Onset of action, Agnostic Behavior Rat, Paul Michael Results from the last study indicate that escitalopram is more than twice as potent as CT in acute test. The chronic study suggests an antidepressant profile. It is recommended to perform follow up studies (follow up study is PCL-106) 1) Complete dose response relationship S- and R-CT, test PCT alone, test combination of R and S, ratio 4:1 2) Onset of action study escitalopram vs CT with daily assessment for 7 days | MLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram has a faster onset of antidepressant action Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Available | | CHMP Jul-00 CHMP Jun-02 CHMP Oct-02 ACHP Dec-00 SOBP May-01 WCBP Jul-01 | | | Poster combines data from PCL-001, PCL-101, 103, SSRIs in anxiety, depression, aggression Poster combines data from PCL-001, PCL-101, 103, SSRIs in anxiety, depression, aggression Poster combines data from PCL-102, PCL-103 and PCL-303 Poster combines data from PCL-102, PCL-106 Abstract can combine data from PCL-102 with PCL-106 |
| PCL-103 | D | Depression, behavior, aggressive mice Neither CT nor its enantiomers inhibited aggressive behavior of isolated mice CT and S-CT but not R-CT inhibited aggressive behavior primarily if they were administered with 1-S-HTP Compared: SSRIs, PCT, 1-S-HTP administration | MLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Available | | ACHP Dec-00 SOBP May-01 CHMP Jan-02 | | | Poster combines data from PCL-102, PCL-103 and PCL-303 |
| PCL-104 | D | Depression/Onset of action, Effect in chronic mild stress model, rat, M. Prapp, Comparison: CT, R-fluoxetine S-CT was as potent as R-fluoxetine, onset of week 1 2 options S-CT compared with R-fluoxetine S-CT compared with CT | MLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability Escitalopram has a faster onset of antidepressant action | Available | | APA May-01 MCDU May-01 WCBP Jul-01 Forum on Mood & Anxiety Disorders Nov-01 SOBP May-02 | | | Poster combines data from PCL-001, PCL-101, 103, SSRIs in anxiety, depression, aggression Psychoneurobiology |
| PCL-105 | D | Depression/Onset of action, HPA axis function. Assessment of baseline and stress induced changes of mRNA POMC expression in anterior pituitary and serum corticosterone in rats treated acutely and chronically, respectively, with S or R- | MLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect | Ongoing, may be discontinued | | | | | |

| Study | Type | Description | Study Director | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Comments |
|---------|------|---|----------------|--|--------------|-------------------|--------------|----------------------------|------------------|--|
| | | | | Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | | | | |
| | | | | Escitalopram has a faster onset of antidepressant action | | | | | | |
| PCL-106 | D | Depression/Onset of action, Agnostic Behavior Paul Mitchell. Results from the first study indicate that escitalopram is more than twice as potent as citalopram in acute test The chronic study suggests an antidepressant profile. It is recommended to perform follow up studies. 1) Complete dose response relationship S- and R- S-citalopram, test R-citalopram alone test combination of R and S, ratio 4:1 2) Onset of action study escitalopram vs citalopram with daily assessment for 7 days Comparator CT, RCT | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability Escitalopram has a faster onset of antidepressant action | Available | | | Sep-01 | | manuscript can combine data from PCL-106 with PCL- 107 poster combines data from PCL-106 and PCL-107 poster combines data from PCL-102 with PCL- 108 |
| PCL-107 | D | Depression, Forced swim test, mice R- fluoxetine, venlafaxine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect | Available | | | Jul-01 | | Journal TBD manuscript combines data from PCL-001, PCL-002, PCL-003, PCL-101, PCL-103, PCL-107, PCL-302, and in vivo uptake inhibition |
| PCL-108 | D | Depression, Chronic mild stress, Venlafaxine, sertraline, paroxetine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is an effective first line treatment for depression Escitalopram is the active isomer of citalopram in terms of antidepressant effect | Planned | | | | | |
| PCL-201 | S | To determine effects on seizure threshold, Effect in models of convulsion/epilepsy, Comparator: SSRIs, CT metabolites alone and with threshold dose of phenytoin | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Available | | | | | Data insufficient to support publication |
| PCL-202 | S | Acute effect of SSRIs, Sexual Behavior male rat, Comparators CT, paroxetine, fluoxetine, R-fluoxetine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram has a favorable side effect profile | Available | | | Mar-01 | Mar-02 | Psychoneuroendocrinology |

| Study | Topic | Direction | Study Director | Key Messages | Final Status | Abstract Due Date | Abstract Date | Abstract Submission Date | Publication Date | Journal/Comments |
|--------|-------|---|----------------|--|--------------|-------------------|----------------------------|--------------------------|------------------|--|
| PC-308 | S | Basal of functional/secretory ability, Effects on plasma oxytocin levels, rat, Comparator: penicillamine | HLU | Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Proposed | | | | | Psychopharmacology |
| PC-308 | S | Sexual/romantic, Efforts/interactions reduced sleep time, Comparator: CT, cospiramine | FRM/HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing | | CIMP Jun-02 EOMP Oct-02 | | | Protein combines data from PC-302, 303, 304, 305, 306, 307; separate studies in vitro and in vivo Protein combines data from PC-302, 303, 304, 305, 306, 307; separate studies in vitro and in vivo |
| PC-310 | S | GI function, Gastrointestinal motility and secretion, rat, Comparator: penicillamine | FRM/HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Proposed | | | | | |
| PC-311 | S | Female sexual dysfunction, Effects on blood flow to vagina and clitoris and NOS activity in rabbits, Sasez de Tapada, Comparator: penicillamine | FRM/HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram has a favorable side effect profile Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | | | | |
| | S | Libido, Female sexual behavior, kidneys, Comparator: penicillamine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs | Proposed | | | | | |

Revised March 5, 2003

| Study | Type | Description | Study Director | Key Messages | Final Phase | Abstract Due Date | Meeting/ Data | Manuscript Submission Date | Publication Date | Journal/Comments |
|---------------------|------|--|----------------|--|------------------|-------------------|---------------------|----------------------------|------------------|--|
| | | | | | | | WCP (WPA) Aug-02 | | | Poster combines data from PCL-304, 322, 320, super selectivity in vitro |
| | | | | | | | ECNP Oct-02 | | | Poster combines data from PCL-302, 306, 320, 322, 308, 304, super selectivity in vitro and in vivo |
| PCL-305 in vitro | MA | Effect S-CT & RCT on rat monoamine transporter binding and function. Comparators: SSRIs, venlafaxine, reboxetine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anxiolytic effect. Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer | Available | | | | | Data insufficient to stand alone, combine with data from depression model and/or anxiety model |
| | | | | Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | | | | |
| PCL-306 in vitro | MA | 5-HT release in synaptosomes. Assessment of 5-HT reuptake properties of S-enantiomer in rat brain synaptosomes. Comparators: CT, fenfluramine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anxiolytic effect. Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Available | | | | | Data insufficient to stand alone, can be combined with other data |
| PCL-307 in vitro | MA | 5-HT transport and electrophysiology in oocytes 1) Studies of 5-HT uptake inhibitory properties of S-, R- and R,S-citalopram in oocytes expressing h5-HTT 2) Studies of effect of S-, R- and R,S-citalopram on ion current properties of h5-HTT, Wiberg Aarhus | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anxiolytic effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing 02-00 | | ECNP Oct-02 | Oct-01 | | Data insufficient to stand alone, can be combined with PCL-310 and PCL-311 Journal TBD |
| | | | | | | Mar-03 | ECNP Sep-03 | | | |
| PCL-308 in vitro | MA | Binding of 3H-S-CT to human 5-HT transporter and its displacement by RCT, Mike Owens | FRUK | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anxiolytic effect. Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing | | | Oct-01 | | Data insufficient to stand alone, can be combined with PCL-310 and PCL-311 Journal TBD |

| Study | Phase | Description | Study Design | Max. Milestone | Final Report | Abstract Due Date | Meeting Date | Monograph Submission Date | Publication Date | Journal Comments |
|--------------------|-------|---|--------------|---|--------------|-------------------|--|---------------------------|------------------|---|
| PCL-310 in vivo | MA | Effect on 5-HT _{2A} receptor mediated inward rectifying potassium current in DRN, rat CT, Serotonin, D. Bupropion | FXR | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anticholinergic effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Proposed | | | | | Data insufficient to stand alone, can be combined with PCL-310 and PCL-311 |
| PCL-310 in vivo | MA | Microdialysis study in rat cortex to measure 5-HT and DA after chronic treatment. Serotonin, Comparator: CT, PCT | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anticholinergic effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing | | CHMP Jan-02 WCP (WPA) Aug-02 ECNP Oct-02 | Oct-01 | | Wait to publish until EU approval Journal TBD pharmacology review poster will include microdialysis data poster combines data from PCL-310, PCL-311, PCL-319 poster combines data from PCL-310, PCL-311, PCL-319 poster combines data from PCL-310, PCL-311, PCL-319 |
| PCL-311 in vivo | MA | Microdialysis study in rat cortex to measure 5-HT after acute systemic and local treatment. Comparator: CT, PCT, paroxetine | HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anticholinergic effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing | | CHMP Jun-02 WCP (WPA) Aug-02 ECNP Oct-02 IFMAD Nov-02 ACNP Dec-02 | Oct-01 | | Wait to publish until EU approval Journal TBD pharmacology review poster will include microdialysis data poster combines data from PCL-310, PCL-311, PCL-319 poster combines data from PCL-310, PCL-311, PCL-319 poster combines data from PCL-310, PCL-311, PCL-319 |
| PCL-313 in vivo | MA | SPECT/RET imaging of 5-HTT in monkeys. Citalopram NMR, Comparator: CT, PCT | FXR | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anticholinergic effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer | Proposed | | | | | |

| Study | Type | Description | Study Director | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Comments |
|--------------------|------|--|----------------|---|--------------|-------------------|--------------|----------------------------|------------------|---|
| PCL-314 in vivo | MA | Effect on D2 receptor binding and expression in chronic mild stress model. Uses tissue from PCL-014, Risperidone | Hu | Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/antidopaminergic effect Escitalopram has a faster onset of antidepressant action | Proposed | | | | | |
| PCL-315 in vivo | MA | Dexamethasone of S- and R-escitalopram and CT concentration in the brain | Hu | Escitalopram represents a new more selective and/or potent generation of SSRIs | Available | | | 09-01 | | Data insufficient to stand alone, can be combined with PCL-310 and PCL-311 Journal TBD |
| PCL-316 in vivo | MA | Effect on dorsal raphe neuron firing rate after chronic treatment, rats. Lethal Abraxane, Comparators Fluoxetine, CT, paroxetine | PRX | Escitalopram is the active isomer of citalopram in terms of antidepressant/antidopaminergic effect Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/antidopaminergic effect Escitalopram has a faster onset of antidepressant action Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing | | | | | |
| PCL-317 ex vivo | MA | Effects of S-, R- and racemic citalopram on 5-HT, MA, and DA uptake by brain synaptosomes and/or platelets to determine relative contribution of S- and R- enantiomers to citalopram's effects on 5-HT transport, J Reusch, Comparators CT, data on other SSRIs on file | PRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/antidopaminergic effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Ongoing? | | | | | Data insufficient to stand alone |
| PCL-318 | MA | h5-HTT mutations, affinity and uptake inhibition Studies of S-, R- and R,S- citalopram in h5-HTT variants expressed in insect cells Affinity and 5-HT uptake inhibition Investigator has been informed on confidentiality and publication limitations Comparators CT, RCT | Hu | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/antidopaminergic effect | Planned | | | | | Data insufficient to stand alone |

| Study | Type | Description | Study Design | Key Message | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Comments |
|---------|------|---|--------------|--|--------------|-------------------|--|----------------------------|------------------|---|
| PCL-319 | MA | Genetic studies assessing for additive properties of escitalopram, Comparators: CT, PCT | MLU | Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer. Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability. | Available | | | Oct-01 | | Data insufficient to stand alone, can be combined with PCL-310 and PCL-311. Journal TBD |
| | | | | Escitalopram represents a new more selective and/or potent generation of SSRIs | | | WCP (WPA) Aug-02 | | | Poster combines data from PCL-310, 311, 319 |
| | | | | Escitalopram is the active enantiomer of citalopram in terms of antidepressant/serotonergic effect | | | EGIP Oct-02 | | | poster combines data from PCL-310, PCL-311, PCL-319 |
| | | | | Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer | | | PTMAD Nov-02 | | | poster combines data from PCL-310, PCL-311, PCL-319 |
| | | | | Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | ACUP Dec-02 | | | poster combines data from PCL-310, PCL-311, PCL-319 |
| PCL-320 | MA | In vivo receptor profile, Comparatory R- fluoxetine, paroxetine, sertraline, venlafaxine, milnacipran, reboxetine | MLU | Escitalopram represents a new more selective and/or potent generation of SSRIs. Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer. Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability. | | | SCWP Apr-02 | | | Poster combines data from PCL-304, 322, 320, super selectivity in vivo |
| | | | | Escitalopram represents a new more selective and/or potent generation of SSRIs | | | Focus on Mood & Anxiety Disorders Nov-01 | | | Poster combines data from PCL-302, 304, 320, 322, 303, 304; super selectivity in vivo and in vivo |
| | | | | Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer | | | WCP (WPA) Aug-02 | | | Poster combines data from PCL-304, 322, 320, super selectivity in vivo |
| | | | | Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | EGIP Oct-02 | | | Poster combines data from PCL-302, 304, 322, 303, 304; super selectivity in vivo and in vivo |
| PCL-321 | MA | Acute effects on DRD11 binding, effects on 5-HT1A receptor mediated effects, Comparators: CT, PCT | MLU | Escitalopram represents a new more selective and/or potent generation of SSRIs. Escitalopram is the active isomer of citalopram in terms of antidepressant/serotonergic effect. Escitalopram has a faster onset of antidepressant action. Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability. | Available | | SCWP Apr-01 | | | poster presents rat data from PCL-322 combined with PCL-321 |
| | | | | Escitalopram represents a new more selective and/or potent generation of SSRIs | | | APA May-01 | | | |
| | | | | Escitalopram is the active isomer of citalopram in terms of antidepressant/serotonergic effect | | | WCP Jul-01 | | | |
| | | | | Escitalopram has a faster onset of antidepressant action | | | | | | |
| | | | | Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | | Oct-01 | | Data insufficient to stand alone, can be combined with PCL-310 and PCL-311. Journal TBD |

| Study | Topic | Description | Study Design | Key Messages | Final Report | Abstract Due Date | Meeting Date | Manuscript Submission Date | Publication Date | Journal/Comments |
|--------------------|-------|---|--------------|---|--------------|-------------------|--|----------------------------|------------------|--|
| PCL-322 | MA | In vitro receptor profile, Computations S-CT, SDOCT, SDOCT | FRX | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anticholinergic effect Escitalopram has improved side effect, drug interaction and safety profiles resulting from the removal of the inactive moiety, the R-enantiomer Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | Available | | Forum on Mood & Anxiety Disorders Nov-01 SZAP Apr-02 ChP Jun-02 | | | Poster combines data from PCL-302, 206, 209, 222, 208, 304, super selectivity in vivo and in vivo Poster combines data from PCL-304, 322, 320, super selectivity in vivo |
| PCL-323 ex vivo | MA | Effects of S-CT on 5-HT uptake in brain synaptosomes after chronic oral treatment | FRX/HLU | Escitalopram represents a new more selective and/or potent generation of SSRIs Escitalopram is the active isomer of citalopram in terms of antidepressant/anticholinergic effect Escitalopram is a refinement of citalopram in terms of antidepressant effect and tolerability | | | WCP (NPA) Aug-02 EQNP Oct-02 WCP (NPA) Aug-02 EQNP Oct-02 | | | Poster combines data from PCL-304, 322, 320, super selectivity in vivo Poster combines data from PCL-302, 206, 304, 322, 208, 304, super selectivity in vivo and in vivo Poster combines data from PCL-001, 003, 101, 103, 223, 320 in anxiety, depression, aggression |
| | MA | Ketamine effects binding of S-CT to 5-HT receptor site | HLU | | Available | | SNM Jun-01 | | | |

Key

- PK - Pharmacokinetics
- PD - Pharmacodynamics
- D - Dose/toxicity
- A - Anxiety (PTO, GAD, SAD)
- S - Side Effects
- MA - Mechanism of Action

Appendix III

APPENDIX IV

PROFESSIONAL MEETING AND SYMPOSIA PLAN

A. PSYCHIATRY

Society of Biological Psychiatry (SOBP):

- 5/15/03 - 5/17/03 in San Francisco, CA
- Expected attendance of 600

American Psychiatric Association (APA):

- 5/17/03- 5/22/03 in San Francisco, CA
- Expected attendance of 18,000

New Clinical Drug-Evaluation Unit Program (NCDEU):

- 5/27/03 – 5/30/03 in Boca Raton, FL
- Expected attendance of 1,000

Collegium Internationale Neuro-Psychopharmacologicum (CINP):

- 10/12/03 – 10/15/03 in Beijing, China
- Expected attendance of 5,000

World Psychiatric Association/World Congress of Psychiatry (WPA/WCP)

- 9/10/03 - 9/15/03 in Cairo, Egypt

American Psychiatric Association Institute on Psychiatric Service (APA-I)

- 10/29/03 – 11/02/03 in Boston, MA
- Expected attendance of 2,000

U.S. Psychiatric Congress

- 11/6/03 – 11/9/03 in Orlando, FL
- Expected attendance of 3,000

APPENDIX IV SYMPOSIA PLAN

American College of Neuropsychopharmacology (ACNP)

- 12/7/03 – 12/11/03 in Puerto Rico
- Expected attendance of 1,300

International Congress of Geriatric Psychoneuropharmacology (ICGP)

- 12/12/03 – 12/14/03 in Puerto Rico

American Association for Geriatric Psychiatry (AAGP)

- 3/12/04 – 3/15/04 in Baltimore, MD
- Expected attendance of 1,200

Anxiety Disorders Association of America (ADAA)

- 3/04
- Expected attendance of 650

PriMed Psychiatry Updates

- Fall 03
- Miami, New York, Chicago, Washington, DC, San Francisco, Los Angeles

B. PRIMARY CARE

American Academy of Family Physicians (AAFP)

- 10/1/02 – 10/5/03 in New Orleans, LA
- Expected attendance of 20,000

American College of Obstetricians and Gynecologists (ACOG)

- 4/26/03 – 4/30/03 in New Orleans, LA
- Expected attendance of 5,000

U.S. Geriatrics and Long Term Care Congress

- 6/19/03 – 6/21/03 in San Francisco, CA
- Expected attendance of 2,000

American College of Physicians-American Society of Internal Medicine (ACP)

- 4/3/03 – 4/5/03
- Expected attendance of 10,000

American Geriatrics Society (AGS)

- 5/14/03 – 5/14/03 in Washington, DC
- Expected attendance of 2,000

Pri-Med Regional Meetings

- Mid-West: 6/19/03 – 6/21/03 in Chicago, IL
- East: 11/7/03 – 11/9/03 in Boston, MA
- Expected attendance of 5,000 at both

C. OTHER ALLIED HEALTH PROFESSIONS

Academy of Managed Care Pharmacy (AMCP)

- 4/19/04 – 4/22/04 in Minneapolis, MN and 11/10/03 – 11/15/03 in Pasadena, CA
- Expected attendance of 4,000

American Medical Directors Association (AMDA)

- 3/4/04 – 3/7/04 in Phoenix, AZ
- Expected attendance of 2,000

American Society of Consultant Pharmacists (ASCP)

- 5/14/03 – 5/16/03 in Tampa Florida and 11/12/03 – 11/14/03 in San Antonio, TX
- Expected attendance of 4,000

APPENDIX VII

PROFESSIONAL ASSOCIATIONS OF PRIORITY

AMERICAN PSYCHIATRIC ASSOCIATION

The American Psychiatric Association (APA) is recognized worldwide as the premier psychiatric society. Its 44,000 U.S. and international physicians specialize in the diagnosis and treatment of mental and emotional illnesses and substance use disorders.

In FY03 Forest Professional Relations provided an unrestricted grant and technical support to create collaboration between APA, AAFP and ACP to develop "reasonable practice" guidelines for the management of chronic depression in primary care practice. The clinical objective is to improve the percent of patients who adhere to the full duration of therapy. The first step, identifying a Standard of Care evaluation instrument, was completed in October 2002.

In 2003 the Workgroup will determine a Standard of Care Intervention Strategy and identify the instructional materials needed to implement the strategy in office setting. The strategy will be tested in each organization's Practice Research Network to validate its ability to improve adherence and prolong duration of therapy. The Workgroup seeks to publish the results of each step in a peer-reviewed Primary Care Journal to begin dissemination of the reasonable practice guidelines.

At the State level, APA Chapters engage in significant lobbying of State Health Departments to maintain mental health care budgets, including support for open Medicaid drug formularies. Forest has expanded its involvement with APA in this regard, creating an information collaboration to assist mutual efforts at the State policy level.

AMERICAN ASSOCIATION OF GERIATRIC PSYCHIATRY

The American Association of Geriatric Psychiatry (AAGP) represents and serves the field of geriatric psychiatry. The mission of AAGP is to enhance the knowledge base and standard of practice in geriatric psychiatry through education and research and to advocate for meeting the mental health needs of older Americans.

In 2002/03 AAGP is developing, for the first time, evidence-based Practice Guidelines for Late Life Depression. Publication is expected in 4Q03. An instructional "toolkit" to assist guideline implementation and an updated depression slide kit will also be issued. Forest Professional Relations is the sole support of these projects, providing an unrestricted grant and technical support.

AMERICAN COLLEGE OF NEUROPSYCHOPHARMACOLOGY

The American College of Neuropsychopharmacology (ACNP) is an elite, research-oriented professional organization with limited membership of 600 nationally recognized scientists. Members are elected based on their original research contributions to the field of neuropsychopharmacology, representing behavioral pharmacology, brain imaging, clinical psycho-pharmacology, epidemiology, genetics, neurology, neurophysiology, psychiatry and psychology.

The principal functions of the College are research and education in mental health, including substance abuse. ACNP provides investigators the opportunity for cross-disciplinary communication at scientific meetings, and promotes a multi-discipline approach to research in the pharmacology of brain and behavior.

Forest is a major contributor to ACNP annual programming, and is a founding sponsor of its newly created International College of Geriatric Psychopharmacology (ICGP).

AMERICAN ACADEMY OF FAMILY PHYSICIANS

The American Academy of Family Physicians (AAFP) is one of the largest national medical organizations, with more than 93,000 members. The Academy has a strong educational and policy platform, representing comprehensive primary care to patients and their families. AAFP has a rich catalog of marketing opportunities and communication vehicles to their members and their patients.

Forest has been a Corporate President's Circle Sponsor of AAFP since 2001, which provides additional marketing opportunities. Forest is also a major sponsor of the Academy's Doctors with Heart philanthropic program.

In conjunction with physician specialty groups (e.g. APA) AAFP develops evidence-based practice guidelines, which must be ratified by their Board of Directors at the Annual Scientific Session. AAFP is actively participating in the Forest-led collaboration with APA to develop reasonable practice guidelines for managing chronic depression in the Primary Care Physician office-setting.

Forest is actively participating in the AAFP's Annual Clinical Focus: "Caring for the Aging in America," a year-long comprehensive educational program (October 2003 – 2004). The objective is to increase the Family Physician's ability to identify and effectively manage health conditions in the elderly. Late Life Depression and Alzheimer's Dementia are key elements of this comprehensive educational program.

AMERICAN COLLEGE OF PHYSICIANS

[PREVIOUS NAME: AMERICAN COLLEGE OF PHYSICIANS - AMERICAN SOCIETY OF INTERNAL MEDICINE]

In 1997 the American College of Physicians (ACP) and the American Society of Internal Medicine (ASIM) merged to form the nation's largest medical specialty society with over 115,000 members. Since 1997, they were known as ACP-ASIM. In May 2004, the College changed its name back to simply ACP.

Over 95,000 of ACP members are general Internists (Internal Medicine), while about 20,000 physicians have a sub-specialty, including cardiology, nephrology, rheumatology, neurology, pulmonology, allergy and immunology, and gastroenterology. Thus, this organization is influential across much of the Forest product portfolio.

ACP is headquartered in Philadelphia and maintains an educational focus for members. Their Washington, D.C. office represents the strong policy arm of the organization and actively lobbies on health care issues. The D.C. office also houses the department responsible for creating office-based programs aimed at improving the practice of medicine.

Forest became a Corporate Sponsor of ACP in FY03, which provides additional marketing opportunities. ACP is actively participating in the Forest-led collaboration with APA to develop reasonable practice guidelines for managing chronic depression in the Primary Care Physician office-setting.

AMERICAN GERIATRIC SOCIETY

The American Geriatric Society (AGS) is the premier physician organization dedicated to improving the health and well being of all older adults. The majority of the 6,000 AGS members are Primary Care Physicians. In the last decade, AGS has become a pivotal force in shaping attitudes, policies and practices regarding health care for older people.

Most AGS members practice Internal Medicine, and may also be members of ACP.

AMERICAN MEDICAL DIRECTORS ASSOCIATION

While the majority of the American Medical Directors Association (AMDA) members are Medical Directors of Long Term Care Facilities and Nursing Homes, the organization has always served the interests of both medical directors and attending physicians. AMDA currently has over 8,700 members and a database of over 2,000 attending physicians, all of whom are Primary Care Physicians.

Forest has been a Corporate Sponsor of AMDA for the last few years. In 2002, AMDA revised their Depression Guidelines for Residents of LTC/NH, and expect to publish them by mid-2003. Forest Professional Relations is the major sponsor of this endeavor, providing financial, technical, and information support.

Forest helped co-sponsor AMDA's major project in drug safety in LTC/NH, Multidisciplinary Medication Management Tool Kit, focusing on reducing errors. Selection of drugs with low potential drug interactions and drugs that are well tolerated by an elderly population are the core themes. These Kits, which were introduced at AMDA's Annual Meeting in March 2003, may be purchased for distribution to LTC/NH as a high-value added program.

Forest has committed to provide major sponsorship of AMDA's Practice Guideline on the Management of Falls in LTC/NH. A body of evidence supports changing the current Guidelines: evaluating medication for potential drug interactions, changing drug therapies to reduce drug interactions and side effects, rather than discontinuing anti-depressants.

Forest has committed to provide major sponsorship of AMDA's Practice Guideline on Dementia, which is scheduled to begin revisions 4th quarter 2003. Publication is estimated as second-half 2004.

AMERICAN ACADEMY OF CHILD AND ADOLESCENT PSYCHIATRY

The American Academy of Child and Adolescent Psychiatry (AACAP) focus is treating children affected by mental, behavioral or developmental disorders, and improving the quality of life for their families. The majority of its 6,500 members are child and adolescent psychiatrists, who actively research, evaluate, diagnose, and treat psychiatric disorders.

During FY04 Forest Professional Relations will work with AACAP to explore the potential for consensus guidelines on treatment of pediatric depression. Results from any AACAP projects will be shared with APA, AAFP and the American Academy of Pediatrics.

NATIONAL ALLIANCE FOR THE MENTALLY ILL

The National Alliance for the Mentally Ill (NAMI) is a nonprofit, grassroots, self-help, support and advocacy organization of consumers, families, and friends of people with severe mental illnesses, such as schizophrenia, major depression, bipolar disorder, obsessive-compulsive disorder, and anxiety disorders. The "traditional" focus of NAMI has been on more severe mental illness, though they have recently begun involvement with more moderate disorders that are managed in a non-psychiatric setting.

Founded in 1979, NAMI has more than 210,000 members who seek equitable services for people with severe mental illnesses, which are known to be physical brain disorders. Working on the national, state, and local levels, NAMI provides education about severe brain disorders, supports increased funding for research, and advocates for adequate health insurance, housing, rehabilitation, and jobs for people with serious psychiatric illnesses.

NAMI has an active lobby effort, operating primarily at the State level with some action at the Federal level. Insurance parity and open formularies are two of their positions.

Forest has been a major Corporate Sponsor of NAMI since 2000.

NATIONAL MENTAL HEALTH ASSOCIATION

Established in 1909, the National Mental Health Association (NMHA) is the country's oldest and largest nonprofit organization addressing all aspects of mental health and mental illness. With more than 340 affiliates nationwide, NMHA works to improve the mental health of all Americans, especially the 54 million individuals with mental disorders, through advocacy, education, research and service.

NMHA's foundation is consumer-oriented education. In recent years, NMHA has become a strong lobby in support of insurance parity and open formularies. Their national/federal lobbying effort is as strong as their chapter-based State activity.

Forest has been a major Corporate Sponsor of NMHA since 2000, and participates in several of their educational conferences.

NMHA has a very effective grassroots organization, which devotes significant effort in lobbying State Health Departments on maintaining mental health care budgets, including supporting an open Medicaid drug formulary. Forest has expanded its involvement with NMHA, creating an information collaboration to assist mutual efforts at the State policy level.

DEPRESSION AND BIPOLAR SUPPORT ALLIANCE

[PREVIOUS NAME: NATIONAL DEPRESSIVE AND MANIC-DEPRESSIVE ASSOCIATION]

The mission of the Depression and BiPolar Support Alliance (DBSA) is to educate patients, families, professionals, and the public concerning the nature of depressive and manic-depressive illnesses as treatable medical diseases; to foster self-help for patients and families; to eliminate discrimination and stigma; to improve access to care; and to advocate for research toward the elimination of these illnesses.

The DBSA is the nation's largest patient-directed, illness-specific organization. Of the 3 largest patient advocacy groups, it is the only one that focuses on depression disorders. DBSA has a nationwide grassroots network of chapters and support groups. It is governed by a 15-member board of directors and guided by a 65-member Scientific Advisory Board composed of the leading researchers and clinicians in the field of mood disorders.

Forest has been a major Corporate Sponsor of DBSA since 2000.

ANXIETY DISORDERS ASSOCIATION OF AMERICA

The Anxiety Disorders Association of America (ADAA) is the only national, non-profit membership organization dedicated to informing the public, healthcare professionals and legislators that anxiety disorders are real, serious and treatable.

Members include clinicians and researchers who treat and study anxiety disorders, individuals with anxiety disorders and their families, and other interested individuals.

ADAA is a relatively small organization, which hopes to expand its influence in the next few years. ADAA is very open to active collaboration with industry, including participation in public relations activities. Forest has been a Corporate Sponsor since 2000.

Marketing opportunities with ADAA will increase when Lexapro labeling expands to include anxiety disorders. At that time, Forest can take advantage of opportunities to disseminate important brand information to their members.

Appendix VIII