

The Intermezzo Brand Team has developed video for PTN. This was done using one of our top Intermezzo speakers and national KOL, [REDACTED] and is the same presentation being provided at Product Theaters that are conducted in conjunction with conferences/conventions. This video program will launch April 19<sup>th</sup> and reach a minimum of 3,000 targeted physicians over a three month period.

### **Intermezzo eMarketing (Healthcare Professionals)**

Intermezzo HCP eMarketing initiatives continued in the first quarter with a multi-channel approach including emails, Online Advertising and Website Visits.

- YTD March, almost two million HCP emails were sent to the 100,000 HCP targets
- Over 800,000 online media impressions were delivered to HCPs via the sites listed in the table below
- Over 64,000 visits to IntermezzoRx.com occurred
- All of these eMarketing initiatives exceed their goals

### **eMarketing (Consumer)**

Intermezzo Consumer eMarketing initiatives continued in the first quarter of 2013. The major initiatives launching included the following:

- Intermezzo Online Banner advertising
- Intermezzo Search advertising on Google, Yahoo and Bing search engines
- Online and Mobile versions of the myIntermezzo.com consumer website
- Consumer Relationship Marketing (CRM) Program

Focused on driving category and product awareness of Intermezzo as an MOTN sleep aid drug, the digital campaign focused heavily on targeted, broad-reaching media vehicles:

- Online Video to maximize the Intermezzo visual impact and extend the brand's TV presence
- PPC to funnel relevant searchers to the Intermezzo site
- Network partnerships to provide efficient reach against core targets
- Content sites to position Intermezzo's brand within trusted and endemic health/lifestyle properties
- We achieved almost 400,000,000 consumer media impressions

As the digital campaign progressed, extensive optimizations were conducted to drive performance, ultimately leading to a \$5.46 Cost-Per-View (CPV) by its conclusion, which was 35% lower than launch.

- Total Visits (driven from Display and Pay-Per-Click (PPC) paid media) also increased dramatically to just over 678,000
- Google Display Network and PPC remained the most efficient tactics, followed by display partners MaxPoint and NBC
- PPC performance, in particular, increased significantly with the introduction of the Intermezzo TV spot in January, which was expected, based on the synergistic relationship between offline and online media

While the CPV for Yahoo! and iVillage were higher than average throughout the campaign, they proved effective in compelling users to take action on myIntermezzo.com (e.g. downloading a Free Trial Offer, Patient Savings Card, etc.), which was a tertiary performance metric.

- Collective, on the other hand, was leveraged largely as a TV frequency strategy due to the vendor's unique cross-platform targeting, especially within the Connected TV space

Overall, digital performance gained significant traction over the course of the campaign and was effective in driving efficient traffic to the DTC site. The brand lift studies, which will be completed in the third quarter, will provide greater insight on increases in consumers' awareness levels of Intermezzo.

Site Name	Total Delivered Impressions (12.17.12-3.31.13)	Total Visits (12.17.12-3.31.13)	Cost-per-Visit (CPV) (12.17.12-3.31.13)
Google Display Network	27,440,519	43,677	\$1.49
MaxPoint	145,084,347	180,101	\$3.90
NBC.com	19,053,667	123,844	\$4.29
Hulu	26,652,084	137,523	\$7.85
EA Pogo	9,575,302	8,693	\$8.62
iVillage	21,859,149	13,699	\$13.04
Yahoo!	71,466,096	32,186	\$14.66
Collective	60,890,302	12,036	\$32.75
WebMD**	7,817,316	6,988	N/A
<b>DISPLAY TOTAL</b>	<b>389,838,782</b>	<b>558,747</b>	<b>\$6.26</b>
<b>PPC TOTAL</b>		<b>119,601</b>	<b>\$1.75</b>
<b>DIGITAL TOTAL</b>	<b>389,838,782</b>	<b>678,348</b>	<b>\$5.46</b>

\*Sites sorted from highest to lowest Total Visits.

\*\*CPV for WebMD not available as the site's cost model is based on Cost-per-Qualified Visitor to the Branded Destination page, set to launch in early March.

Visits to myIntermezzo.com were over 380,000 with Display media driving 70% of visits and Paid Search driving 22% of visits.

- Approximately 1,200 consumers have registered on the site to receive the Intermezzo Welcome Kit and be registered in the Consumer CRM program.

Jan - Mar 2013 Site Performance	
Total myIntermezzo.com Visits	380,392
Non-Media Visits	44,881
Display Visits	250,788
Paid Search Visits	84,723
myIntermezzo.com Registrations	1,197

An email was sent to over 1,000,000 consumers that had experience with zolpidem in the recent past. This list was provided via a third-party resource that generates patient data-bases that are created when patients “opt-in” to the service.

- That single eMail was opened over 120,000 times resulting in almost 15,000 visits to myIntermezzo.com.
- Many visitors downloaded savings cards and registered for the CRM program.

### **Purdue Laxatives Brands**

The most significant initiative during the first quarter related to gaining exposure for both Colace and Senokot via social media. Colace and Senokot now have Facebook pages. In addition, a Twitter campaign was initiated for Colace and Senokot. Both of these initiatives are aimed at expanding awareness of both products with a new generation of consumers. More traditional print advertising continued during the first quarter. Advertisement placement in magazines such as Women’s Day, Better Homes and Gardens, and Readers Digest gained exposure to our traditional target consumer, to maintain loyalty to the brands. During the first quarter the Customer Relationship Marketing (CRM) program continued. This is aimed at establishing an ongoing “relationship” with loyal customers. This is achieved via an opt-in process and eMarketing technology.

National Account Managers implemented forty-six in-store promotions across their retail pharmacy chains and independent networks. This included a Senokot Laxatives “Instant Coupon,” a Senokot “Sweepstakes” Free Standing Insert (FSI) and a Senokot/Senokot-S “Bonus Pack” promotion at select retailers e.g. Walgreens and Wal-Mart.

### **Managed Care Update**

The tables below depict the formulary status of Purdue products in three major payer channels. Included in the tables are the percentages and number of lives in each formulary category/tier, and a brief summary follows each channel with major customers and developments/status changes in the first quarter of 2013.

<b>Commercial Formulary Status</b> ~ 210 Million lives in this channel	OxyContin		Butrans		Intermezzo	
	Lives (mm)	%	Lives (mm)	%	Lives (mm)	%
Preferred/2nd tier	177.8	85	65.8	32	22.6	10
Preferred/3rd tier	8.9	4	103.1	49	54.2	26
Step Edit/Prior Auth	7.6	4	19.2	9	55.1	26
Not Covered	15.7	7	21.9	10	78.1	38

### **OxyContin (Commercial)**

OxyContin continues to maintain “best in class” access and is the only extended-release opioid brand with more “unrestricted” access than restrictions. The 2013 objective is to maintain the current level of preferred-brand/2<sup>nd</sup> Tier status of 85% of live covered. OxyContin commercial national market share exceeds 26%.

With Opana ER having generic competition, Opana ER brand has increased its rebates to commercial plans nationally. Nucynta ER has also increased rebates for preferred formulary status, and there is increased pressure for Purdue to provide deeper rebates for OxyContin as new contracts are negotiated in order to maintain the current formulary status levels.

### **Butrans (Commercial)**

Butrans continues to achieve improved formulary access (32% of commercial lives in a preferred position). The 2013 objective is to achieve a minimum of 35% of lives covered in a preferred-brand/2<sup>nd</sup> Tier position.

In mid-fourth quarter 2012, Aetna’s commercial prescription plan elevated Butrans to a preferred formulary position (approximately 8 mm lives nationally). This new formulary position was followed by an extensive national pull-through program that was initiated with non-representative and ASF implemented activities during the first quarter. Aetna is averaging 835 RXs per month since formulary elevation. The previous four months prior to the formulary elevation, Aetna was averaging 664. This is an increase of 26% prescriptions per month during the initial pull-through efforts.



### Intermezzo (Commercial)

Since launch, the commercial channel has been the focus for Intermezzo coverage. As we began 2013, approximately 71% of all commercial prescriptions submitted via claims to managed care plans, were filled. Of the remaining 29%, 21% were rejected by managed care plans (not covered on formulary), with 9% reversed by patients at the pharmacy (cost). Additionally, 6.6% of prescriptions were “abandoned” (never picked up/dispensed to patient).

A large formulary removal took place at CVS/Caremark, a large national PBM, effective January 1, 2013. Caremark removed Intermezzo from their formulary. They now require their patients to pay 100% for the cost of the Intermezzo prescription. Up until Caremark’s decision on January 1, 2013, Caremark was one of the highest adjudicators for Intermezzo prescriptions, at 3rd tier co-pay. Therefore, this decision has increased the “non-coverage” in the above table significantly.

Negotiations with Caremark are ongoing. Dr. Landau has been in contact with Caremark’s Chief Medical Officer, to discern the foundation for Caremark’s negative decision. Efforts are underway to conduct a face-to-face meeting between Caremark and Purdue’s medical teams to present Intermezzo in an effort to reverse the decision. As these meetings take place, efforts are underway to negotiate a contract that would provide rebates for Intermezzo at a more favorable formulary position.

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<b>Medicare Part D</b> ~ 31 Million lives in this channel	OxyContin		Butrans		Intermezzo	
	Lives ( <i>mm</i> )	%	Lives ( <i>mm</i> )	%	Lives ( <i>mm</i> )	%
Preferred	15.1	48.9	0.2	1.0	0.009	0.3
Non-Preferred	2.1	7.0	2.5	8.0	2.2	6.8
Step Edit/Prior Auth	2.1	6.0	1.3	4.0	0.8	2.5
Not Covered	11.7	38.1	27.0	87.0	27.9	90.4

### OxyContin (Medicare Part D)

OxyContin continues to have favorable status for 2013 Medicare Part D formularies, with just less than 49% of eligible patients having access to a preferred formulary position and the corresponding favorable copay.

OxyContin Medicare Part D national market share exceeds 20%. Generic fentanyl patch (market share of 27.2%), generic extended- release morphine (market share of 30.4%), and methadone (market share of 15%) all have market share increases in the last 12

months in this channel. During the first quarter, 84% of all extended-release opioid prescriptions filled in this channel were for generics.

There is continuing pressure from health plans that provide Medicare Part D prescription plans as negotiations for 2014 formularies moved forward during the first quarter, as formularies for 2014 need to be established by July 2013. The pressure relates to reducing the costs of prescriptions and providing deeper rebates for branded products, especially in categories where there are ample generic/therapeutic alternatives, such as the extended-release opioid category.

OxyContin's national formulary status has been negatively impacted in the first quarter, with a recent decision by United Healthcare affecting their Medicare Advantage (Medicare Part D benefit design (MA-PD)) to not cover OxyContin in 2013. Gross OxyContin sales for 2012 through this plan design are estimated to be \$65mm annually.

### **Butrans (Medicare Part D)**

Butrans has had a slow uptake in the Medicare Part D channel, due mostly to two factors. First, the payers advocating increased generic utilization across their formularies and increased tactics to encourage substitution of all branded extended-release opioids.

<b>Medicaid ~ 53</b> <b>Million lives in</b> <b>this channel</b>	OxyContin		Butrans		Intermezzo	
	Lives (mm)	%	Lives (mm)	%	Lives (mm)	%
On PDL Formulary	1.5	2.0	8.4	16.0	2.9	5.2
Prior Auth Required	51.5	98.0	44.6	84.0	50.1	94.8

The Medicaid market continues to be a channel dominated by the individual States' mandating use of generics. State budget shortfalls dominate the news and many States believe these shortfalls are accelerated by expenditures from their Medicaid recipients.

There was a recent success in the State of Wisconsin. They added Butrans to the Preferred Drug List without us having to provide a supplemental rebate. This would be in addition to the mandated rebate. The most recent rebate data that was submitted provides actual sales in Wisconsin through the end of 2012. Purdue sales show how formulary coverage combined with an effective representative-driven pull-through program can accelerate sales. Sales for the first two quarters of Butrans coverage were \$126,858 (3Q12) and \$163,420 (4Q12). These current sales compare very favorably to

the previous four quarter average sales for Butrans through Wisconsin Medicaid which were \$46,341.

### **Forecasting, Analytics and Market Research**

During the first quarter we spent a large portion of our time supporting the development of the 10 year plan. As part of this process, we performed forecasting research for ONU and HYD. We also performed, and are in the process of performing, managed care focus groups, as well as pricing research.

The research is providing clarity with regard to market challenges that will need to be overcome for these products. The research has helped to identify the clinical endpoints, and rebates, required to overcome the challenges.

Regarding HYD, we have initiated an in-depth, secondary study to understand chronic usage of hydrocodone/ APAP and the potential of these patients to “step up” to an extended release opioid. In addition, we are progressing in our initiative to consolidate all of our sales and marketing data to perform analytics that will ultimately lead to predictive modeling of response to our marketing measures at the individual customer level.

The projects listed below represent a non-comprehensive sample of key undertakings by Forecasting, Analytics and Market Research with respect to our in-line products.

<b>INTERMEZZO Objectives</b>	<b>Key results</b>	<b>Recommended Actions/Potential Actions</b>
<p><b><u>Pre-DTC Consumer Awareness Study- fielded mid-Dec 2012</u></b></p> <ul style="list-style-type: none"> <li>- Establish baseline awareness and usage levels of Intermezzo prior to DTC campaign</li> <li>- Understand consumer satisfaction with current insomnia medications</li> </ul>	<ul style="list-style-type: none"> <li>- About one-half of MOTN sufferers say they avoid taking prescription medications in the middle of the night due to concerns about grogginess in the morning, so some take a partial tablet when they wake in the middle of the night.</li> <li>- One in five reports that their doctor recommended taking a partial tablet in the middle of the night.</li> <li>- Ambien CR has the highest ratings for satisfaction with help staying asleep, with 41%</li> </ul>	<ul style="list-style-type: none"> <li>- None. Baseline for DTC campaign / designed as a pair of studies. No recommendation until after post DTC campaign awareness study.</li> </ul>

	<p>selecting 9, 10, or 11 on an 11 point satisfaction scale.</p> <ul style="list-style-type: none"> <li>- 5% of consumer and 4% of MOTN consumers reported awareness of Intermezzo.</li> </ul> <p>Less than 1% had taken Intermezzo in the past 12 months.</p>	
<p><b><u>Post-DTC Consumer Awareness Study- fielding soon.</u></b></p> <ul style="list-style-type: none"> <li>- Establish awareness and usage levels of Intermezzo after DTC campaign</li> <li>- understand frequency with which consumers request Intermezzo with physician.</li> </ul>	TBD	<ul style="list-style-type: none"> <li>- understand effectiveness of DTC campaign on building awareness of Intermezzo among consumers could lead to recommendations to continue, discontinue or tweak the campaign going forward.</li> </ul>
<p><b><u>Intermezzo Speaker Program (refresh with Jun-Oct cohorts)</u></b></p> <p><u>Completed 3<sup>rd</sup> QTR 2012</u></p> <ul style="list-style-type: none"> <li>- To Determine TRx impact and ROI of Speaker Program</li> </ul>	<ul style="list-style-type: none"> <li>- Incremental full costs ROI: 0.13</li> <li>- Incremental TRx lift/HCP: 0.85 (not Statistically significant)</li> <li>- There appears to be sensitivity to call frequency post attendance</li> <li>- Psychiatrists with Sleep Market Decile 10 had the highest responsiveness while market decile 6-9 still had positive TRx lift over control, albeit at a reduced level</li> <li>- Mid to high market decile PCPs, but low/non-Intermezzo decile appear to have TRx lift, but trails Psychiatry significantly</li> <li>- Intermezzo Super Core targets appear to have higher responsiveness than Core</li> </ul>	<ul style="list-style-type: none"> <li>- Make all effort to enroll insomnia market decile 10 HCPs</li> <li>- Recruitment of high decile Psychiatrists, high market decile PCPs (although lower responsiveness), and possibly Neurologists will likely improve program effectiveness</li> <li>- Continue engagement through field force post speaker event</li> </ul>

	<p>targets</p> <ul style="list-style-type: none"> <li>- Number of rep calls delivered post speaker event corresponds to higher percentage of HCPs with positive TRx lift</li> <li>- Noncurrent Intermezzo prescribers appear to have higher responsiveness. However, the number of current Intermezzo prescribers is low</li> <li>- ROI may improve with time</li> </ul>	
OXYCONTIN Objectives	Key results	Recommended Actions/Potential Actions
<p><b><u>Sources of higher strength and tablets dispensed declines (internal)</u></b></p> <ul style="list-style-type: none"> <li>- Understand the sources of decline of the OxyContin's 40, 60 and 80mg strengths since the launch of the reformulation</li> <li>- understand the sources of the declines of the tablets dispensed across all strengths</li> </ul>	TBD	<ul style="list-style-type: none"> <li>- Potential actions could include marketing and sales tactics to counter declines, possibly following additional analysis at the physician level.</li> </ul>
<p><b><u>OxyContin Relationship Marketing (RM) Pilot to "Closed IDNs" - Boston, Seattle and Washington</u></b></p> <p><u>Completed 4<sup>th</sup> QTR 2013</u></p> <p>Determine TRx impact and ROI of RM programs in the three selected areas</p>	<ul style="list-style-type: none"> <li>- Boston and Seattle: no overall impact</li> <li>- Washington: <ul style="list-style-type: none"> <li>- Incremental full costs</li> </ul> </li> </ul> <p>ROI: 0.05</p> <ul style="list-style-type: none"> <li>- Incremental TRx lift/HCP: 0.01 or 0.5% (Statistically significant)</li> <li>- Majority of HCPs that were reached by RM were PCPs</li> </ul>	<ul style="list-style-type: none"> <li>- Make all effort to reach existing high and medium/low OxyContin and ERO prescribers as there is higher responsiveness from existing prescribers of OxyContin</li> <li>- Continue to reach across spectrum of HCPs as cost of RM for no-access HCPs are minimal compared to</li> </ul>



	<ul style="list-style-type: none"> <li>- Overall, RM did not appear to change OxyContin prescribing behavior in Boston</li> <li>- Only 22% of Boston HCPs are OxyContin decile 8-10 compared to 55% for Seattle and 47% for Washington</li> <li>- PCPs appear to be responsive in Seattle</li> <li>- "Conversions" initiative and "eDetail" both appear to be responsive tactics in Seattle and Washington. Many of the HCPs were reached by both "Conversions" and "eDetail"</li> <li>- Washington cohort responsiveness corresponds with higher decile ERO and OxyContin</li> </ul>	other traditional means
OTC Objectives	Key results	Recommended Actions/Potential Actions
<p><b><u>Slow Mag Attitude and Usage Analysis</u></b></p> <p>Detailed profile of Slow Mag consumers and why they purchase Slow Mag.</p>	<p>Slow Mag consumers are different from other magnesium supplement users: more likely to be men, somewhat younger, and have a higher income. Slow Mag consumers more likely to be interested in fitness activities such as running, hiking, biking, etc.</p>	<p>Sales presentation developed to maintain &amp; help expand retail distribution by pointing out unique customer. Continue to target active, fitness oriented men through selective media.</p>
<p><b><u>Betadine OTC Line Extension Focus Groups</u></b></p> <ul style="list-style-type: none"> <li>• Test perceptions of swab sticks distributed by Mundipharma</li> </ul>	<p>Consumers generally familiar with Betadine through hospital association so most consider it a strong, effective germicide. It is viewed as "old-</p>	<p>Determine retailer interest in stocking swab sticks and understand potential costs for modifications necessary to sell in U.S.</p>

	fashioned” and its strongest association is staining (negative association). Swab sticks generally viewed more positively than current forms due to less possibility of staining & potential for away-from-home use.	
<b><u>Laxative Market Events Timeline</u></b>	Purdue 2012 Laxative growth was driven by Colace, with key growth Feb – May 12, 2012 aligned with TV, Sweepstakes, FSI, IRCs, and promo activity at CVS & Walgreens synergistically driving increases. The Senokot Brands also benefitted from combination marketing efforts driving sales for Senokot in 2012 between Aug – Oct, with a leveling off with Senokot-S declines.	Target key SKUs at key retailers for potential new distribution. Based on evidence from 2012 strive to gain retailer commitment to promotions timed to FSI/Sweepstakes/IRC, etc. to maximize impact.
<b><u>Laxative Attitude and Usage Analysis</u></b> Update understanding of laxative category and brand behavior and ultimately what motivates the consumer to purchase a product._	Key factors determining purchase outlined such as doctor recommendation, value, efficacy, motivating benefits and language	Results shared with traditional, digital, SEO/SEM and PR agencies. Working together with the Brand Team to determine 2014 brand plans, media and promotions based on results.
<b>BUTRANS Objectives</b>	<b>Key results</b>	<b>Recommended Actions/Potential Actions</b>
<b><u>Butrans Fibromyalgia Quantitative Study Underway</u></b>  To determine the feasibility of a new indication for Butrans.	Identify key dynamics in the fibromyalgia market that will impact market potential and adoption of this new indication.  Understand physicians'	Results will be used to determine if Purdue should pursue a fibromyalgia indication for Butrans or publish articles in medical journals.

<p>To measure uptake of Butrans for the treatment of fibromyalgia.</p>	<p>approaches to treatment and map key treatment algorithms.</p> <p>Understand current treatment practice for Fibromyalgia patients.</p> <p>Gain reaction to the varying product profile combinations.</p> <p>After exposure to each scenario, measure uptake of the new product.</p> <p>Identify the impact this new indication will have on prescribing in comparison to currently-available Fibromyalgia products.</p>	
<p><b><u>Butrans Hospital Spillover Effect</u></b></p> <p>To understand the impact hospital formulary acceptance has on Butrans retail prescriptions.</p>	<p>Determine the financial value of gaining formulary acceptance for Butrans at hospitals. Hospitals provide a natural opportunity to broaden both awareness and physician experiences with the product. If hospitals put Butrans on formulary, physicians and other healthcare providers will treat the chronic pain patients that have started on the product. This will cause the level of awareness of Butrans to grow as more physicians try the product and/or hear of chronic pain patients that have been well treated with the product. Office based physicians who are aware of Butrans on a hospital</p>	<p>Results will be used to determine if Purdue should increase current efforts on gaining hospital formulary status for Butrans. Also, which types of hospitals would provide the most impact.</p>

	formulary may be more inclined to prescribe the product.	
<p><b><u>Butrans BrandVision Study Wave #3</u></b></p> <p>To evaluate Butrans and its competition in the opioid market on key dimensions that affect market share.</p>	<p>Analyze market penetration, differentiation and relationships. Measure: brand awareness, access, usage, adoption, advocacy, “buzz”, etc. Inform the Butrans brand team in regards to its branded competitors and the Butrans market in general. To gain a better understanding of current trends and changes.</p>	<p>Results will be used to adjust Butrans marketing efforts to respond to competitive threats and changes in the market.</p>
<p><b><u>Butrans Relationship Marketing (RM) – Boston, Seattle and Washington</u></b></p> <p>Completed 3<sup>rd</sup> QTR 2013</p> <p>To Determine TRx impact and ROI of RM programs in the three selected areas</p>	<p>- Incremental full costs ROI/TRx Lift:  - Boston: 0.85 / 0.05 (Statistically Significant)  - Seattle: 0.34 / 0.02 (Not Statistically Significant)  - Washington: 1.32 / 0.10 (Statistically Significant)  - “Initiations” initiative generated positive response across all 3 areas of interest  - Majority of HCPs that were reached by RM were PCPs  - Majority of HCPs are non Butrans prescribers  - There are low number of responders: 3 (Boston), 8 (Seattle), 3 (Washington)  - NP/PAs appear to be responsive in both Seattle and Washington  - ERO decile 10 HCPs did not appear to be responsive. Responsive HCPs varied across regions and spans</p>	<p>- Make all effort to reach existing Butrans prescribers as there is higher responsiveness from existing prescribers of Butrans  - Continue to reach across spectrum of HCPs as cost of RM for no-access HCPs are minimal compared to other traditional means</p>

	<p>between ERO decile 4-9</p> <ul style="list-style-type: none"> <li>- There were several Butrans “non-prescribers” who responded. However, Rx lift trails that of HCPs that recently prescribed Butrans.</li> </ul>	
<p><b><u>Butrans Experience Program (refresh)</u></b></p> <p>To Determine TRx impact and ROI of Patient Experience Program</p>	<ul style="list-style-type: none"> <li>- Incremental Full Costs ROI: 1.4 at 6 month follow- up</li> <li>- Cumulative Incremental TRx lift over control is 1.57 TRx per enrollee (89% TRx lift) at 6 month follow-up</li> <li>- There appears to be sensitivity to call frequency prior to enrollment</li> <li>- HCPs with enrolled patients appear to outperform HCPs without enrolled patients.</li> <li>- Primary Specialty appears to have the largest Rx lift while PCPs appear to have responsiveness but is less than Primary Specialty.</li> <li>- Responder Rx lift corresponds with Butrans deciles.</li> <li>- 32% of the enrolled “non-Butrans” prescribers began prescribing post enrollment and appear to be associated with increased call frequency post enrollment.</li> <li>- 46% of HCPs who ceased to prescribe Butrans in the 6 months prior to enrollment began prescribing post enrollment.</li> </ul>	<p>Continue program. ROI is positive.</p> <p>Make all effort to enroll high ERO and brand decile HCPs and Primary Specialists that have prescribed Butrans in the previous 6 months.</p> <ul style="list-style-type: none"> <li>- Communicate with HCPs on the importance of enrolling patients into the program.</li> <li>- Increased calls to Butrans “non-prescriber” HCPs post enrollment appears to elicit positive performance. However, Rx lift may not be as high as HCPs who have written for Butrans prior to enrollment</li> </ul>

### **BuTrans Qualitative and Quantitative Market Research Results Summarized**



Based on qualitative and quantitative market research, there were several issues uncovered that are impeding Butrans' growth. Below is a top-line of key findings from the market research:

- Butrans is not yet "front of mind" to HCPs twenty-four months post launch
- HCPs perceive Butrans as not yet having broad coverage/patient access by Managed Care providers
- 56% of Butrans patients discontinue at day 35 (in line with ERO category)
- Initial Butrans dose is often being initiated with a 5 mcg/hour when it should be the 10 mcg/hour.
- 83% of patients who discontinue Butrans do not titrate from their initial starting dose.
- Physicians are not providing a PRN/supplemental analgesic, along with Butrans as often as needed

The results of the research have been provided to the Butrans brand team. Actions to address the issues have been incorporated into current promotional strategies and tactics.

Sales & Marketing material, eMarketing initiatives and other promotional efforts reflect messaging that reinforces appropriate initiation and titration of Butrans. The need for supplemental analgesia, along with Butrans, and ongoing messaging around managed care coverage and the Patient Savings Program.

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## **MANUFACTURING / SUPPLY CHAIN / PHARMACEUTICAL TECHNOLOGY**

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Sustain Compliance across operational areas by auditing, monitoring key metrics and planned system upgrades/improvements (FDA, DEA, OSHA and EPA, CIA and HR policy) without major disruption to supply. Maintain continuous supply of commercial and new products to all customers, on time across the major product lines. Ensure project milestones are met and product moves into commercialization. Attain operational and management efficiency, continuously improving and assuring cost effectiveness.

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### **Key Metrics: Manufacturing, Supply Chain and Pharmaceutical Technology**

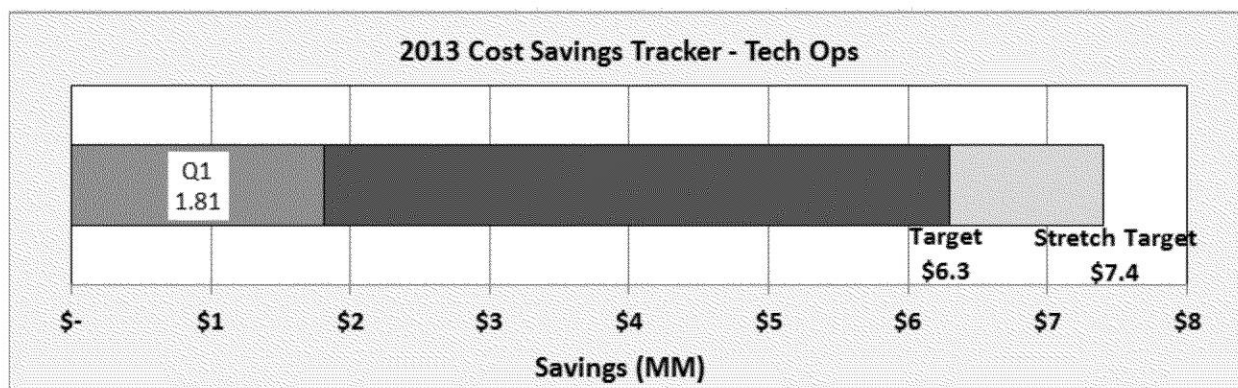
2013 Manufacturing, Supply Chain, and Pharmaceutical Technology					
Manufacturing and Supply Chain	Q1 YTD			Full Year	
	Actual	Budget	Var	2013 Budget	2012 Actual
Tablets Manufactured (MM)	170	171	(1)	726	691
OxyContin	103	106	(3)	394	486
MS / MSER	64	65	(1)	246	196
Oxy APAP	-	-	-	86	-
Oxy Export	3	-	3	-	9
Export Packaging Bottles (000)					
Bottles Packed	64	-	64	-	310
Orders Shipped On-Time					
Wilson	99.0%	99.0%	0.0%	99.0%	99.6%
Rhodes	100.0%	99.0%	1.0%	99.0%	97.0%
3rd Party	100.0%	99.0%	1.0%	99.0%	99.0%
Orders Shipped In-Full					
Wilson	99.0%	99.0%	0.0%	99.0%	99.0%
Rhodes	100.0%	99.0%	1.0%	99.0%	100.0%
3rd Party	100.0%	99.0%	1.0%	99.0%	100.0%
Inventory On-Hand (Months)					
OxyContin	2.4	2.5	(0.1)	2.5	2.1
BuTrans	0.9	3.0	(2.1)	3.0	5.5

Pharmaceutical Technology	Q1 YTD			Full Year	
	Actual	Budget	Var	2013 Budget	2012 Actual
Research and Development Hours	8,110	10,703	(2,593)	-	29,878
Production Hours	1,116	1,743	(627)		3,233
Support Hours	6,994	8,959	(1,965)		26,645
Development Batches Manufactured	18	37	(19)	77	83

### Comments on Key Metrics Table

BuTrans Inventory On-Hand is low due to issues with LTS West Caldwell manufacturing site transfer project. Supply from LTS in Germany has recommenced, and market outages will be avoided.

### 2012 Savings



Through Q1, 2013, Technical Operations recorded ~ \$1.8 mm in forecasted annual savings. These savings were driven by \$1.7 mm negotiated savings of raw materials through favorable contracted pricing of Morphine. Additional savings were realized through process improvements implemented on the manufacturing floor and in the laboratory (\$0.1 mm).

### **Infrastructure / Capital Projects**

The first new packaging line was installed, and the line is fully operational for OxyContin and MS Contin / MSER.

### **Rx / OTC Highlights**

- Intermezzo – Manufacturing for fresh supplies of Intermezzo started at Patheon in March 2013, and will be packaged at Sharp in April 2013.
- Dilaudid (Injectables) – Purdue successfully completed a three year supply agreement with Hospira for the injectables business. Purdue is evaluating alternative supply and API sources for the long term supply of this product line.
- Betadine – We are evaluating a change in our supply source for the Betadine line from Thatcher to Aplicare, as well as Betadine line extensions from some of our Mundipharma affiliates.

### **Risk Mitigation: Back-up of Key Products and Materials**

- Sumitomo - Final qualification batches at Wilson are now scheduled for July 2013.
- Dow - A new custom specification has been finalized, and Dow has updated their DMF to incorporate the process changes to produce this grade of Polyox. This will address the degradent issue. This custom Polyox will also be used by our affiliates in Europe.

## New Facility

- Final site selection process and incentive negotiations are underway, in parallel with the detailed facility design. Expect to have detailed facility design completed at end Q2, 2013, in line with the final site selection timeline.

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## QUALITY

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Sustain compliance with all laws and regulations related to cGxP from drug development through commercialization. Support the accurate and timely release of approved quality product. Assure integrity and qualification of all new product development, technology transfer and regulatory filings.

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## Sustained Compliance

- ONF Support Activities: As previously reported, a single stability lot of ONF 10 mg tablets (WBL51) showed Out of Trend (OOT) results for unknown degradents. These degradents were identified, specifications filed and submitted to *in vivo* genotoxicity testing. The testing is completed with favorable results, and the reports are in progress. Once the final reports are received, the issue will be closed by filing of a final field alert report with the Atlanta District Office.
- Two additional phases of the Trackwise implementation were completed on schedule.
  - Phase V: Commercial and Clinical Complaints (January 28, 2013)
  - Phase III: Change Control and Planned Deviations (March 25, 2013)
- There was no significant change in the number or types of product complaints received in 1Q2013. The processes remain in control and meet procedural timelines.

## External Manufacturing

- Dilaudid - The final field alert concerning the Dilaudid 1mg/mL ampule for a missing label identified via a complaint was filed on February 5, 2013. The investigation conducted by Hospira concluded this was an isolated incident.
- Butrans

- An Out of Specification (OOS) test result was reported on January 10, 2013, for the degradant Buprenorphine N-Oxide at the 3-month 40°C/75%RH stability sample for a 7.5 mg clinical lot produced at LTS West Caldwell. This lot supported the planned regulatory submission of this intermediate strength.
- Subsequently, on January 21, 2013, a similar OOS result was reported at the 3-month stability interval for the 40°C/75%RH 5mg validation lot produced to support the introduction of the first batches produced at West Caldwell to the market. Investigation into the root cause is on-going. No commercial product produced at West Caldwell has been released to the market.
- Slow-Mag Support - Investigations into the DEM issue continue, and to date no root cause has been determined. The final report for the *in vivo* genotoxicity testing has been received. The final response to the FDA 483 to provide this update is in preparation.
- On March 20, 2013, Purdue received written confirmation from the FDA's New Jersey District Office, that the FDA considers the recall for Colace Stool Softener 100 mg in 30 count bottles (Lot OJ8151) completed and terminated. This recall was initiated in April 2011 due to an OOS.

#### **Support for New Products**

- The 3-month testing of stability samples supporting regulatory filings for ONF in Latin America / Asia Pacific regions was successfully completed.
- The Korean FDA inspected the Wilson manufacturing site on March 11 – 14, 2013. In the wrap-up meeting, the site received one major observation related to specific requirements in the Korean regulations for validation of dirty and clean holding times for equipment. Twelve additional remarks to be classified as minor observations and/or recommendations in the final inspection report were also presented. The final report is scheduled for receipt within one month of the completion of the inspection.



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## RESEARCH & DEVELOPMENT

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R&D's goal is to efficiently and effectively advance each pipeline project to and through the defined stage gates as described within each program's strategic development plan. R&D's objectives for 2013 are reflected in Purdue's Business Scorecard and focus on progress or completion of major milestones for each pipeline project. While there are many components within each program, emphasis is placed on those items whose progress, quality and outcome drive stage gate decisions and as a consequence, project progress to NDA submission, approval, or termination. Through 1Q2013 substantial progress has been made toward the budgeted plan.

Each of the following pipeline projects are addressed herein:

- Reformulated OxyContin® (OTR/ORF)
- Butrans® (BTDS)
- Targin® (ONU)
- Hydrocodone QD (HYD)
- TRPV-1 (VND)
- ORL1 (OAG)
- Intermezzo (INT)
- Abuse Deterrent Immediate Release Oxycodone / ADIR – (OCI)

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### **Reformulated OxyContin (OTR/ORF)**

**All R&D scorecard activities for reformulated OxyContin remain on track:**

- Pre-approval labeling supplement (revised product label)
- Messaging regarding a) evidence base for use of opioids to treat chronic, non-cancer pain, and b) abuse deterrent properties / outcomes driven by reformulated OxyContin
- Pediatric exclusivity research program

Revised product labeling is under active negotiation between Purdue and FDA. While PDUFA (target) date of March 14<sup>th</sup> was not met, negotiations are positive and are expected to conclude prior to April 16<sup>th</sup>. As of this time, the label includes detailed text characterizing the physicochemical properties of the formulation, in vitro testing results, intranasal in vivo abuse potential data and label claims for both.

A comprehensive, objective and data-driven report presenting the evidence base (data) supporting the use of opioid medications for the treatment of chronic, non-cancer pain was submitted to FDA on Friday, March 22<sup>nd</sup>. The data analyzed and presented in this submission are sourced from Purdue-sponsored studies, as well as non-Purdue studies

published in peer reviewed journals. Multiple publications, abstracts, posters and presentations of these data are planned for 2013 and beyond.

#### Support for Independent Associated Companies

Purdue assistance, including support from R&D (Cranbury) and Manufacturing (Wilson) continues with Independent Associated Companies for ORF approval. Mundipharma registrations were initiated in the Philippines (Feb 6), Brazil (March 15) and Taiwan (March 22). New submissions are planned for Hong Kong (April 2013), Thailand, Indonesia, Singapore, and Malaysia 2Q2013, Mexico July 2013 and Vietnam 4Q2013. Mundipharma request for registrations in 7 Gulf Central Committee States was received March 18. Questions / requests for information for pending registrations received from health authorities in Korea, Australia and New Zealand 1Q2013.

#### 10mg ORF

Preliminary results indicate that the combined in vivo micronucleus/ comet assay in rats was not genotoxic. The weight of evidence indicates that neither ORF degradant poses a genotoxic risk to humans. Timing for the final reports of these studies is targeted for 2Q2013.

#### Pediatric Program

OTR3001 (Safety Study) Enrollment		
Milestone/Target by December 2013	Rating	Current Status
≥ 127 patients	5	91 patients enrolled of N=154 as of April 12, 2013
119 patients	3	
< 112 patients	1	

The pediatric exclusivity research program remains on-track for sNDA submission in January 2016.

#### Butrans® (BTDS)

**All R&D scorecard activities for Butrans remain on track:**

- Progress Butrans PREA (pediatric research) program
- Stage-gate analysis required to make go/no-go decision for 2<sup>nd</sup> generation and higher strength patches

## **Other Butrans Updates**

The Pre-Approval Supplement supporting registration of Butrans 15 mcg/hr patch is targeted for submission by March 29<sup>th</sup>, with an FDA approval date of September 29<sup>th</sup>, 2013.

An out-of-specification (OOS) stability investigation for 7.5 mcg/hr patches is under way at the LTS facility in West Caldwell. The root cause for the OOS has not been identified. Commercial production in West Caldwell is on hold until the investigation is completed. Submission of intermediate strengths (7.5 and 15 mg/hr) - Prior Approval Supplement (PAS) is delayed pending completion of the OOS investigation.

Draft results from the Higher Dose Thorough QTc trial (BUP1025) are under review; results appear to confirm that of BUP1011 which demonstrated small, but positive effect (per ICH E14 Guideline) on delaying the QT interval with treatment of Butrans 40mcg/hr (achieved with 2 X 20mcg/hr patches).

The Law Department is assessing IP/exclusivity timelines relative to the latest 2<sup>nd</sup> Generation development and BUP1025 results.

The 2<sup>nd</sup> Generation PK data from Study BUP1504 indicated that the 2<sup>nd</sup> Generation formulation was not reproducible. LTS is working to correct the formulation. Planning is underway to determine a revised timeline and whether it will support the current registration/launch strategy.

Financial assessments are being updated to include new scenarios incorporating delays in 2nd Generation development and IP/exclusivity assessment

## **Abuse Deterrent Immediate Release Oxycodone /ADIR - (OCI)**

**All R&D scorecard activities for OCI remain on track:**

- Initiate abuser panel study in June
- Complete clinical and registration batches in Wilson plant

Based on data from the OCI1001 trial, 7.5% sodium lauryl sulfate (SLS) was selected for abuse deterrence properties.

Manufacture of clinical materials was initiated the week-of March 25 in Wilson. An End-of-Phase 2 meeting is scheduled with FDA on May 21 to seek advice and guidance on the proposed OCI Development Program.

### **ONU (Targin/TarganIQ)**

**The following R&D scorecard activities are presented below:**

- The initial NDA filing is on track for September, 2013.
- Twin pivotal studies required to support planned sNDA submission (opioid induced constipation) are enrolling at a rate inconsistent with current submission and launch plan.

The NDA submission (for the indication of Pain with abuse deterrent properties) is on track for September 2013. If approved, the product label is expected to characterize TarginIQ as a safe and effective opioid analgesic with pharmacologic abuse deterrent properties. The favorable safety and tolerability data (inclusive of GI events) generated in the single US pivotal study (ONU3701) will be submitted for inclusion in the product label.

A multifaceted plan to expedite enrollment in the replicate pivotal studies (ONU3704/3705) required to support label expansion (OIC treatment) is being implemented. These two pivotal studies define the critical path for sNDA submission and all efforts are being made to expedite their conduct and completion; the revised sNDA submission date is 4Q2015.

### **Hydrocodone QD (HYD)**

**All R&D scorecard activities for HYD remain on track:**

- Complete enrollment in the single pivotal study required to support NDA submission and approval in the US.

NDA filing in 2Q2014 and 3Q2015 launch dates remain on track. If priority review is granted (high probability, given abuse deterrent features of the HYD formulation), the launch date could be as early as 1Q2015.

### **TRPV1 Lead (VND)**

**All R&D scorecard activities for TRPV-1 remain on track:**

- Complete enrollment in two Proof-of-Concept studies in support of go/no-go decision

Two human Proof-of-Concept studies (Osteoarthritis and Post -Herpetic Neuralgia) initiated in September, 2012 and are recruiting on schedule; a go/no-go decision for

one or both potential indications (general nociceptive pain and neuropathic pain) is targeted for late 2013/early 2014.

### **ORL1 (OAG)**

**All R&D scorecard activities for ORL1 remain on track:**

- Complete non-clinical studies to determine whether lower exposures in humans are capable of producing desired analgesic outcome with satisfactory adverse event and tolerability profile.

The First-in-Human, single ascending dose study (OAG1001) was paused after three cohorts of dosing to allow for thorough analysis of adverse event (somnolence) and pharmacokinetic (low bioavailability) data.

- A plan of nonclinical experiments designed to better understand the cause of these adverse events was conducted and suggest that human efficacy may be achieved at doses (exposures) lower than those associated with the observed AEs.
- A focused human efficacy trial (using a dental pain model) leading to a Go / No Go decision has been agreed with Shionogi and is anticipated to commence in 2H2013.

### **TRPV1 Back-up (VAN)**

**All R&D scorecard activities for VAN remain on track:**

- Progress first-in-human experiment under Japanese IND

The First in Human clinical trial (Single Ascending Dose) has been successfully conducted in Japan. A Multiple Ascending Dose study has begun in Japan and includes Caucasian subjects.

### **Intermezzo (INT)**

**All R&D scorecard activities for Intermezzo remain on track:**

- Submit final protocol for a “Clinical Use” study to meet FDA’s Post-Marketing Requirement described to Purdue in the NDA approval letter
- Plan to initiate pediatric (PREA) research program in to address FDA’s Pediatric Post-Marketing Requirement
- Advance publication plan in support of product launch