

## NuPathe (PATH)

**Initiating Coverage of PATH with an OUTPERFORM Rating and Fair Value of \$20: Novel Drug Delivery for Better Patient Compliance.**

July 25, 2011

Price  
**\$7.06**

Rating  
**OUTPERFORM**

Fair Value Estimate  
**\$20**

Liana Moussatos, Ph.D.  
(415) 263-6626  
liana.moussatos@wedbush.com

Richard Lau  
(415) 274-6851  
richard.lau@wedbush.com

- **NuPathe is an emerging pharmaceutical company applying proprietary drug delivery technologies to improve patient compliance.** The company's lead candidate, Zelrix™, is a proprietary patch delivery of sumatriptan for acute migraine treatment. The company is targeting patients with gastrointestinal symptoms of nausea and vomiting who have difficulty completely swallowing an oral medication.
- **We project cash runway through Zelrix™ launch.** The company ended Q1 2011 with about \$32.8 million in cash, investments, and cash equivalents and management guided to runway into H1 2012 which includes the anticipated launch of Zelrix™. Although there is potential for non-dilutive funding from one or more partnerships, we anticipate the company may conduct a financing to hire a sales force and for marketing preparation and launch of Zelrix, if approved on time.
- **We anticipate a major near-term catalyst could significantly impact PATH's valuation.** The NDA for Zelrix™ has a prescription drug user fee act (PDUFA) deadline of August 29, 2011 for FDA approval. We believe the clean clinical trial results established efficacy and estimate a 75% chance of first-pass approval, with at least 20% upside for PATH and the potential to double versus 20%-40% downside if approval is delayed.
- **In our view, PATH is undervalued at about \$7 per share compared with our fair value of about \$20.** We calculate PATH's fair value based on a 30% annual discount and a 1x-10x premium range on our net peak annual sales estimate for each product and indication in the clinic to reflect risk. With PATH trading at only about one-third of our \$300+ million peak sales potential for their lead acute migraine treatment candidate, Zelrix™, we believe NuPathe is an attractive investment. We are conservative in our first two years' projections of a new product launch due to the time it takes to achieve full reimbursement. However, our projections become bullish in the third launch year in 2014 as we and the Street project profitability.

### Company Information

Shares Outst (M)	14.6
Market Cap (M)	\$103
52-Wk Range	\$5.06 - \$10.22
Book Value/sh	\$1.70
Cash/sh	\$1.48
Enterprise Value (M)	\$81
LT Debt/Cap %	37

### Company Description

NuPathe is developing novel delivery methods including its proprietary SmartRelief and LAD for approved APIs as treatments for large unmet medical needs in acute migraine, Parkinson's disease, schizophrenia, bipolar disorder, and related CNS conditions.

FYE Dec	2010A	2011E			2012E		
REV (M)	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	\$0.0A	--	--	--	--	--
Q2 Jun	--	0.0E	0.0E	--	--	--	--
Q3 Sep	--	0.0E	0.0E	--	--	--	--
Q4 Dec	--	0.0E	0.0E	--	--	--	--
Year*	\$0.6A	\$0.0E	\$0.0E	--	\$16.6E	--	\$20.3E
Change	--	--	--	--	--	--	--
EPS	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	(\$0.26)A	--	--	--	--	--
Q2 Jun	--	(0.42)E	(0.46)E	--	--	--	--
Q3 Sep	--	(0.54)E	(0.52)E	--	--	--	--
Q4 Dec	--	(0.71)E	(0.64)E	--	--	--	--
Year*	(\$4.39)A	(\$1.92)E	(\$1.89)E	--	(\$2.42)E	--	(\$2.30)E
P/E	NMx	NMx	--	--	NMx	--	--
Change	--	--	--	--	--	--	--

Consensus estimates are from Thomson First Call.  
\* Numbers may not add up due to rounding.



Source: Thomson Reuters

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## I. INVESTMENT THESIS

### COMPANY SUMMARY

NuPathe, located in Conshohocken, PA, is an emerging pharmaceutical company applying its proprietary delivery technology to improve patient convenience and tolerability for existing drugs. The company's lead product, Zelrix™ is a sumatriptan iontophoretic patch developed using its proprietary SmartRelief technology for acute migraine with gastrointestinal symptoms and is in FDA review with an August 29, 2011 PDUFA. The company also has two preclinical candidates with a 2011 IND for NP201 to treat Parkinson's disease and an IND expected in 2012 for NP202 to treat schizophrenia and bipolar disorder. We believe approval of Zelrix™ is likely to result in one or more lucrative commercial partnerships and the company is a likely acquisition target.

### KEY POINTS

**Figure 1: We believe NuPathe has reduced pipeline risk as its lead product has already passed Phase 3.**

Product	Pre-Clinical	Phase 1	Phase 2	Phase 3	NDA Review	Launch
<b>Zelrix™</b> Acute Migraine Sumatriptan SmartRelief iontophoretic transdermal patch	✓	✓	✓	✓	PDUFA 8/29/11	H1:12 (Guidance)
<b>NP201</b> Parkinson's disease Ropinirole LAD implant	✓					
<b>NP202</b> Schizophrenia and bipolar disorder Atypical antipsychotic LAD implant	✓					

Sources: NuPathe and Wedbush Securities

NuPathe currently has its lead product, Zelrix™, under review at the FDA for approval to treat acute migraine in patients experiencing gastrointestinal symptoms of nausea and vomiting and who have difficulty swallowing oral medication. The PDUFA deadline is August 29, 2011; and with approval, the company anticipates launch in the first half of 2012. In addition, the company is developing NP201 as a treatment for Parkinson's disease as well as NP202 to treat schizophrenia and bipolar disorder and plans to take them into the clinic with a partner.

**We estimate initial product launch in H1 2012 could lead to full-year breakeven/profitability in 2014.**

We project Zelrix™ for acute migraine is likely to be approved in 2011 and launched in 2012 with gross peak annual sales conservatively reaching over \$300 million. With launch of Zelrix™ in 2012, we project 2014 to be the first breakeven/profitable year with estimated GAAP EPS of about \$1.24 on sales of about \$101 million which is at the high end of analysts' estimates. We are confident about sales due to headache specialists confirming that they have subsets of patients who would prefer patch delivery, especially among those experiencing nausea and vomiting and who have difficulty swallowing oral medication. NuPathe ended Q1 2011 with about \$33 million in cash, and we project runway into Q2 2012. We project the second product launch to be NP201 for Parkinson's disease in 2016 with worldwide gross sales reaching over \$350 million. We project a 2017 launch for NP202 in Schizophrenia and Bipolar Disorder, with worldwide gross sales approaching \$500 million each for these larger markets. We presume that NuPathe has a commercial partner for ex-US territories and for primary care in the US for Zelrix™ and is likely to partner NP201 and NP202 prior to clinical development.

### Estimated Milestones (\*our estimates)

<b>August 29, 2011</b>	<b>Zelrix™ PDUFA date</b>
<b>2011/2012*</b>	<b>Potential partnerships for Zelrix™, NP201, NP202</b>
<b>H1:12</b>	<b>U.S. commercial launch of Zelrix™</b>

**We see major value drivers in 2011 and 2012.**

In the near-term, we anticipate the main value drivers to include potential approval of Zelrix™ by or on the August 29, 2011 PDUFA deadline as well as a potential commercial partnership for Zelrix™ and/or development & commercial partnerships for NP201 and NP202 in 2011 or 2012 and launch of Zelrix™ in 2012. We believe approval of Zelrix™ is likely to trigger one or more commercial partnerships.

**Figure 2: We believe PATH is trading at an attractive valuation.**

PATH Product Pipeline Valuation		Eligible # Patients	Pricing \$/Patient	Gross Peak Sales WW	Net Peak Revs	Revs Year	Peak Penetration	Multiple	Launch	Discount Rate	MktCap Fair Value	Stock Fair Value
Product	Indication											
<b>Zelrix</b>	<b>Acute Migraine</b>	<b>15,000,000</b>	<b>\$1,620</b>	<b>\$332,147</b>	<b>\$208,228</b>	<b>2017</b>	<b>1%</b>	<b>8</b>	<b>3/1/2012</b>	<b>30%</b>	<b>\$293,583</b>	<b>\$20.15</b>
NP201	Parkinson's disease	3,000,000	\$2,698	\$387,359	\$102,548	2021	22%	2	11/1/2016	30%	\$13,786	\$0.95
NP202	Schizophrenia	6,600,000	\$3,854	\$491,133	\$94,733	2022	7%	1	11/1/2017	30%	\$4,898	\$0.34
NP202	Bipolar Disorder	30,000,000	\$3,854	\$468,750	\$92,656	2022	1%	1	11/1/2017	30%	\$4,791	\$0.33
We use multiples to account for clinical and regulatory risk at various stages of development.			Total Peak Revs:		\$405,510			7/20/11	Stock	MktCap	Upside Potential	
1x: in preclinical testing	6x: passed Phase 2 / in Phase 3											
2x: passed preclinical	7: positive Phase 3											
3x: IND filing accepted	8: regulatory review											
4x: Phase 1 data	9: approved											
5x: Phase 2 data	10: launched											
										<b>Late Stage Products Fair Value</b>		
										<b>\$20.15</b>	<b>\$293,583</b>	<b>181%</b>
										<b>Current Quarter's Est Net Cash (000):</b>		
										<b>\$1.48</b>	<b>\$21,613</b>	
										<b>Total Technology Value</b>		
										<b>\$21.77</b>	<b>\$317,058</b>	<b>203%</b>
										<b>Total PATH Value:</b>		
										<b>\$23.25</b>	<b>\$338,671</b>	<b>224%</b>
										<b>Current PATH Value:</b>		
										<b>\$7.18</b>	<b>\$104,586</b>	

Source: Wedbush Securities

**We believe that PATH is currently at an attractive valuation as it is trading around \$7 versus our fair value of about \$20 per share or about \$290 million market capitalization.** We believe approval of Zelrix™ is likely to lead to a commercial partnership. We view NuPathe as a \$23 per share acquisition target for the whole pipeline. We calculate our fair value based on a 30% annual discount and a 1x-10x premium range on our net peak annual sales estimate for each product and indication in the clinic, depending on stage of development to reflect risk. Our fair value includes candidates/disease areas which, in our view, have at least shown proof-of-concept clinical efficacy. Since Zelrix™ has already completed Phase 3 clinical trials and is under NDA review at the FDA, we only include our fair value for Zelrix™ in our fair value for PATH.

#### RISKS TO ATTAINMENT OF OUR FAIR VALUE INCLUDE:

**Clinical Risk** NuPathe is an early-stage company which has completed late-stage clinical development for their lead product candidate, Zelrix™, and has submitted a NDA which has been accepted for filing and is being reviewed by the FDA. Even though Zelrix™ successfully completed a pivotal Phase III clinical trial, it is still susceptible to inherent risks of failure at any stage of drug development such as the appearance of unexpected adverse events. The company has two preclinical candidates, NP201 and NP202 as potential treatments for Parkinson's and for schizophrenia, respectively. Because the company is not expected to release initial top line results from mid-to-late stage clinical candidates, we do not believe clinical risk is high in 2011. However, the company's business model involves in-licensing product candidates and its resources are limited in a competitive environment; moreover, the pipeline gap between Zelrix™ and the next clinical candidate NP201 is substantial and may not be filled in a timely manner to provide a staggered portfolio of product candidates to support consistent long-term growth.

**Regulatory Risk** NuPathe has never obtained marketing approval for a drug candidate but submitted a NDA for its lead product candidate, Zelrix™, on October 29, 2010 which the FDA accepted for filing and has assigned an August 29, 2011 prescription drug user fee act (PDUFA) date as a deadline for a marketing approval decision. As Zelrix™ is currently being reviewed by the FDA; regulatory risk is high as a decision is expected in 2011. Despite what we believe were positive Phase 3 results, the FDA could determine that the clinical program or the NDA was deficient or that Zelrix™ is not approvable and may require additional trials or manufacture additional validation batches. For example, the FDA could require that NuPathe conduct a second pivotal Phase 3 trial and/or a skin sensitization study despite the fact that the company believes it is not required to do so based on its discussions with the FDA. If the FDA requires additional studies or data, the resulting increased costs and delays in the marketing approval would likely increase financing risk. Even after conducting such trials and submitting new data, the FDA may find these to be insufficient or may not agree with the analysis and still may not approve the NDA. Any delay in obtaining, or an inability to obtain, marketing approvals would increase financing risk by delaying Zelrix™ commercialization as well as potential profitability. Regulatory risk can involve turnover in regulatory decision makers which can change policy and approval criteria after the trial is conducted. Agency statisticians may choose a different analytical process than was conducted in the NDA and conclude that the trials failed to achieve statistical efficacy. Changes in standard-of-care occurring while the trial is ongoing may also result in the design being found to be obsolete during regulatory review. Even if a product is approved, the designated patient population may be much smaller than expected which could limit sales potential. Post-approval clinical studies may be required as well as limits on sales and marketing practices and materials. If unexpected adverse effects emerge the drug can be withdrawn from the market. Regulatory requirements also vary among different countries and may result in requirements for additional clinical trials.

**Manufacturing Risk** NuPathe lacks manufacturing capability and plans to continue to rely on third parties to supply its product candidates. In addition, the company does not have any executed agreements for long-term commercial supply for its lead candidate Zelrix™, and if it executes such a contract, it is likely to be a single-source supplier. Manufacturers of product candidates must follow FDA rules relating to the FDA's current good manufacturing practice (cGMP) regulations which apply to organization of personnel, buildings, facilities, equipment, control of components, drug product containers, closures, production and process, packaging and labelling, holding and distribution, laboratory procedures, records and reports, as well as returned or salvaged products. The

manufacturing facilities must pass a pre-approval inspection and will also have periodic inspections by the FDA and other regulatory authorities. Failure to comply can result in a manufacturer receiving warning letters, having products seized or recalled, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and/or criminal penalties. As it is our view that third parties are less motivated toward NuPathe's pipeline than NuPathe employees, we feel that manufacturing risk is somewhat higher than normal. The company has its lead product candidate, Zelrix™, in regulatory review which is a time when manufacturing processes have to be scaled up and inspected. Third parties may also be less motivated to have sufficient quantities of product candidates which could result in delays in commercialization. LTS manufactures Zelrix™ using sumatriptan and components purchased from third parties. Although LTS has experience manufacturing passive transdermal drug patches, it does not have experience in manufacturing active transdermal patches, such as Zelrix™. In order for LTS to produce a commercial supply of Zelrix™, there are multiple activities which need to be completed including transferring technology and production capabilities from LTS' German facility where Zelrix' clinical supply was produced to the commercial manufacturing facility in New Jersey, assemble the commercial scale manufacturing equipment for Zelrix™ using components purchased from third party suppliers, and validate the customized machinery and production process. Because the machinery must be customized for Zelrix™, NuPathe is funding its purchase. If LTS is unable to assemble, customize and validate Zelrix™ commercial scale production at its New Jersey facility, there could be shortages. Also, maintenance issues with customized equipment could result in shortages of Zelrix™ due to the extra time it may take LTS to obtain replacement parts, to finish repairs and to revalidate customized equipment and production. Other risks associated with reliance on third party manufacturers include increased risk associated with regulatory compliance and quality assurance, possible breach of manufacturing agreements, possible termination or nonrenewal of the agreements, and disruption and costs associated with changing suppliers.

**Commercialization Risk** NuPathe's business model is to develop and commercialize clinical candidates. As NuPathe is a small company, we view commercialization risk as somewhat higher than normal; however, this is offset by not relying on third parties for all commercial activities as we understand NuPathe plans to market Zelrix™ to headache specialists in the US. We anticipate NuPathe is likely to partner commercial activities for primary care and outside the US. We consider NuPathe's commercial plan to be optimal for leveraging potential profits from Zelrix™ sales for a small company. By having its own sales force, collaboration risks are likely to be reduced including significant competition obtaining collaborators, implementing collaborations, obtaining optimal terms, maintaining collaborators' priority in their resources and efforts, successfully negotiating disagreements, and avoiding early terminations.

**Competition Risk** NuPathe is a relatively small company with limited resources which increases competition risk. Companies with relatively large budgets for sales and marketing may counter detail against NuPathe's future products and limit its sales. Given that its lead product, Zelrix™, is a novel patch delivery method for sumatriptan and triptans represent the majority of prescribed treatments in oral, nasal and injectable delivery methods, Zelrix™ is likely to have significant competition among acute migraine treatments even if approved by the FDA and launched. We believe competition risk is high, despite pursuing a novel niche—migraine patients with severe nausea and vomiting in which swallowing pills or other oral forms of delivery are not optimal. Physicians treating migraine have told us that many of their migraine patients who experience nausea and vomiting are still able to swallow but the pill may be expelled if they vomit. They also believe some of their patients would prefer a patch delivery. On the other hand, we believe competition risk is lowered by Zelrix™ incorporating sumatriptan which is frequently the first treatment prescribed by headache specialists. In 2010, sumatriptan sold over 70 million units in the U.S. which included about 10 million units of GlaxoSmithKline's (GSK:NYSE) branded Imitrex and Treximet. Maxalt from Merck (MRK:NYSE) sold about \$496 million in the U.S. in 2010 and was the top seller; however, patent exclusivity is expected to expire between 2012 and 2014 and other triptan patents are expected to expire between 2013-2017. Following expiration, inexpensive generic versions of branded triptans are likely to compete with Zelrix™, if approved. Because of lower cost, insurers are likely to promote use of a generic triptan prior to prescribing Zelrix™. Additional competition in the future may come from drug candidates in clinical development, including Merck's telcagepant and Levadex from MAP Pharmaceuticals (MAPP:Nasdaq) which are in late-stage clinical development or regulatory review, respectively. In addition to competition for Zelrix™, NuPathe's early-stage product candidates, NP201 and NP202, are likely to face competition in the future if they are approved. Specifically, NP201, a biodegradable, subcutaneous, injectable polymer implant combined with ropinirole, is likely to have competition from generic immediate-release and extended release versions of ropinirole and pramipexole, as well as from continuous delivery treatments, including a levodopa gel and an injectable apomorphine. NP202 is a biodegradable, subcutaneous, injectable polymer implant combined with an atypical antipsychotic medication and is likely to have competition from branded and generic versions of antipsychotic medications and other sustained-delivery depot formulations of atypical antipsychotics. The nature of the biopharmaceutical industry yields many breakthroughs and new and improved products and processes may be developed by outside companies at any time which could become best-in-class and limit the uptake of NuPathe's products. Due to the company's small size and limited resources, it may be unable to acquire additional product candidates or technologies from third parties as more established companies are also pursuing their acquisition. Increased competition may lead to fewer opportunities and less favorable terms.

**Intellectual Property Risk** Because the composition of matter patents covering the active pharmaceutical ingredients (APIs) of Zelrix™, NP201, and NP202, have expired, competitors will be able to offer and sell products with the same API so long as these competitors do not infringe upon any of NuPathe's product, formulation and method-of-use patents, or violate any marketing exclusivity period in the intellectual property (IP) estate. Since Zelrix™ is NuPathe's lead product candidate and is being reviewed by the FDA; we believe its IP risk is important. Two patents have been issued (US 6,745,071) or allowed (US 2008/0287497) and the intellectual property protecting NuPathe's current clinical pipeline shouldn't begin to expire until 2027 with the potential for extension to 2029. The issued patent was licensed by NuPathe and covers an iontophoresis drug delivery system. NuPathe and its licensors have filed US and foreign patent applications. In order to develop and commercialize Zelrix™, NuPathe must have a license for LTS's intellectual property



and its development and license agreement has a provision that if LTS is the commercial manufacturer, it will be exclusive and LTS will grant NuPathe an exclusive, worldwide, royalty-free license to LTS's intellectual property for commercialization of Zelrix™. However, if commercially reasonable terms cannot be reached, NuPathe would need to develop equivalent or alternative intellectual property, which would significantly delay commercialization of Zelrix™ and involve additional cost. NuPathe is a relatively small company with limited resources so larger companies with more resources may use litigation to weaken its intellectual property position. Because NuPathe relies on third parties, like LTS, to protect the licensed intellectual property, NuPathe may not have any input or control over the filing, prosecution or enforcement of such intellectual property rights and these patents may be found to be invalid or unenforceable. Any enforcement of intellectual property rights, or defense of any claims asserting the invalidity thereof, may be subject to the cooperation of the third parties who may find that their business interests do not support enforcement of these patents. NuPathe has financial obligations associated with intellectual property licenses with third parties, such as University of Pennsylvania for their IP related to LAD technology used to develop and commercialize licensed products (e.g. NP201 and NP202) and to SurModics Pharmaceuticals for their IP for NP201. Clinical and regulatory milestones for NP201 and NP202 can trigger payments at a time of insufficient cash which could delay development and commercialization and even cause termination of the licenses. NuPathe also relies on trade secrets and proprietary know-how as part of its intellectual property. Despite requiring confidentiality agreements, the company is exposed to the potential for unauthorized disclosure which could lead to enablement of competitors to duplicate or surpass NuPathe's technology and weaken its competitive position. Although NuPathe maintains general liability and product liability insurance with limits, subject to deductibles, of \$2 million for general liability, \$1 million for umbrella liability coverage for payments that exceed the general liability limits and \$2 million for product liability, this insurance may not fully cover potential liabilities. Product liability lawsuits could reduce the commercial potential of any product candidates successfully developed. NuPathe plans to have international business relationships for the development and commercialization of its product candidates. Additional risks associated with international business relationships include different regulatory requirements for drug approvals, potentially weaker intellectual property rights, potential for parallel importing, changes in tariffs, trade barriers and regulatory requirements, economic weakness, compliance with tax, employment, immigration and labor laws for employees traveling abroad, foreign taxes, foreign currency fluctuations, labor unrest, production shortages, and interruptions resulting from geo-political actions or natural disasters.

**Financing Risk** NuPathe is an emerging pharmaceutical company with a lead product candidate being reviewed for market approval by the FDA and the company has not commercialized any products or generated sales. If Zelrix™ is approved by the August 29, 2011 PDUFA deadline, we project first product sales in 2012 and anticipate breakeven/profitability in 2014. The company has funded operations primarily with equity, warrants, convertible notes, and debt facilities and ended Q1 2011 with about \$32.8 million in cash, investments, and cash equivalents. Management has guided to runway into H1 2012 which includes the anticipated launch of Zelrix™. Consequently, we believe there is some financing risk in 2011. Although there is potential for non-dilutive funding from one or more partnerships, we anticipate the company may require financing to fund the hiring of a sales force and marketing preparations for Zelrix™, if approved on time, as well as additional clinical development for NP201 and NP202 and potential in-licensing of additional product candidates prior to our estimate of full-year breakeven/profitability in 2014. If approval for Zelrix™ is delayed, we anticipate the company is likely to require financing to meet any additional requirements for approval. In addition, because some of the manufacturing equipment for Zelrix™ is customized, the company is also obligated to pay for these costs. The company executed a Loan Facility in May 2010 with MidCap Funding III, LLC, and Silicon Valley Bank and received \$5 million. On June 24, 2011, a First Loan Modification Agreement was announced in which the Term B Loans were increased from \$6 million to \$10 million, \$3 million Term C Loans were provided until August 31, 2011, maintenance of at least \$3 million in unrestricted cash, and reduction of LIBOR from 8.75% to 8.5%. With the execution of this Amendment, NuPathe drew down an additional \$10 million term loan under its secured credit facility in order to prepare for the launch of Zelrix™ expected in the first half of 2012. NuPathe issued warrants to purchase 59,748 shares of PATH at \$7.95 per share. Due to restrictions in the May 2010 Loan Facility and the pledge of NuPathe's assets as collateral, there are potential limits to additional debt financing. The company's debt and contractual commitments, including an equipment funding agreement with LTS could tie up cash to pay interest and principal and reduce working capital, capital expenditures, and product development. In addition, because the May 2010 Loan Facility has variable rate interest, the company's debt is exposed to increases in the market rate of interest which could decrease cash runway. Also, the company is exposed to currency exchange fluctuations as payments under the equipment funding agreement with LTS are in Euros.

## II. FINANCIAL MODEL

NuPathe Inc. (NASDAQ: PATH)						Wedbush Pac Grow Life Sciences				
Historical and Projected Income Statement						Liana Moussatos, Ph.D.				
(In thousands except per share data)						Richard Lau				
	2010A	2011E				2012E	2013E	2014E	2015E	
	FY:10A	Q1A	Q2	Q3	Q4	FY:11E	FY:12E	FY:13E	FY:14E	FY:15E
Gross Sales										
Zelrix			-	-	-	-	\$ 19,642	\$ 58,563	\$ 127,647	\$ 206,657
NP201(Parkinson's Disease)			-	-	-	-	-	-	-	-
NP202 (Schizophrenia)			-	-	-	-	-	-	-	-
NP202 (Bipolar Disorder)			-	-	-	-	-	-	-	-
Total Gross Sales	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 19,642	\$ 58,563	\$ 127,647	\$ 206,657
Revenues:										
Net Product Sales	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 16,629	\$ 48,599	\$ 99,270	\$150,339
Zelrix	-	-	-	-	-	-	16,629	48,599	99,270	150,339
Grant Revenue	650	-	-	-	-	-	-	-	-	-
Royalty and License Revenues	-	-	-	-	-	-	-	-	2,174	7,060
Zelrix	-	-	-	-	-	-	-	-	2,174	7,060
NP201(Parkinson's Disease)	-	-	-	-	-	-	-	-	-	-
NP202 (Schizophrenia)	-	-	-	-	-	-	-	-	-	-
NP202 (Bipolar Disorder)	-	-	-	-	-	-	-	-	-	-
Total Net Revenues	\$ 650	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 16,629	\$ 48,599	\$ 101,444	\$157,399
Cost and Expenses:										
Cost of Goods	-	-	-	-	-	-	4,989	14,580	29,129	42,981
R&D	17,064	1,574	3,090	3,121	3,152	10,936	12,926	13,451	13,997	14,565
SG&A	4,772	1,970	2,490	4,265	6,807	15,532	32,993	34,333	35,727	37,177
Other	-	-	-	-	-	-	-	-	-	-
Total Operating Expenses	\$ 21,835	\$ 3,544	\$ 5,580	\$ 7,385	\$ 9,959	\$ 26,469	\$ 50,908	\$ 62,363	\$ 78,852	\$ 94,723
Operating Income (Loss)	(21,186)	(3,544)	(5,580)	(7,385)	(9,959)	(26,469)	(34,279)	(13,764)	22,591	62,675
Net Interest Income (Expense)/Other Income	(3,671)	(179)	(487)	(470)	(456)	(1,592)	(1,307)	(359)	(114)	(34)
Other Income (Expense)	-	-	-	-	-	-	-	-	-	-
Income Before Income Taxes	\$ (24,856)	\$ (3,723)	\$ (6,067)	\$ (7,855)	\$ (10,416)	\$ (28,060)	\$ (35,586)	\$ (14,123)	\$ 22,478	\$ 62,642
Provision (Benefit) for Income Taxes	(500)	-	-	-	-	-	-	-	4,042	11,558
Net Income (Loss)	\$ (24,356)	\$ (3,723)	\$ (6,067)	\$ (7,855)	\$ (10,416)	\$ (28,060)	\$ (35,586)	\$ (14,123)	\$ 18,436	\$ 51,083
EPS (GAAP,Taxed,Diluted)	(\$4.39)	(\$0.26)	(\$0.42)	(\$0.54)	(\$0.71)	(\$1.92)	(\$2.42)	(\$0.96)	\$1.24	\$3.41
Weighted Shares Outstanding (Basic and Diluted)	6,126	14,554	14,566	14,591	14,616	14,582	14,679	14,779	14,879	14,979
Cash	\$38,918	\$32,768	\$36,136	\$27,716	\$16,735	\$16,735	(\$28,412)	(\$50,121)	(\$34,763)	\$13,862
Net Cash per share	\$5.50	\$1.90	\$1.48	\$0.94	\$0.23	\$0.23	(\$2.30)	(\$3.39)	(\$2.34)	\$0.93
Annual (Burn)/Generation	\$34,992					(\$22,183)	(\$45,147)	(\$21,708)	\$15,358	\$48,625

Source: Wedbush Securities

	Q2:11	Q3:11	Q4:11	FY:11	FY:12	FY:13	FY:14	FY:15
<b>Consensus Revenues</b> (\$ millions)	\$0	\$0	\$0	\$0	\$20.30 \$7.30-\$26.02	\$53.16 \$46.3-\$62.47	\$95.77 \$86.1-\$114	\$162 \$162-\$162
<b>Wedbush difference</b> (\$ millions)	\$0	\$0	\$0	\$0	~\$(4) In-range	~\$(4) Low end	~\$5 High end	~\$(5) In range
<b>Consensus EPS</b> \$(0.54)-\$(0.42)	\$(0.47) \$(0.54)-\$(0.42)	\$(0.53) \$(0.63)-\$(0.42)	\$(0.64) \$(0.73)-\$(0.59)	\$(1.89) \$(2.07)-\$(1.72)	\$(2.30) \$(3.58)-\$(1.53)	\$(1.30) \$(2.21)-\$(0.44)	\$0.24 \$(0.52)-\$1.03	\$2.36 \$2.36-\$2.36
<b>Wedbush difference</b>	\$0.05 High end	\$(0.01) In range	\$(0.07) Low end	\$(0.03) In range	\$(0.12) In range	\$0.34 In range	\$1.00 High end	\$1.05 Above

Sources: Thomson One Analytics and Bloomberg

We tend to be relatively conservative in our first two years of product launch; however, due to headache specialists comments about having a group of patients who would prefer patch delivery, we become relatively bullish in year three (2014) which is our breakeven/first full year of profitability. With over 40 million migraine patients worldwide, we believe Zelrix™ sales can reach our projected peak of over \$300 million.

### III. MANAGEMENT

We believe execution risk is lowered by the significant experience and accomplishments of NuPathe's management team. The team has extensive experience in pharmaceutical development.

Name	Position and Past Experience
<b>Jane H. Hollingsworth</b>	<b>Co-Founder and CEO since January 2005.</b> Ms. Hollingsworth has served as a director and Chief Executive Officer since January 2005. Prior to founding NuPathe, Ms. Hollingsworth co-founded and served as Executive Vice President, Secretary and General Counsel of Auxilium Pharmaceuticals, Inc., a specialty pharmaceutical company. Prior to co-founding Auxilium, Ms. Hollingsworth served as Vice President, Secretary and General Counsel of IBAH, Inc., a multinational contract research organization. Prior to this, Ms. Hollingsworth practiced law at the law firm of Montgomery, McCracken, Walker & Rhoads. Ms. Hollingsworth holds a BA from Gettysburg College and a JD from the Villanova University School of Law.
<b>Terri B. Sebree</b>	<b>President since February 2005.</b> Ms. Sebree is one of NuPathe's founders and has served as President since February 2005. Prior to founding the company, Ms. Sebree served as Senior Vice President of Development at Auxilium. Prior to joining Auxilium, Ms. Sebree served as Executive Vice President, U.S. Operations at IBAH. Before IBAH, Ms. Sebree served in a variety of management roles with Abbott Laboratories for over nine years. Ms. Sebree holds a BS from Texas A&M University.
<b>Keith A. Goldan</b>	<b>Vice President and CFO since November 2008.</b> Mr. Goldan, CPA has served as NuPathe's Vice President and Chief Financial Officer since November 2008. From October 2004-2008, Mr. Goldan was Chief Financial Officer and served on the board of directors of PuriCore plc, a medical technology company. Prior to Puricore, Mr. Goldan served as Vice President and Chief Financial Officer of Biosyn, Inc., a specialty pharmaceutical company, in a variety of roles with ViroPharma Inc., Century Capital Associates, a specialty consulting firm focusing on capital strategy for healthcare companies, and the Healthcare & Life Sciences Practice of KPMG LLP. Mr. Goldan achieved a B.A. from the Robert H. Smith School of Business at the University of Maryland and an MBA from The Wharton School at the University of Pennsylvania.
<b>Mark W. Pierce, M.D., Ph.D.</b>	<b>Vice President and CSO since October 2006.</b> Dr. Pierce has served as NuPathe's Vice President and Chief Scientific Officer since October 2006. Prior to NuPathe, Dr. Pierce was Senior Vice President of Pfizer's Global Research and Development from July 2002 – October 2005. Dr. Pierce has a B.A. and a Ph.D. from Northwestern University and an M.D. from Northwestern University Medical School. He did his training in internal medicine at Peter Bent Brigham Hospital and Massachusetts General Hospital in Boston. Dr. Pierce was an Instructor and Associate Professor of Medicine at Harvard Medical School.
<b>Gerald W. McLaughlin</b>	<b>Vice President of Commercial Operations since September 2007.</b> Gerald W. McLaughlin has served as NuPathe's Vice President of Commercial Operations since September 2007. Previously, Mr. McLaughlin held positions at Endo Pharmaceuticals, a specialty pharmaceutical company, including Senior Director, Strategic Marketing from January 2007 through August 2007, Regional Sales Director from July 2005 through December 2006, Group Marketing Director, Pain Products from November 2002 through June 2005 and Marketing Director. Prior to Endo, Mr. McLaughlin held various marketing and sales roles at Merck for 11 years. Mr. McLaughlin has a BA from Dickinson College and an MBA from Villanova University.
<b>Ezra H. Felker</b>	<b>Vice President Business Development since January 2006.</b> Mr. Felker has served as NuPathe's Vice President of Business Development since January 2006. Previously, he served as an Entrepreneur in Residence at BioAdvance, an initiative by the Commonwealth of Pennsylvania focused on funding early stage life sciences companies, from June 2005 through December 2005. Prior to BioAdvance, Mr. Felker was Associate Vice President of BTG Ventures at BTG International Inc., Manager, Business Development at Icagen, Inc. and as a protein chemist at Hybritech and Biosite Diagnostics. Mr. Felker holds a BS from the University of California, San Diego and an MBA from the Weatherhead School of Management at Case Western Reserve.
<b>Michael F. Marino</b>	<b>Vice President and General Counsel since October 2010.</b> Mr. Marino has served as NuPathe's Vice President and General Counsel since October 2010. Prior to joining the company, Mr. Marino practiced law at Morgan, Lewis & Bockius LLP from March 2005 to October 2010 and at WilmerHale LLP from October 2001 to March 2005. While at Morgan, Lewis & Bockius and WilmerHale, Mr. Marino's practice focused on advising life science and other companies on mergers and acquisitions, securities offerings, corporate financings, securities law compliance, corporate governance, and other general corporate matters. Mr. Marino has a B.S. in Accountancy from Villanova University and a J.D. from Boston College School of Law.

Sources: NuPathe and Wedbush Securities



#### IV. INTELLECTUAL PROPERTY

We understand that the earliest expiration of US patent protection for Zelrix™ is 2027.

Number	Title	Priority/Filing Date	Status
PCT/US07/09000 WO 2007/120747*	Transdermal Methods and Systems for the Delivery of Anti-migraine Compounds Related Applications	04/13/06 4/12/07	Pending PCT
US 2008/0287497(Continuation of 0900□ above)	Transdermal Methods and Systems for the Delivery of Anti-migraine Compounds Related Applications	04/13/06 07/28/08	Allowed
US Appl. 61/264,095	User Activated Self contained Pre-packaged Iontophoretic Drug Delivery System	11/24/09 11/24/10	Pending US provisional
6,745,071**	Iontophoretic Drug Delivery System	2/21/03	Issued
PCT/US03 028980** + WO2004/075980	Iontophoretic Drug Delivery System	2/21/03 09/13/03	Pending PCT
US 2009/0318847 A1	Polyamine Enhanced Formulations for Triptan Compound Iontophoresis	06/19/08	Pending U.S. Utility Office Action Pending
PCT/US2008/81837* WO 2009/154648	Polyamine Enhanced Formulations for Triptan Compound Iontophoresis	06/19/08 10/30/08	Pending PCT
US2009/0317450 A1	Pharmacokinetics of Iontophoretic Sumatriptan Administration	06/19/08	Pending U.S. Utility Office Action Pending
PCT/US2008/081841*** WO2009/154649	Pharmacokinetics of Iontophoretic Sumatriptan Administration	06/19/08 10/30/08	Pending PCT
US 2010/0262066 A1	Electronic Control of Drug Delivery System	12/30/08 12/29/09	Pending US Utility
PCT/US09/69673	Electronic Control of Drug Delivery System	12/30/08 12/29/09	Pending PCT
US2011/0066100-A1	Methods for Iontophoretically Treating Migraine and Nausea	08/10/09 08/10/10	Pending US Utility
PCT/US10/045045 WO 2011/019732	Methods for Iontophoretically Treating Migraine	08/10/09 08/10/10	Pending PCT

\* Australia, Brazil, Canada, China, Europe, Japan, Mexico, New Zealand, South Africa, Eurasia, India, Israel

\*\* Australia, Canada, China, Europe, Japan, Korea

\*\*\* Australia, Brazil, Canada, Europe, Japan, Mexico, New Zealand, South Africa, Eurasia, Israel

+ Fully paid, exclusive license from Travanti Pharma, Inc. ("Travanti") in the field of migraine

Sources: NuPathe and Wedbush Securities

Two patents relevant to Zelrix™ under NuPathe's intellectual property estate have been issued or allowed with the last one expiring in 2027. The others are in various stages of the process and could extend the exclusivity to 2029 if they are issued. NuPathe also owns exclusive worldwide rights to both SmartRelief and Long-Acting Delivery (LAD) technologies.

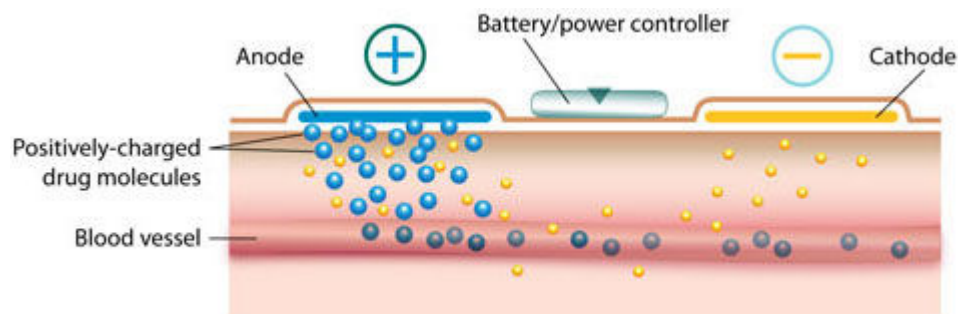
#### V. TECHNOLOGY PLATFORMS

We believe NuPathe's proprietary drug delivery technologies enhance patient convenience and tolerability. NuPathe's drug development incorporates two proprietary drug delivery technologies: SmartRelief and Long-Acting Delivery (LAD) technologies. Zelrix™ utilizes SmartRelief while NP201 and NP202 both use LAD.

##### SmartRelief

NuPathe's SmartRelief technology utilizes iontophoresis to actively deliver drug through the skin. The iontophoresis process begins with two reservoirs, one with positively charged drug and the other with negatively charged counter ion. When a mild electric current is applied, drug travels out of the reservoir and into the skin where it's absorbed and disbursed by blood vessels. As compared to passive transdermal technologies, iontophoresis offers several advantages including the ability to control the amount and rate of drug delivery and the ability to deliver a variety of medications such as proteins and peptides. In our opinion, iontophoresis has been validated as a drug delivery technology through the approval of two pharmaceuticals products, Johnson & Johnson's IONSYS system and Vysteris, Inc.'s LidoSite topical system for analgesia, and multiple iontophoretic medical devices. Zelrix™ utilizes the SmartRelief technology for controlled delivery over four hours of Sumatriptan.

Figure 3: SmartRelief Technology



Source: NuPathe, reprinted with permission

### Long-Acting Delivery (LAD) Technology

LAD is NuPathe's proprietary drug delivery technology which utilizes a small biodegradable implant. The implant is made of a biodegradable polymer matrix injected just below the skin. It can also be removed via a minor surgical procedure for early termination of therapy if needed. Thus far, the company has tested the LAD technology using several different neuropsychiatric compounds in multiple animal models. Based on the results, NuPathe believes patients can potentially be treated for one to three months with a single application. We believe the LAD technology has the potential to increase efficacy through better patient compliance and/or lead to a more favorable side effect profile through lower peak drug levels.

## VI. CLINICAL PIPELINE

NuPathe's lead candidate, Zelrix™ is being reviewed by the FDA for potential marketing approval and has a PDUFA deadline of August 29, 2011. In addition, the company has two additional candidates in IND-enabling preclinical studies.

Figure 4: Pipeline

Product	Pre-Clinical	Phase 1	Phase 2	Phase 3	NDA Review	Launch
<b>Zelrix™</b> Acute Migraine Sumatriptan SmartRelief iontophoretic transdermal patch	√	√	√	√	PDUFA 8/29/11	H1:12 (Guidance)
<b>NP201</b> Parkinson's disease Ropinirole LAD implant	√					
<b>NP202</b> Schizophrenia and bipolar disorder Atypical antipsychotic LAD implant	√					

Sources: NuPathe and Wedbush Securities

### Late-Stage Product: Zelrix™

Indication: Acute Migraine

Annual Gross Peak Sales Potential: over \$300 million worldwide

**Market Opportunity.** Migraine is a chronic and debilitating neurological condition characterized by episodic attacks of moderate to severe headache pain. Associated symptoms often include nausea and vomiting, photophobia (light sensitivity), phonophobia (sound sensitivity), and visual disturbances or aura. The condition affects up to approximately 12% of people in the United States and Europe, with approximately 30 million affected in the former. However, about half of migraine sufferers in the U.S. experience symptoms severe enough to seek medical therapy. Most migraines last between four and 24 hours, and according to Lipton RB et al, *Neurology* 2007

68(5): 343-349, 63% experience between one and four migraines per month while 31% experience three or more migraines per month. We anticipate that NuPathe will partner Zelrix™ prior to pursuing ex-US regulatory approvals.

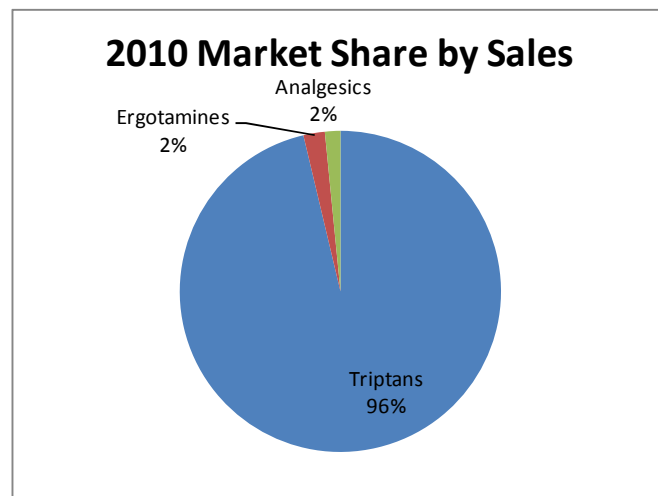
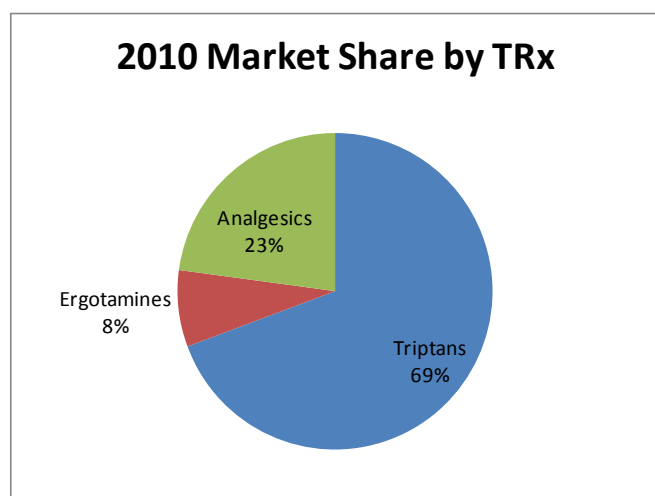
**Figure 5: Overall 2010 Migraine Market by Drug Class**

2010	TRx Quantity	TRX MBS Dollars	% share (Qty)	% share (\$)
Triptans	113,262,064	\$1,830,530,617	69%	96%
Ergotamines	12,823,332	\$40,648,955	8%	2%
Analgesics	37,324,673	\$29,589,541	23%	2%
<b>Total</b>	<b>163,410,069</b>	<b>\$1,900,769,113</b>		

Source: Wolters Kluwer Health and Wedbush Securities

**Current Treatment Options.** The two main types of migraine treatments are acute and preventive. Acute treatments dominate the migraine market and are designed to stop a migraine attack quickly, lessen the severity, reduce short-term recurrence, and to maintain the patient's ability to function. The three main classes of acute migraine treatments are triptans, analgesic combinations, and ergotamines, including dihydroergotamine (DHE). Triptans dominate the acute migraine market and, according to data published by Wolters Kluwer Health, the 2010 total revenue for prescription migraine drugs was approximately \$1.9 billion in the U.S., with \$1.8 billion for triptans representing 96% of the market. There are currently seven main triptan brands on the market available by oral, injectable or nasal administration. Generic sumatriptan is the market leader with 2010 sales of \$625 million representing 54% of the market on a quantity basis. In the U.S., the 2010 triptan market can be further broken down into oral (\$1.51 billion), injectable (\$230 million) and nasal (\$91 million).

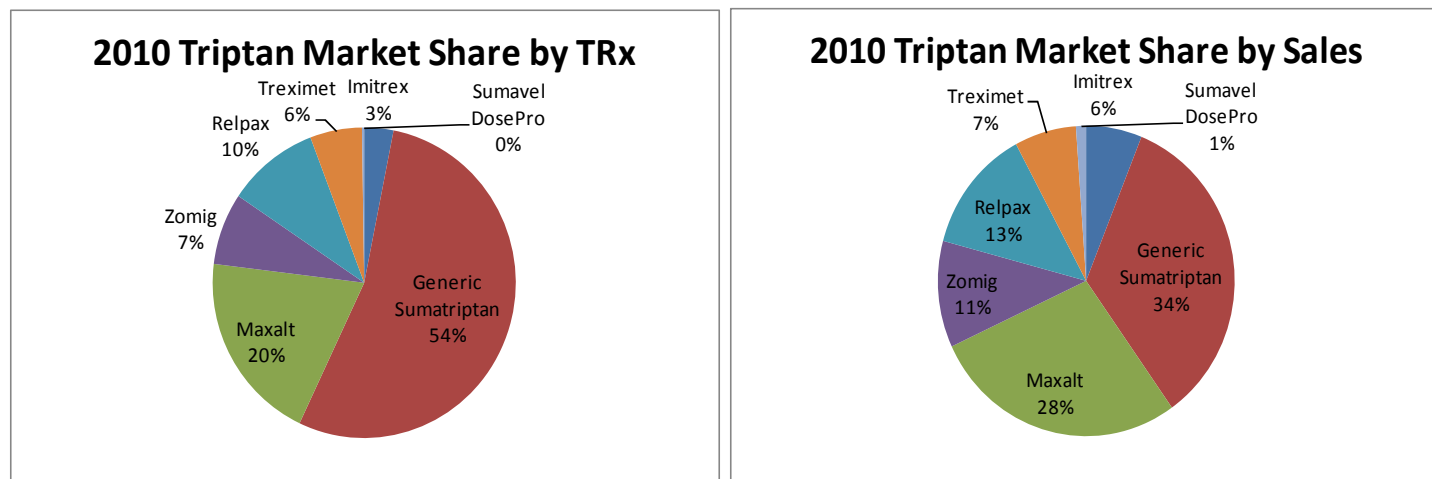
**Figure 6: Triptans are the Market Leader**



Source: Wolters Kluwer Health and Wedbush Securities

**Despite multiple treatment options, inadequate migraine relief occurs in a significant number of individuals.** Unfortunately for migraine sufferers, both triptans and DHE have limitations. The triptans provide pain relief slowly (often 45 to 90 minutes after dosing), individual drugs do not work in 30-40% of patients, and the class is accompanied by arterial constriction which can raise blood pressure. Headache specialists have indicated to us that they will try different oral triptans and different modes of delivery for triptans prior to changing class of active ingredient. Meanwhile, although DHE is a safe drug used clinically for over 50 years, it is only available intravenously and subcutaneously (from a healthcare provider) or nasally (where absorption can lead to inconsistent dosing), and is often accompanied by nausea, particularly when given intravenously. We note that Map Pharmaceuticals is developing Levadex, inhaled DHE, which has a PDUFA date of March 26, 2012. In our opinion, the migraine market is sufficiently large to support multiple products, especially given that about 79% of migraineurs would try a new medication while over 80% of patients on a triptan have used a different triptan in the past and 48% have used two or more different triptans, according to Bigal ME et al, *Headache* 2007 47(4):475-479.

Figure 7: Generic Sumatriptan is the Market Leader Among Triptans



Source: Wolters Kluwer Health and Wedbush Securities

Figure 8: Zelrix™



Source: NuPathe, reprinted with permission

**Summary.** Zelrix™ is an active, single-use transdermal patch that provides controlled delivery of sumatriptan for four hours. It was designed using NuPathe's SmartRelief technology to address the limitations of current migraine therapies. The clinical development of Zelrix™ included eight Phase 1 trials, one skin irritation study, one pivotal Phase 3 trial (completed in July 2009), and two long-term, open-label Phase 3 trials (one has completed). The company submitted an NDA for Zelrix™ to the FDA in October 2010 via the 505(b)(2) registration pathway. The PDUFA deadline is August 29, 2011, and with approval, NuPathe anticipates launch in the first half of 2012.

**Migraine-related nausea and vomiting may be avoided with Zelrix™'s transdermal delivery system.** Migraine-related nausea and vomiting (MRNV) can be a significant impediment to successful oral migraine treatment due to administration challenges.

According to Silberstein SB *Headache* 1995 35(7):387-396, 52% of all migraineurs experience nausea and 22% experience vomiting in a majority of migraines. Additionally, 48% of migraineurs have reported that nausea or vomiting causes them to delay or avoid treatment. We estimate that this segment of the migraine population consists of approximately 10 to 15 million patients in the U.S. and the ideal target population for Zelrix™ treatment.

**Zelrix™ may improve consistency of response due to a more predictable PK profile.** Migraine-associated gastroparesis is a condition in which migraineurs experience paralysis of the stomach muscles resulting in a slower digestion and inconsistent migraine relief due to poor absorption of oral medications. Conversely, Zelrix™ is not dependent on gastrointestinal absorption due to its transdermal delivery system and may provide more consistent migraine relief over oral delivery by avoiding the hurdles from migraine-associated gastroparesis. Furthermore, it may minimize triptan-related adverse events through tighter delivery of sumatriptan and a lower peak plasma level.

## CLINICAL TRIAL RESULTS

Figure 9: Pivotal Phase 3 Clinical Trial Results

ITT Analysis – Last observation carried forward	Zelrix (n=226)		Placebo (n=228)		% Difference	p-value
	Total	%	Total	%		
Symptom Two Hours After Patch Application						
Headache pain free	40	17.7%	21	9.2%	8.5%	0.0092
Headache pain relief	119	52.9%	65	28.6%	24.3%	<0.0001
Nausea free	189	83.6%	144	63.2%	20.4%	<0.0001
Photophobia free	116	51.3%	83	36.4%	14.9%	0.0028
Phonophobia free	125	55.3%	89	39.0%	16.3%	0.0002

Source: NuPathe and Wedbush Securities

**Phase 3 Results.** The company completed the pivotal Phase 3 trial in July 2009. The trial met its primary endpoint of proportion of patients pain-free at two hours versus placebo with statistical significance ( $p=0.0092$ ). Furthermore, key secondary endpoints were met with statistical significance including proportion of patients with pain relief ( $p<0.0001$ ), nausea free ( $p<0.0001$ ), photophobia free ( $p=0.0028$ ), and phonophobia ( $p=0.0002$ ) versus placebo. Four additional secondary endpoints were also met with statistical significance including: 1) headache pain relief within one hour ( $p=0.0123$ ; 29% Zelrix™ versus 19% placebo); 2) freedom from nausea within one hour ( $p=0.0251$ ; 71% Zelrix™ versus 58% placebo); 3) freedom from migraine at two hours ( $p=0.0135$ ; 16% Zelrix™ versus 8% placebo); and 4) decreased use of rescue medication within 24 hours ( $p<0.0001$ ; 40% Zelrix™ versus 60% placebo using rescue medication). Furthermore, a retrospective analysis showed sustained pain relief from two to 24 hours in patients (no or mild pain at all time points) who had originally achieved pain relief at two hours ( $p=0.0251$ ; 34% Zelrix™ versus 21% placebo).

**Figure 10: Pivotal Phase 3 Safety Data**

Adverse Event, n (%)	Zelrix (n=234)	Placebo (n=235)
Application site pain	54 (23%)	34 (15%)
Application site paresthesia	28 (12%)	44 (19%)
Application site pruritis	18 (8%)	16 (7%)
Application site reaction	16 (7%)	13 (6%)

Source: NuPathe and Wedbush Securities

head.” There were no serious AEs or deaths in the trial.

#### **Zelrix™ maintains efficacy in patients with MRNV.**

According to a post-hoc sub-analysis of the Phase 3 data, 54% of patients with nausea at baseline had headache pain relief at two hours which is similar to the overall population in the Phase 3 trial. This suggests to us that the effectiveness of Zelrix™ is maintained in patients with MRNV. We believe this is important given that patients with MRNV often experience limited effectiveness with oral sumatriptans, particularly due to vomiting.

**Pivotal Phase 3 Study Design.** The pivotal Phase 3 trial included a randomized, double-blind, placebo controlled design to evaluate the safety and efficacy of Zelrix™ versus an active transdermal placebo patch in acute migraine patients. Inclusion criteria required patients to have experienced moderate to severe pain during a migraine, had migraines for at least one year, and reported one to six migraines per month. Patients remained in the trial until they treated one migraine with a patch or two months post randomization, whichever occurred first. The trial included a total of 469 patients with a mean age of 41 years at 38 sites in the U.S. Patient populations were balanced with the Zelrix™ population consisting of 197 women and 37 men and the placebo population consisting of 201 women and 34 men.

The primary endpoint was the proportion of patients who were pain free at two hours after patch application as measured by a standard migraine diary. Key secondary endpoints included: 1) proportion of patients nausea free at two hours; 2) proportion of patients photophobia free at two hours; and 3) proportion of patients phonophobia free at two hours. Safety assessments included: 1) adverse events; 2) investigator skin irritation exam scores; and 3) subject skin irritation self-exam scores.

The primary endpoint was the proportion of patients who were pain free at two hours after patch application as measured by a standard migraine diary. Key secondary endpoints included: 1) proportion of patients nausea free at two hours; 2) proportion of patients photophobia free at two hours; and 3) proportion of patients phonophobia free at two hours. Safety assessments included: 1) adverse events; 2) investigator skin irritation exam scores; and 3) subject skin irritation self-exam scores.

**Phase 3 12-Months Open-Label Trial (NP101-008).** This was an open-label extension study to the pivotal Phase 3 trial. A total of 183 patients enrolled in the trial and more than 2,000 patches were applied. Top-line data was initially released in October 2010 and the full data were presented at the American Headache Society 53<sup>rd</sup> Annual Scientific Meeting (AHS June 2-5, 2011 Denver). Overall efficacy was similar to that seen in the Phase 3 trial with 23.8% of patients being headache pain free, 58.2% experiencing headache pain relief, 79% being nausea free, 60.1% being phonophobia free, and 53.4% being photophobia free two hours after treatment. Furthermore, as shown in Figure 12, the treatment effect was relatively consistent through the entire 12 month study period. On average, patients used about 1.6 patches per month with the majority being used to treat an initial migraine (1933 patches used to treat initial migraine and 156 patches used as rescue medication).

**Phase 3 Safety.** 50% of Zelrix™ patients (117) and 40% of placebo patients (103) experienced at least one treatment-emergent adverse event. The most common AE reported by Zelrix™ patients were related to the application site, including application site pain and tingling. Skin tolerability of Zelrix™ is comparable to other transdermal products with mild to moderate redness upon patch removal. There was a low incidence of triptan-related AE's with Zelrix™, with 1.7% experiencing atypical sensations and 1.7% experiencing pain and other pressure sensations (both mild severity). One patient reported a moderate intensity “cold sensation

**Figure 11: Phase 3 Sub-analysis in Patients with Nausea at Baseline**

Post-hoc analysis	Zelrix (n=95)		Placebo (n=119)	
Timepoint	1 hour	2 hour	1 hour	2 hour
Headache pain free	4%	14%	2%	7%
Headache pain relief	22%	54%	13%	22%
Nausea free	44%	68%	32%	43%
Photophobia free	31%	55%	26%	34%
Phonophobia free	42%	64%	37%	37%

Source: Zelrix™ data presented at the 52<sup>nd</sup> annual American Headache Society conference (AHS June 24-27, 2010 Los Angeles) and Wedbush Securities



Figure 12: 12-month Efficacy and Safety Data

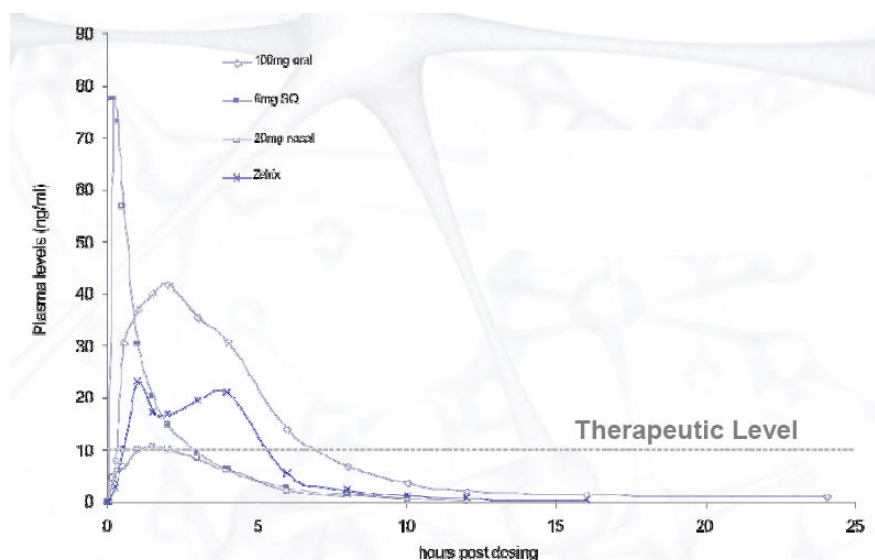
Symptom Two Hours After Patch Application	Headache pain relief (Range)	Nausea free (Range)	Adverse Event	Safety Population N=183
Months 1-4	56 – 62%	72 – 78%	Any adverse event	107 (58.5%)
Months 5-8	51 – 63%	76 – 84%	Application-site pruritus	40 (21.9%)
Months 9-12	51 – 68%	70 – 86%	Application-site pain	39 (21.3%)
			Application-site hypersensitivity	11 (6%)

Source: Zelrix™ data presented at AHS 2011 and Wedbush Securities

The 12-month safety and tolerability of Zelrix™ is consistent with successive uses of the patch. There was no cumulative skin irritation with continued patch use. Furthermore, the incidence of triptan-related AEs (i.e. atypical sensation and chest discomfort) was a low 1.6% of patients during the first month and 0% during months two through 12. 41% of patients experienced at least one treatment-emergent adverse event during month one of the study with the most commonly reported AEs being related to application site and were mild/moderate and transient. After month one, the incidence of adverse events was consistent and ranged from 11 – 19% for months two to six and from 8 – 15% for months seven to 12.

**Phase 1 Clinical Trials.** NuPathe has completed eight Phase 1 trials plus an additional skin irritation study of Zelrix™. In four of the Phase 1 trials, various Zelrix™ prototypes were tested in healthy volunteers to establish proof of concept. In the fifth Phase 1 trial, the pharmacokinetics (PK) of Zelrix™ was compared to oral sumatriptan in migraine patients. In the sixth clinical trial, the PK of Zelrix™ was compared to the three other routes of administration of sumatriptan (20mg nasal spray, 100 mg tablet, and 6 mg injection) in healthy volunteers. In the seventh Phase 1 trial, the PK of Zelrix™ was compared in the elderly and young adults and by site of administration (upper arm and thigh). The eighth Phase 1 trial was a confirmatory bioavailability and PK study.

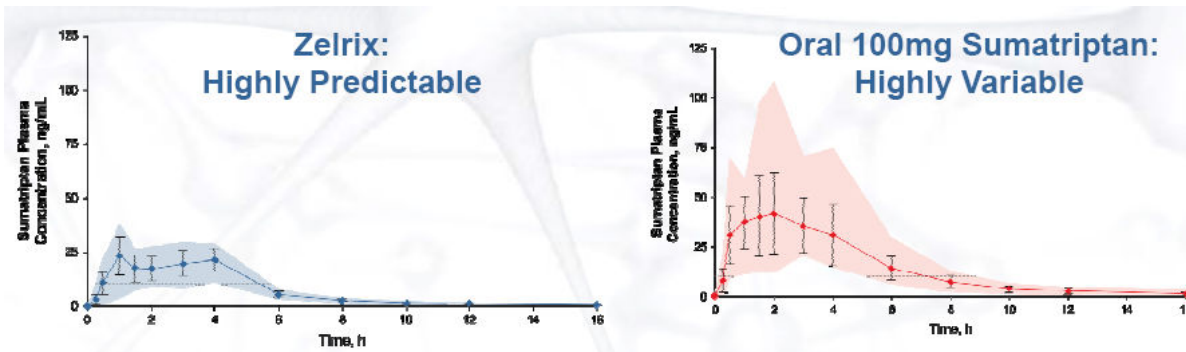
Figure 13: Pharmacokinetic Comparison by Routes of Administrations



Source: NuPathe, reprinted with permission

**Pharmacokinetics.** When compared to the three other routes of administration of sumatriptan—20mg nasal spray, 100 mg tablet, and 6 mg injection—Zelrix™ resulted in sumatriptan plasma levels between the 20 mg Imitrex nasal spray and the 100 mg Imitrex oral tablet. Furthermore, therapeutic plasma concentrations (10 ng/mL) were achieved within 30 minutes after Zelrix™ application and maintained for approximately five hours. Importantly, Zelrix™ resulted in less variability in sumatriptan plasma levels compared to both 20 mg Imitrex nasal spray and 100 mg Imitrex oral tablet potentially supporting the idea that transdermal administration provides more predictable delivery by bypassing absorption through the gastrointestinal system. Furthermore, the  $C_{max}$  of Zelrix™ is about one fourth that of the 6 mg injection and about half that of the 100 mg oral dose.

Figure 14: Zelrix™ Results in Consistent Release of Sumatriptan



Source: NuPathe, reprinted with permission

Figure 15: Pharmacokinetic Profile

Treatment Group	AUC <sub>0-inf</sub> (hr*ng/mL)	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hr)	T <sub>1/2</sub> (hr)
Zelrix (n=17)	113.5	24.8	1.7	2.9
SQ 6 mg (n=23)	113.6	82.2	0.3	2.2
Nasal 20 mg (n=23)	50.3	12.5	1.5	2.2
Oral 100 mg (n=23)	247.1	51.6	2.2	4.8

Source: Zelrix™ data presented at the 50<sup>th</sup> annual American Headache Society annual conference (AHS June 26-29, 2008 Boston) and Wedbush Securities

**Safety – Zelrix™ avoids C<sub>max</sub> related AEs.** A Phase 1 clinical trial showed that at the time of patch removal, more than 75% of Zelrix™ patients had no or minimal skin redness. Furthermore, within 48 hours after patch removal, all patients had no or minimal skin redness. The trial also showed that all triptan-related AEs occurred when sumatriptan plasma levels exceeded 50 ng/mL. As Figure 16 shows, no triptan related AEs were seen with Zelrix™ treatment given that plasma levels never went above 50 ng/mL while still maintaining therapeutic levels (10 ng/mL).

Figure 16: Summary of Triptan Adverse Events by Route of Administration

Adverse Events		Number of Subjects Reporting Event (%)			
Categorization	Preferred Term	Zelrix (n=17)	Nasal Spray (n=23)	Injection (n=23)	Oral (n=23)
Atypical Sensation					
	Any adverse events	-	-	14 (60.9%)	
	Burning sensation mucosal	-	-	3 (13.0%)	
	Ear discomfort	-	-	1 (4.3%)	
	Facial pain	-	-	1 (4.3%)	
	Feeling hot	-	-	2 (8.7%)	
	Flushing	-	-	6 (26.1%)	
	Head discomfort	-	-	1 (4.3%)	
	Hot flush	-	-	3 (13.0%)	
	Sensation of heaviness	-	-	1 (4.3%)	
	Sensation of pressure	-	-	1 (4.3%)	
Pain and Pressure Sensation					
	Any adverse events	-	-	2 (8.7%)	4 (17.4%)
	Neck pain	-	-	-	2 (8.7%)
	Sensation of heaviness	-	-	1 (4.3%)	1 (4.3%)
	Sensation of pressure	-	-	1 (4.3%)	1 (4.3%)

Source: NuPathe and Wedbush Securities

**Commercial Strategy.** NuPathe plans to launch Zelrix™ with approximately 100 sales reps to target neurologists and headache specialists (approximately 10,500 physicians) covering 30% (53 million migraine units) of the migraine opportunity. We believe the company is likely to partner in order to reach the primary care physicians as well as all physicians ex-US.

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**Preclinical Product: NP201****Indication: Parkinson's Disease****Annual Gross Peak Sales Potential: approximately \$387 million worldwide**

**Market Opportunity.** Parkinson's disease is a progressive, degenerative disorder of the central nervous system caused by the loss of neurons in the brain controlling movement. Early in the disease, symptoms are characterized by tremor, rigidity, slowness of movement, and impaired balance and coordination. Later in the disease, cognitive and behavioral symptoms may arise with dementia common in the advanced stages of the disease. The average age of onset is 60. There are approximately seven to 10 million Parkinson's patients worldwide with about one million in the U.S., according to the Parkinson's Disease Foundation.

**Summary.** NP201 is a long-acting formulation of ropinirole that NuPathe is developing using their LAD technology. Ropinirole is a generic, FDA approved dopamine agonist that is also known under the brand name Requip and is used for the treatment of Parkinson's disease and restless leg syndrome. NP201 is designed to continuously deliver ropinirole for up to two months. The company believes NP201 has the potential to increase efficacy while decreasing side effects of ropinirole based on a preclinical study in a validated animal model. NuPathe expects to file an IND for NP201 with a partner.

**Unmet Need.** There are currently no cures for Parkinson's disease. Symptomatic treatments include dopamine agonists, like ropinirole, and dopamine replacement therapy through levodopa. However, these oral treatments have their limitations, including variable drug levels due to intermittent dosing (1-3 times daily). Published literature suggests that variable drug levels may hasten disease progression due to deterioration of the remaining dopamine receptors. Furthermore, intermittent dosing may result in more frequent and serious AEs. When polled during the recent 15<sup>th</sup> International Congress of Parkinson's Disease and Movement Disorders (ICPDMD June 5-9, 2011 Toronto, Canada), Parkinson's specialists indicated that a once-daily treatment that maintained blood levels in the therapeutic range was at the top on their wish list for new treatments.

**NP201 Advantages.** NP201 could potentially be a superior treatment option to oral therapy due to its continuous delivery of ropinirole for up to two months. Published literature suggests that continuous delivery may circumvent abnormal movements caused by over medication.

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**Preclinical Product: NP202****Indication: Schizophrenia, Bipolar Disorder, Atypical Antipsychotic****Annual Gross Peak Sales Potential: almost \$500 million worldwide each for schizophrenia and bipolar disorder**

**Market Opportunity.** Schizophrenia is a mental disorder characterized by losing touch with reality and interferes with one's ability to think clearly, manage emotions, make decisions and have social interactions. Onset typically occurs in young adulthood. Schizophrenia is estimated to affect over two million people in the U.S., according to the National Alliance on Mental Illness.

Bipolar disorder, or manic depression, is a mental disorder that causes extreme shifts in mood, energy, and functioning. Onset typically occurs in late adolescence or young adulthood. Bipolar disorder is estimated to affect over ten million people in the U.S., according to the National Alliance on Mental Illness.

**Summary.** NP202 is a long-acting formulation of an FDA-approved antipsychotic using LAD technology. NP202 is being designed to continuously deliver an antipsychotic medication for up to three months with a single dose. The company expects to file an IND for NP202 with a partner.

**Unmet Need.** A major problem with the treatment of schizophrenia is patient compliance. According to The Clinical Antipsychotic Trials in Intervention Effectiveness (CATIE) study, 74% of schizophrenia patients become non-compliant with their medication within 18 months of initiating therapy. Furthermore, noncompliant patients are more than twice as likely to relapse as compared to compliant patients. In order to improve patient compliance, physicians use depot injections of medications such as Risperdal Consta, Invega Sustenna, and Zyprexa Relprevv. However, these depot injections only provide therapy for two to four weeks per dose.

**NP202 Advantages.** The company believes that NP202 could potentially be a significant improvement over current treatment options due to its continuous delivery of medication for up to three months. Furthermore, NP202 is being designed to allow physicians to remove the implant at any time providing a way to stop therapy. With depot injections, it is not possible to stop therapy which discourages use by some physicians and patients due to concerns about AEs. The company hopes to develop the product as a pre-loaded injectable implant that can be stored at room temperature.

## **Summary**

NuPathe is developing novel delivery methods including their proprietary SmartRelief and long-acting delivery (LAD) platforms using approved active pharmaceutical ingredients (APIs) as treatments for large unmet medical needs in acute migraine, Parkinson's disease, schizophrenia, bipolar disorder, and related central nervous system (CNS) conditions. We believe NuPathe's novel drug delivery systems are likely to improve patient compliance as its product candidates reduce the reasons patients have for missing a dose. In addition to Zelrix™—the marriage of SmartRelief patch delivery with sumatriptan treatment of acute migraine—the company is applying long-acting delivery (LAD) technology to treatments for Parkinson's disease, schizophrenia, and bipolar disorder. Patients having these conditions frequently miss a treatment when multiple daily doses are required. Physicians believe physical deterioration may accelerate from uneven control and prefer once daily dosing. We believe the FDA PDUFA deadline for Zelrix™ on August 29, 2011 is likely to materially impact PATH's valuation. We estimate a 75% probability of first-pass approval with about 20% upside to a potential doubling versus 20-40% downside risk if approval is delayed.

### **Covered public companies mentioned in this report:**

<b>Company</b>	<b>Ticker</b>	<b>Price (intraday 7/25/11)</b>	<b>Rating</b>	<b>Fair Value</b>
Map Pharmaceuticals	MAPP	\$16.30	O	\$25

### Analyst Certification

I, Liana Moussatos, Ph.D., Richard Lau, certify that the views expressed in this report accurately reflect my personal opinion and that I have not and will not, directly or indirectly, receive compensation or other payments in connection with my specific recommendations or views contained in this report.

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### Wedbush Equity Research Disclosures as of July 25, 2011

Company	Disclosure
NuPathe	1
MAP Pharmaceuticals	1,3,4,5,7

### Research Disclosure Legend

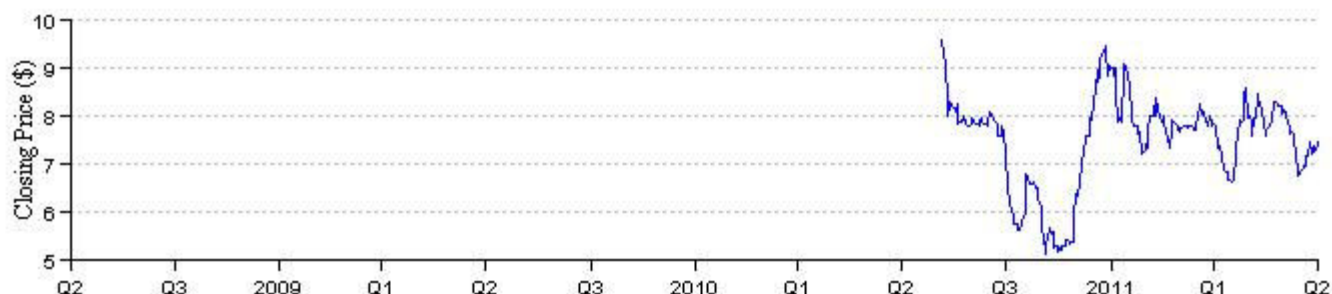
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# PATH



# MAPP

1) 03/03/09	2) 05/26/09	3) 07/14/09	4) 08/05/09	5) 09/14/09	6) 01/11/10	7) 03/02/10	8) 09/29/10
Buy \$12	Buy \$15	Outperform \$15	Outperform \$16	Outperform \$17	Outperform \$21	Outperform \$22	Outperform \$23
9) 11/05/10	10) 12/10/10	11) 12/15/10	12) 03/01/11	13) 05/03/11	14) 06/13/11		
Outperform \$24	Neutral \$24	Outperform \$24	Outperform \$26	Outperform \$24	Outperform \$25		



\* WS changed its rating system from (Strong Buy/Buy/Hold/Sell) to (Outperform/ Neutral/Underperform) on July 14, 2009. Please access the attached hyperlink for WS' Coverage Universe: <http://www.wedbush.com/services/cmg/equities-division/research/equity-research> Applicable disclosure information is also available upon request by contacting Ellen Kang in the Research Department at (213) 688-4529, by email to [ellen.kang@wedbush.com](mailto:ellen.kang@wedbush.com), or the Business Conduct Department at (213) 688-8090. You may also submit a written request to the following: Business Conduct Department, 1000 Wilshire Blvd., Los Angeles, CA 90017.

## OTHER DISCLOSURES

**RESEARCH DEPT. \* (213) 688-4505 \* [www.wedbush.com](http://www.wedbush.com)**

**EQUITY TRADING** Los Angeles (213) 688-4470 / (800) 421-0178 \* **EQUITY SALES** Los Angeles (800) 444-8076

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# WEDBUSH

EQUITY RESEARCH DEPARTMENT  
(213) 688-4529

DIRECTOR OF RESEARCH  
Mark D. Benson (213) 688-4435

## RETAIL AND CONSUMER

### Consumer Products

Rommel T. Dionisio (212) 938-9934  
Kurt M. Frederick, CFA CPA (213) 688-4459

### Entertainment: Toys

Edward Woo, CFA (213) 688-4382

### Healthy Lifestyles

Kurt M. Frederick, CFA CPA (213) 688-4459

### Specialty Retail: Hardlines

Joan L. Storms, CFA (213) 688-4537  
John Garrett (213) 688-4523

### Specialty Retail: Softlines

Betty Chen (415) 273-7328

## RETAIL/CONSUMER MARKET RESEARCH

Gabriella Santaniello (213) 688-4557

## CLEAN TECHNOLOGY AND INDUSTRIAL GROWTH

### Aerospace and Defense

Kenneth Herbert (415) 274-6875  
Andrew Doupé (415) 274-6876

### Clean Technology

Craig Irwin (212) 938-9926  
David Giesecke (212) 938-9925

### Environmental Services

Al Kaschalk (213) 688-4539  
Kevin Lee (213) 688-4303

### Industrial Biotechnology

Liana Moussatos, Ph.D. (415) 263-6626  
Christopher N. Marai, Ph.D. (415) 274-6861

### Water and Renewable Energy Solutions

David Rose, CFA (213) 688-4319

## TECHNOLOGY, MEDIA AND TELECOM

### Communications Equipment

Rohit Chopra (212) 668-9871  
Sanjit Singh (212) 938-9922

### Entertainment: Retail

Michael Pachter (213) 688-4474  
Nick McKay (213) 688-4343  
Alicia Jenks (212) 938-9927

### Entertainment: Software

Michael Pachter (213) 688-4474  
Edward Woo, CFA (213) 688-4382  
Nick McKay (213) 688-4343

### Computer Services: Financial Technology

Gil B. Luria (213) 688-4501  
Nick Setyan (213) 688-4519  
Roham Medifar, CFA (213) 688-4429

### Internet and E-Commerce

Edward Woo, CFA (213) 688-4382

### Media

James Dix, CFA (213) 688-4315

### Movies and Entertainment

Michael Pachter (213) 688-4474  
Nick McKay (213) 688-4343  
Alicia Jenks (212) 938-9927

### Semiconductors

Betsy Van Hees (415) 274-6869  
Ryan Jue (415) 263-6669

### Telecommunications Infrastructure

Suhail Chandy (213) 688-4380  
Scott P. Sutherland, CFA (213) 688-4522

### Telecommunications Software

Scott P. Sutherland, CFA (213) 688-4522  
Suhail Chandy (213) 688-4380

### Wireless Equipment

Scott P. Sutherland, CFA (213) 688-4522  
Suhail Chandy (213) 688-4380

## LIFE SCIENCES

### Biotechnology/Biopharmaceuticals/BioDefense

Gregory R. Wade, Ph.D. (415) 274-6863  
David M. Nierengarten, Ph.D. (415) 274-6862  
Christopher N. Marai, Ph.D. (415) 274-6861

### Cardiac, Hepatic and Regenerative

Duane Nash, MD JD MBA (415) 263-6650  
Akiva Felt (415) 263-6648

### Emerging Pharmaceuticals

Liana Moussatos, Ph.D. (415) 263-6626  
Richard Lau (415) 274-6851  
Christopher N. Marai, Ph.D. (415) 274-6861

### Healthcare Services - Managed Care

Sarah James (213) 688-4503  
Daniel Patt (212) 938-9937

### Medical Diagnostics and Life Sciences Tools

Zarak Khurshid (415) 274-6823

## EQUITY SALES

Los Angeles (213) 688-4470 / (800) 444-8076  
San Francisco (415) 274-6800  
New York (212) 938-9931  
Boston (617) 832-3700

## EQUITY TRADING

Los Angeles (213) 688-4470 / (800) 421-0178  
San Francisco (415) 274-6811  
New York (212) 344-2382  
Boston (617) 832-3700

## CORPORATE HEADQUARTERS

1000 Wilshire Blvd., Los Angeles, CA 90017-2465  
Tel: (213) 688-8000 www.wedbush.com