

## Highlights

### Lead product entering Phase III for treatment of acute migraine

NuPathe's lead product, NP101, is entering the pivotal Phase III trial for the treatment of acute migraine. Results are expected 1Q09. Based on a proprietary transdermal formulation of sumatriptan, NP101 will be following a 505(b)2 regulatory pathway. NDA filing is expected in 3Q09 with approval occurring in 2010.

### Significant market opportunity identified for NP101

NP101 is the first and only transdermal treatment for acute migraine. It should provide patients unprecedented control over the migraine – eliminating issues associated with nausea, improving consistency, and reducing treatment-limiting side effects.

*According to market research, NP101 could capture more than 30% of the current \$2.3B US migraine market.*

### Opportunity to commercialize NP101 through specialty sales strategy while leveraging PCP market with partners

Over 25% of triptans, the leading class of acute migraine therapies, are prescribed by neurologists and headache specialists (\$575M), making it a viable segment for a specialty sales strategy. Moreover, promotional intensity in the migraine market has dropped precipitously in the last several years, creating an environment where promotion can be cost effective and efficient.

PCPs account for nearly 60% of migraine scripts or \$1.4B in sales. NuPathe projects that the PCP component of NP101 could generate over \$350M in annual sales, making it an attractive licensing or co-promotional opportunity for a variety of pharmaceutical companies.

### Management team experienced in specialty pharmaceutical development and commercialization

The NuPathe team was previously successful in building Auxilium Pharmaceuticals and IBAH Clinical Research. The team also has direct experience in marketing migraine and transdermal products.

## Management Team

### Mike Cola – Chairman

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### Jane Hollingsworth – CEO

Auxilium, IBAH

### Terri Sebree – President

Auxilium, IBAH, Abbott

### Mark Pierce, MD, PhD – CSO

Pfizer, Warner Lambert, Abbott

### Joel Sussman – CFO

Adolor, BioRexis, TetraLogic, CardioKine

### Jerry McLaughlin – VP, Com. Ops.

Endo, Merck

### Ezra Felker, MBA – VP, Bus. Dev.

BioAdvance, BTG, Icagen, Biosite

## 2008/9 Goals

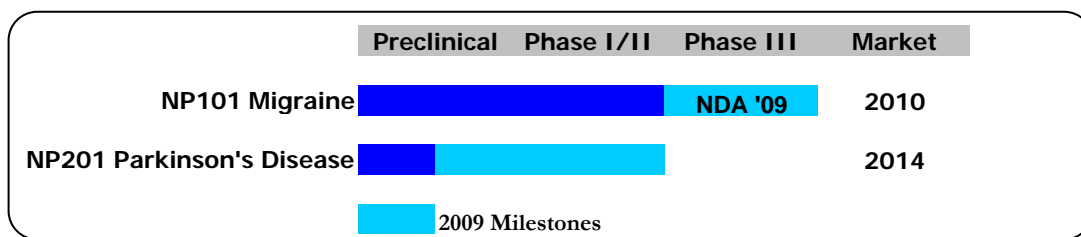
- Complete clinical development and file NDA for NP101
- Complete in vivo POC of NP201 and initiate human studies
- Finalize NP101 commercial strategy and establish marketing partnerships

Highlights	<b>Executive Summary</b>	NP101 Acute Migraine	NP201 Parkinson's disease
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## EXECUTIVE SUMMARY

NuPathe Inc. is a specialty pharmaceutical company developing innovative therapeutic products for the treatment of neurological and psychiatric diseases. NuPathe's mission is to identify and address the needs of patients, their families, and health care professionals that are insufficiently met by current treatments. The NuPathe team has a proven track record developing and commercializing specialty pharmaceutical products.

NuPathe's current portfolio consists of two products, the first and only transdermal patch for the treatment of acute migraine, a \$4B market, and a long-acting formulation of a dopamine agonist for the underserved Parkinson's disease and restless leg markets. The Company's products are based on reformulations of approved pharmaceuticals using NuPathe's proprietary delivery technologies, SmartRelief™ and LAD™. Combining these technologies with known molecules can provide significant clinical advantages over existing therapeutic options.



NuPathe's products are being developed under the accelerated 505(b)2 regulatory and clinical development pathway. The Company's most advanced product is NP101, a transdermal patch for the treatment of acute migraine. NuPathe expects NP101 to enter the market in 2010.

<b>NP101 Acute Migraine SmartRelief™</b>	<p>NP101 is the first and only transdermal treatment in clinical development for acute migraine. Today, only 50% of migraine patients are satisfied with their migraine treatment due to issues such as migraine-associated nausea/vomiting, inconsistent relief, and side-effects. NP101 was designed to address these issues, providing patients with superior control over their migraine as compared to currently available oral and non-oral options.</p> <p>NP101 is based on NuPathe proprietary SmartRelief™ technology, a breakthrough in iontophoretic patch technology that utilizes low-level electrical energy to transport drugs through the skin in a safe and effective manner.</p>
<b>NP201 Parkinson's disease LAD™</b>	<p>NP201 is a significant advance in the long-term management of Parkinson's disease. By providing 2-3 months of stable drug levels with each administration, NP101 may significantly improve the efficacy, tolerability, and convenience associated with daily dosing regimens.</p> <p>NP201 is based on NuPathe's proprietary LAD™ (long acting delivery) technology, which enables drugs to be delivered with unparalleled control, consistency, and convenience for 1-12 months via a single biodegradable dose.</p>

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## THERAPEUTIC OPPORTUNITY – NEURO-PSYCHIATRIC DISEASE

The worldwide market for products treating neuro-psychiatric diseases is over \$35B, not-including protein based therapeutics. However, despite numerous innovative treatments, neuro-psychiatric diseases are still poorly treated.



Treatment is often limited by poor patient compliance and suboptimal ADME/PK, leading to incomplete symptom control and adverse effects. Clinicians and patients recognize these issues and are anxious for improvements.

NuPathe's strategy is to identify areas of particular medical need and determine the key deficits with existing products. Specifically targeting these deficits, NuPathe identifies, acquires, and develops novel formulations of existing products utilizing emerging technologies.

NuPathe separates itself from many other companies in that it does not identify a product and then search for a need. NuPathe only acquires and develops formulations that provide clear and significant clinical benefits that can be recognized by clinicians, patients, and payers.

## NUPATHE DELIVERY PLATFORMS

NuPathe is developing products based on two proprietary delivery platforms. Each platform provides unique technical features that, when combined with the appropriate drug, translates into significant clinical and commercial advantages.

### **SMARTRELIEF™ - ELECTRONICALLY ASSISTED DRUG DELIVERY (IONTOPHORESIS)**

Iontophoresis is a non-invasive technology that utilizes low-level electrical energy to transport drugs through the skin. The rate and amount of drug delivered is controlled electronically, so that the patient receives consistent therapy each and every time.

**SmartRelief™ represents a breakthrough in iontophoretic patch technology - a thin, self-contained, disposable patch.**

Up until now iontophoresis was limited to office-based or chronic applications where cumbersome and costly electronics were acceptable. SmartRelief™ is the next generation of iontophoresis – easy and cost-effective. Each SmartRelief™ patch is self-contained, pre-programmed, and disposable.

SmartRelief™ is an ideal option for transdermal delivery where speed and/or control are required or for molecules that are not delivered effectively through passive means.

## **LAD™ LONG-ACTING DELIVERY TECHNOLOGY**

Effective long-term therapy of neuropsychiatric conditions requires constant, stable drug levels over prolonged periods of time. Unfortunately, patient compliance and drug pharmacokinetics present significant obstacles to consistent therapy. NuPathe is addressing these issues through its proprietary LAD™ long acting delivery technology. LAD™ enables drugs to be delivered with unparalleled control, consistency and convenience for 1-12 months from a single dose.

- ▶ **Superior Compliance**
- ▶ **Improved Efficacy**
- ▶ **Better AE Profile**

- ▶ **1-3 month drug delivery**
- ▶ **Biodegradable**
- ▶ **Stable release profile - no burst/dose-dumping**
- ▶ **Administered via injection**

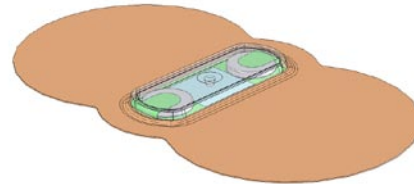
LAD™ is comprised of a biodegradable polymer matrix, formed into a small rod that is administered via injection, just below the skin. It slowly releases drug to the patient and degrades over a defined period of time, eliminating the need for removal. After a defined period, the patient receives an additional dose if continued treatment is desired. If necessary, the product can be removed prior to complete degradation.

LAD™ has been formulated with several neuropsychiatric compounds and tested in multiple animal models. Results indicate that LAD™ provides a safe, convenient, and consistent option for drug delivery.

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## NP101 – MIGRAINE SMARTRELIEF™: MIGRAINE HAS MET IT'S PATCH

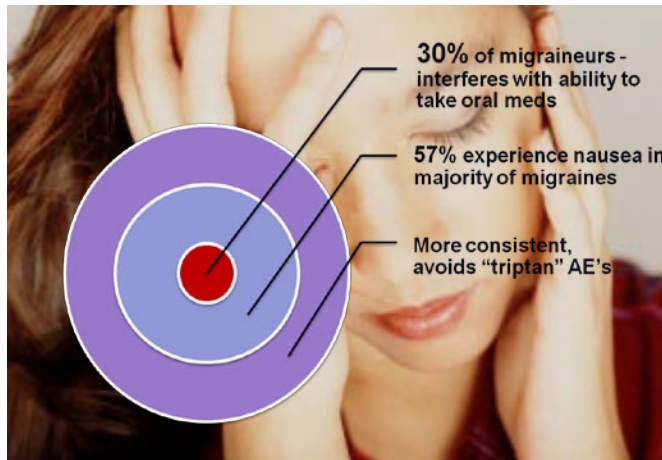
Migraine headache impacts approximately 28 million adult Americans, primarily women. This painful and often disabling disorder costs the US economy over \$13B in lost work and productivity. Acute migraine therapy consists primarily of triptans, the treatment standard since the 1992 introduction of sumatriptan (Imitrex™). As a class, triptans generate over \$2.3B in US annual sales. Despite the additional entrants, sumatriptan remains the gold standard within the class, garnering approximately 50% of the market.



**Rapid  
Consistent  
Tolerable**

NP101 is a novel transdermal formulation of sumatriptan, based on NuPathe's proprietary SmartRelief™ technology. NP101 is a thin, disposable, single use patch for the treatment of acute migraine. NP101 was designed to address the most common complaints of patients – nausea, inconsistent relief, and adverse events. Through precise control of dosing and by-passing the GI tract, NP101 may be able to provide a clinically superior solution to current medications.

### CLINICAL NEED



Over 90% of migraine patients experience nausea and/or vomiting. For approximately 30% of migraineurs, nausea interferes with their ability to take oral medication.

Migraine-associated nausea and gastric symptoms have been linked to poor drug absorption, resulting in delayed or inconsistent relief (eg sometimes drug works, sometimes it doesn't). Physicians report that inconsistent relief, the most common complaint of patients, occurs in as many as half of patients. Other patients complain that their medication produces too many side-effects and are unable to continue use.

These issues have real clinical impact. Patients delay treatment until nausea subsides, employ coping techniques, wait until the migraine becomes severe before taking medication, or don't treat their migraine at all. The end result is the same. Too often, patients are poorly or not treated, absent from work and unable to continue a normal life.

**SmartRelief™ represents an empowering alternative for migraine patients – convenient, consistent, and controlled delivery of their migraine medication regardless of nausea, vomiting, or other gastric symptoms common with migraine.**

## COMMERCIAL OPPORTUNITY

For years the migraine market has been plagued by minimal innovation and inattention to clinically meaningful patient and physician needs. Newly introduced products provided little, if any, differentiation from their predecessors. As such, marketers attempted to inundate the market with promotion in order to gain share. Ultimately, the new products largely disappointed patients, physicians, and marketers as they failed to better address patient needs.

Today, the dynamics of the migraine market are shifting. Promotional intensity has dropped significantly as attempts to create differentiation have been unsuccessful. Consumers, who were once happy with any improvement in their condition, are now looking for better solutions. Approximately half of all migraine patients are dissatisfied with their current treatment. Most indicate a strong readiness to move to a new option.

Unfortunately, there are not any options currently available that address patient's primary concerns. The migraine market is primed for a new approach that can circumvent migraine-associated nausea, mitigate typical triptan adverse events, and improve consistency of response. NP101 was identified and is being developed to address these issues.

**NP101 has the potential to become a new standard in the treatment of acute migraine and provides a unique commercialization opportunity:**

- **Readily identifiable and motivated patient population**
- **Highly differentiated product designed to address key patient needs**
- **Competitive dynamics and value proposition support attractive pricing**
- **Promotional efficiency due to reduction in competitive efforts**

With innovation becoming an increasingly rare commodity in the pharmaceutical industry, new technologies that bring a measurable and meaningful improvement to patient care possess a high degree of commercial attractiveness. NP101 offers the promise of moving the triptan market beyond the era of "me-too" offerings.

## DEVELOPMENT STATUS

NP101 is being developed under the 505(b)2 regulatory pathway. Supporting pharmacokinetic and preclinical studies have been completed. The pivotal Phase III trial has been initiated and will be complete 1Q09.

In a comparative Phase I trial vs. oral, nasal, and injectable formulations of sumatriptan, NP101 demonstrated:

- Rapid achievement of therapeutic drug levels
- More consistent pharmacokinetics
- Superior adverse event profile

Phase III – On-Going  
NDA File – 3Q09  
Product Approval – 2010

## NP201 – PARKINSON'S DISEASE LAD™

Parkinson's disease affects over 600,000 people in the United States alone. The disease is characterized by movement disorders caused by the loss of dopaminergic control. Parkinson's disease is treated by replacing lost dopamine with an exogenous source, such as levodopa/carbidopa and dopamine agonists. Dopamine agonists currently account for approximately \$1B in US sales.

The treatment of Parkinson's disease is very sensitive to drug levels - low levels of dopamine result in Parkinsonian symptoms, while high levels produce motor response complications or, in extreme cases, psychosis. Many experts also believe that inconsistent (eg pulsatile) stimulation of the dopamine receptor may hasten disease progression.

In order to address these issues, NuPathe has developed a two month formulation of an approved dopamine agonist. NP201 represents a major step forward in the management of Parkinson's disease. Administered subcutaneously, NP201 provides consistent and sustained dopamine levels, effectively controlling the disease while limiting the high and low dose effects associated with other similar treatments.

NP201 is a completely unique delivery approach to the treatment of Parkinson's disease and carries great promise as a convenient, effective treatment that reduces the dose requirements and side effects of current treatments. By maintaining the dose in a consistent therapeutic range, experts in the field believe that NP201 has the potential to slow neuronal deterioration and disease progression.

Animal proof-of-concept studies are scheduled to be completed in 2008. Clinical studies will follow.