

Adolor Corporation
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adolor

a·do·lor(ā·dō·lōr) without pain

2 0 0 0 A n n u a l R e p o r t





Adolor's Commercial Opportunities

ADOLOR CORPORATION is a publicly held research-based analgesia product company in Exton, PA, committed to the development of novel analgesics and pain-related therapeutics based upon recent advances in proprietary medicinal chemistry and recombinant opioid receptor technology. Adolor is developing next generation centrally and peripherally acting non-addictive analgesics for the treatment of hyperalgesia (inflammatory pain), pruritis (itch), mild-to-moderate pain, and moderate-to-severe pain. The company is also

Adolor Corporation

developing products that are designed to greatly diminish most of the prevalent and dose-limiting side effects of current opioid narcotic therapy. Adolor is unique in combining near-term clinical opportunities with a longer-term approach to developing novel opioid analgesics based upon a new molecular understanding of opioid receptor function.

Redefining Pain Management Therapy

- ADL 8-2698 in late-stage clinical trials for:
 - Post-operative ileus (in Phase 3)
 - Opioid bowel dysfunction
(Initiation of Phase 3 expected 2001)
- Commercial opportunities in five market segments of more than \$1 billion each
- Extensive pain management product pipeline
- Multiple product candidates with demonstrated beneficial clinical results and safety
- Established partnerships:
 - GlaxoSmithKline
 - Santen Pharmaceutical Co.
- First in class, patent-protected products

Over 100 million patients experience acute or chronic pain annually in the United States. Because pain impairs one's ability to carry out a productive life, acute and chronic pain are serious health and economic issues. Adolor re-defines this large market opportunity by using its patented receptor technology and chemistry to develop product candidates that are designed to reach five distinctly different but related markets. The first opportunity described in the chart is Adolor's promising *first in class* product candidate that will treat the inevitable gastrointestinal complications that occur as the result of abdominal and other surgical procedures. The second opportunity described addresses the side effects of the opioid analgesics currently being prescribed for acute and chronic pain. The third, fourth and fifth opportunities reflected in the chart describe existing pain management markets into which our peripheral opioid analgesic product candidates are expected to provide significant advances over currently marketed products.

Five Market Opportunities Greater than \$1 Billion

Indication	U.S. Market/Year
Post-Operative Ileus	> 5 Million patients with "at risk" surgeries*
Opioid Bowel Dysfunction	> 125 Million narcotic prescriptions**
Dermal Pain & Itch	> \$1.2 Billion**
Moderate-to-Severe Pain	> \$3.5 Billion**
Mild-to-Moderate Pain	> \$4.6 Billion**

*Company estimate. **IMS Health, 12 months ending 8/00

Product Pipeline

Product	Research	Preclinical	Phase 1	Phase 2	Phase 3
ADL 8-2698					
Post Operative Ileus	•	•	•	•	•
Opioid Bowel Dysfunction	•	•	•	•	•
Opioid/2698 Combo Analgesic	•	•	•	•	•
ADL 2-1294					
Ophthalmic Pain	•	•	•	•	•
Dermal Itch	•	•	•	•	•
Dermal Pain	•	•	•	•	•
Joint Pain	•	•	•	•	•
ADL 10-0101					
Visceral Pain	•	•	•	•	•
Dermal Itch	•	•	•	•	•
Ophthalmic Itch	•	•	•	•	•
ADL 10-0116					
Visceral pain and Itch	•	•	•	•	•
ADL 1-0398					
Visceral Pain and Itch	•	•	•	•	•



The Year 2000

Adolor: a unique company dedicated to pain management

It is a pleasure to be writing this first letter to our stockholders as a public company. Since Adolor's founding in 1994, we have focused on becoming a research-based product development company specializing in pain management. We have succeeded in our endeavor by creating a broad pipeline of first-in-class product candidates that address significant clinical issues in pain management, specifically the severe side effects commonly associated with currently marketed opioid narcotics and the need for better analgesics with fewer side-effects. At the same time, we have begun to build a first class commercial organization

Dear Stockholders

with a highly flexible commercial strategy to successfully market our first products.

For everyone at Adolor, the year 2000 was filled with tremendous growth and change as we evolved from a discovery/early development company to a late stage development company. We reported highly positive clinical results with our lead product candidate in two separate indications, and moved it into Phase 3. We made solid advances with several other products in our pipeline, and added significantly to our capabilities in the drug development, regulatory affairs and marketing areas, capabilities critical to our success as we continue our progress towards full commercialization. Finally, in November Adolor became a public company with an initial public offering of 6.9 million shares, giving us a solid financial footing as we move forward with our long-term plans.

Pain Management – the Adolor Solution

Pain management remains one of the most difficult challenges facing the medical community today. Due to the troubling side effects of currently marketed opioid narcotics, patients are frequently undertreated for pain or may receive inappropriate therapy. As these issues gain prominence, pain management becomes a high priority for both patients and physicians.

While all currently marketed opioid narcotic analgesics work by stimulating pain relief receptors in the brain and spinal cord (central nervous system), they also frequently produce severe central nervous system and gastrointestinal tract side effects. By concentrating on the design and development of compounds that target opioid receptors outside of the central nervous system, Adolor has developed two new, related classes of pain management product candidates: analgesics that stimulate the opioid pain relief receptors at the site of injury or disease without any central nervous system side effects, and blockers of the severe gastrointestinal side effects associated with currently marketed opioid narcotics.

A Focused Commercial Strategy

We believe there is a large and growing opportunity for more effective pain management products with fewer side effects. In the United States alone, millions of people suffer function loss due to chronic pain at a huge cost annually in medical fees, lost productivity, litigation and treatment. With year 2000 prescription sales over \$11 billion, an increase of 28 percent over 1999, the market for pain management products is exploding.

Product Development

ADL 8-2698

- Completed successful Phase 2 Post-Operative Ileus trial
- Completed four successful Phase 2 Opioid Bowel Dysfunction trials
- Confirmed anti-nausea/ vomiting clinical effect; paves way for combination product candidate and additional post-operative claims
- Initiated Phase 2/3 trial for Post-Operative Ileus
- Had three successful meetings with FDA delineating development path
- Signed contract for commercial supply of drug

ADL 10-0101

- Completed Phase 1 safety trial in normal volunteers
- Initiated Phase 1 and Phase 2 trials for preliminary efficacy in pain and itch

ADL 10-0116

- Initiated preclinical development of oral product candidate for pain and itch

Partnering

- Signed ADL 2-1294 ophthalmic pain license with Santen Pharmaceuticals

Financial

- Raised \$49.0 million in two up rounds of private financing
- Raised \$103.6 million in a successful Initial Public Offering

Other

- Hired key personnel in clinical development, research, regulatory and commercial functions

We expect to concentrate our initial marketing efforts on a number of key segments, specifically surgeons, major hospitals, and those physicians who are high opioid narcotic analgesic prescribers – markets best served by a focused sales force. The success of our recent IPO gives us the financial strength to retain valuable market rights to our product candidates and the organizational flexibility to move quickly to develop and deliver those products to the patients that need them. As we move closer to approval and launch, we plan to create our own internal marketing and sales teams to exploit the full potential of our portfolio.

The Year Ahead

In 2001, we expect to achieve a number of important new clinical milestones. We began, and plan to be near completion of all Phase 3 clinical studies with our lead product candidate, ADL 8-2698 for post-operative bowel paralysis (ileus), and plan to initiate the Phase 3 program for opioid bowel dysfunction. In light of ADL 8-2698's performance in previous trials, we are on target to file our first New Drug Application for the management of post-operative ileus in the second quarter of 2002 and a supplementary NDA for opioid bowel dysfunction in 2003.

We, or our partners, expect to begin and complete additional Phase 1 and Phase 2 trials with our peripheral opioid analgesics ADL 2-1294, ADL 10-0101 and ADL 10-0116. On the strategic front, we will continue to seek out new marketing and co-marketing opportunities that fit our commercial strategy for both classes of compounds.

Finally, we want to take this opportunity to recognize all those who contributed to our success last year. We could not have achieved as much as we did without the dedication and hard work of our employees and the strong support of our investors. As we move into our first full year as a public company, we look forward to advancing our groundbreaking work in pain management and to create even greater value for our stockholders.

John J. Farrar, Ph.D.
President, Chief Executive Officer and Director





Adolor's Dual Path to Pain Management

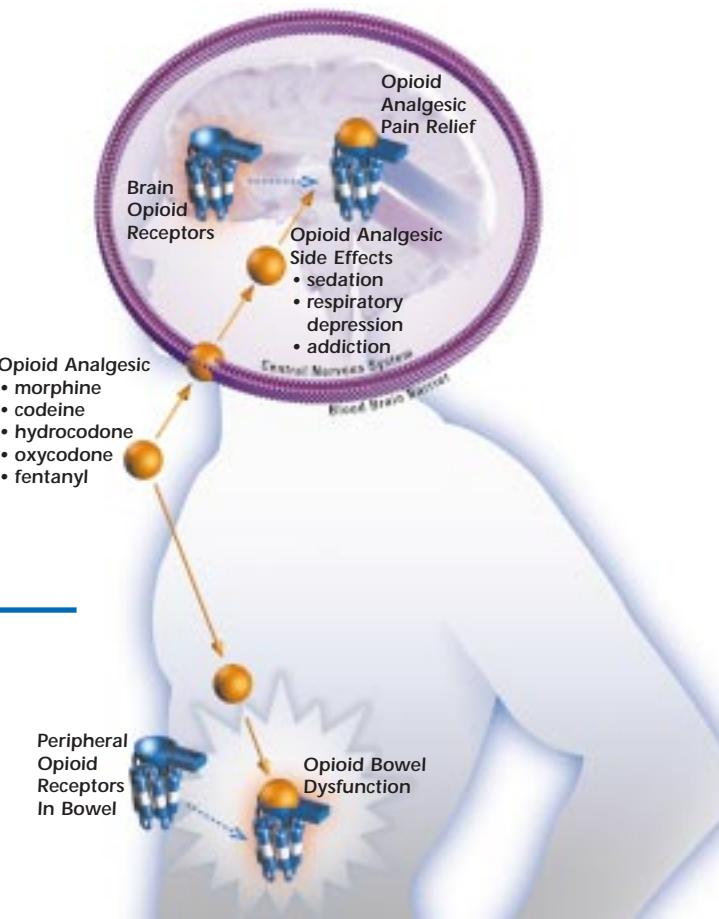
More than just an unpleasant sensation, the experience of pain is both a physical and psychological event. When tissues become inflamed or injured, pain receptors in those tissues send signals through nerve fibers into the spinal cord and from there to pain centers in the brain. Opioid narcotics like morphine bind to opioid receptors on the nerve surface and block transmission of those pain signals. Currently prescribed opioid narcotic analgesics work by stimulating pain relief receptors in the brain and spinal cord (the central nervous system) but they produce severe central nervous system side effects such as sedation, slowing of breathing and the potential for addiction. Additionally, when these same opioid receptors that are also located throughout the gastrointestinal tract are stimulated by opioid narcotics, side effects such as nausea, vomiting and constipation are produced.

By targeting our drugs to opioid receptors **outside** the central nervous system, Adolor has developed two different classes of pain management product candidates that 1) share

In Phase 2 trials, ADL 8-2698 not only shortened bowel recovery time for patients, but allowed them to leave the hospital nearly one and a half days sooner.

Typical opioid narcotic analgesic drugs target mu opioid receptors in the brain and in the periphery. Their desirable analgesic action is accompanied by adverse effects in the brain such as sedation and respiratory depression. In the periphery, opioid narcotic analgesics may produce abdominal pain, bloating, and opioid induced constipation which are symptoms of "Opioid Bowel Dysfunction" (OBD).

a common scientific approach 2) utilize common technology platforms and 3) most importantly, provide solutions to the basic side effect deficiencies of the currently marketed opioid narcotics. The first class of drugs effectively blocks the gastrointestinal side effects of opioid narcotics such as nausea, vomiting, constipation and the bowel paralysis that follows abdominal surgery. The second class of drugs are analgesics that stimulate peripheral pain relief receptors on the primary pain sensing nerves at the site of injury or disease. In essence, these drugs are designed to shut down the pain signal at its origin before it gets into the central nervous system to be recognized by the body as pain. The goal is powerful narcotic-like analgesic pain relief without the central nervous system side effects of drugs like morphine or codeine.



ADL 8-2698

Post Operative Ileus
Opioid Bowel Dysfunction
Opioid/2698 Combo Analgesic



Path 1: Blocking the Gastrointestinal Side-Effects of Opioid Narcotics

Gastrointestinal Tract – Restricted Opioid Narcotic Antagonists

ADL 8-2698 is an orally-administered drug that is not absorbed from the gastrointestinal tract. It is designed to work locally in the gastrointestinal tract to block the adverse effects of opioid narcotics on the intestine. Patients who would potentially benefit from ADL 8-2698 include approximately 3 million who take opioid narcotics for

ADL 8-2698

protracted periods of time for pain relief and approximately 5 million surgical patients who have post-operative bowel paralysis (ileus).

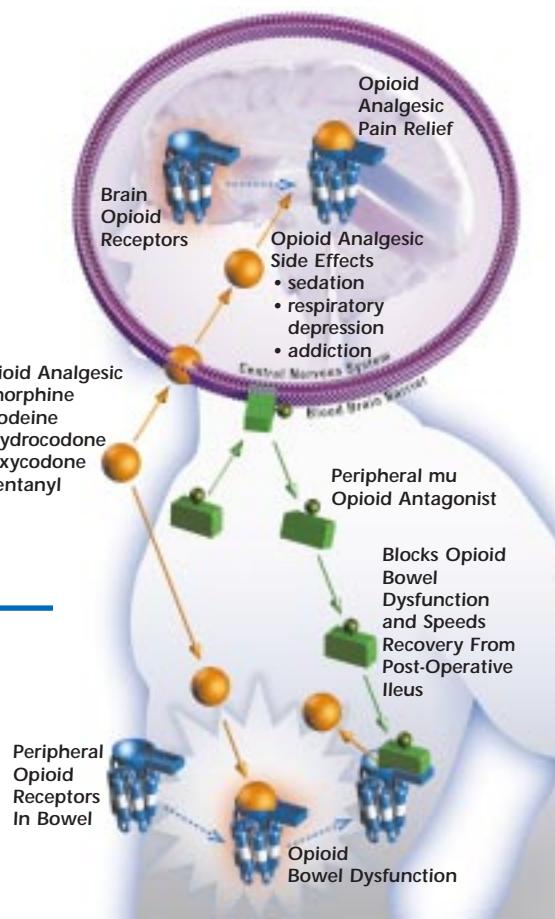
ADL 8-2698 has a number of important advantages:

- It is a small, easily synthesized molecule
- It is an orally administered capsule for better patient compliance
- It is not systemically absorbed, greatly reducing the chances of systemic side effects
- It is safe in animal toxicology studies at > 7,000x therapeutic dose.

ADL 8-2698 selectively targets mu opioid receptors in the GI tract and blocks symptoms of Opioid Bowel Dysfunction without blocking opioid narcotic analgesia in the brain. Adolor's Phase 2 clinical studies show that this action may be useful in restoring normal bowel function following surgery (post-operative ileus), in blocking post-operative nausea and vomiting and in protecting against opioid constipation in patients receiving chronic opioid narcotic analgesic therapy. ADL 8-2698 has not reversed the beneficial analgesic effects of morphine and other opioid narcotics in over 300 patients studied to date.

Opioid Bowel Dysfunction

Extreme constipation is a debilitating and treatment limiting side effect for patients treated with morphine and other opioid narcotics for protracted periods of time. To date, we have completed multiple Phase 1 and Phase 2 clinical trials with ADL 8-2698 in over 400 normal volunteers and patients. In four Phase 2 double-blind and placebo-controlled clinical trials, ADL 8-2698 reversed Opioid Bowel Dysfunction (OBD) in 80-100 percent of patients receiving narcotics for chronic pain. In addition, ADL 8-2698 did not block pain relief, did not cause narcotic withdrawal and was well tolerated at the therapeutic doses given. Phase 3 clinical trials for OBD are projected to begin in the 2nd quarter of 2001. In short, the trials have shown that the compound is safe and effective in OBD.





Post-Operative Ileus

Post-operative ileus is the delayed recovery of bowel function following surgery. It often causes extended hospital stays and adds significantly to the cost of treating surgical patients. It is estimated that there are more than five million patients per year with surgeries that result in ileus, increasing health care costs as much as \$10 billion annually. In a Phase 2 double-blind and placebo-controlled clinical trial, ADL 8-2698 shortened the time to recovery of bowel function for these patients by one to two days and allowed patient discharges from the hospital 1.4 days sooner. ADL 8-2698 also reduced post-operative nausea and vomiting by 50-100 percent. Adolor's first Phase 3 clinical

ADL 8-2698

trial with ADL 8-2698 for the reduction of post-operative ileus began in the first quarter of 2001.

ADL 8-2698/Opioid Narcotic Combination Product

Adolor is currently exploring the further use of ADL 8-2698 co-formulated in the same capsule with an opioid narcotic analgesic to create the "G.I. side-effect free opioid narcotic". An oral formulation of ADL 8-2698 combined with a narcotic analgesic in a single capsule may have the potential to capture a significant portion of the acute and chronic care oral opioid narcotic market with a product that gives effective pain relief for moderate-severe pain without causing nausea or constipation. Additional Phase 1 and 2 studies are planned for this candidate.

Path 2: Peripheral Opioid Analgesics

Adolor's analgesic product candidates target *mu* and *kappa* opioid receptors on the primary pain-sensing peripheral nerves at the site of injury or disease. In preclinical studies, several of our peripheral opioid analgesics have been shown to be as effective as narcotic analgesics in relieving the pain associated with inflammation. Because they block the pain signal directly at the site of inflammation with far fewer side effects than narcotics, peripheral opioid analgesics have the potential to revolutionize pain management, cut healthcare costs, and improve patient quality of life by reducing patient dependence on opioid narcotics. In addition, our scientists and collaborators have shown that peripheral opioid analgesics are effective in preclinical models of pruritis (itch).

Adolor is working to create topical, injectable and oral formulations of these peripheral analgesics that will specifically target conditions as varied as eczema, arthritis, post-surgical pain and visceral pain. In total, these are significant market opportunities.

Peripheral Mu Analgesics- Topical Product Candidates

Adolor's topical peripheral opioid analgesic product candidates target the *mu* opioid receptor and are based on ADL 2-1294 as the active ingredient. ADL 2-1294, like morphine, is a potent *mu* opioid agonist. Unlike morphine,

however, ADL 2-1294 is unable to cross the blood brain barrier and therefore exhibits no CNS side effects or potential for opioid addiction.

Dermal Applications In two clinical trials, Adolor demonstrated that ADL 2-1294 causes a statistically significant reduction in pain following experimental skin burns. The product candidate has been licensed to GlaxoSmithKline for further clinical development for dermal pain and itch. Recently, GlaxoSmithKline succeeded in developing an improved formulation for further Phase 2 trials and is expected to initiate a Phase 2 eczema itch trial in the 2nd quarter of 2001.

ADL 2-1294

Ophthalmic Applications In two Phase 2 clinical trials Adolor demonstrated that ADL 2-1294 provides pain relief following eye surgery or eye injury without any dose limiting side effects. We subsequently licensed the product

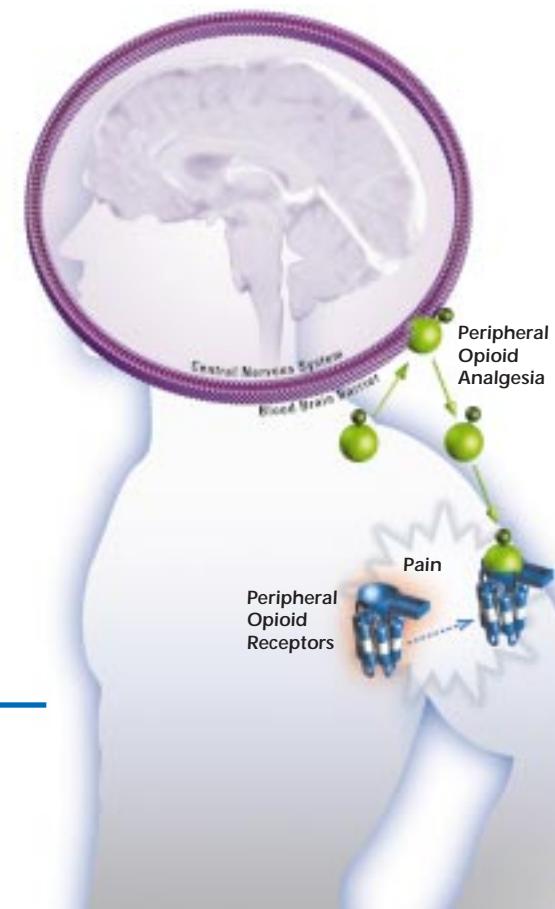
to Santen Pharmaceuticals for further development. We expect Santen to enter clinical trials with an improved formulation later in 2001.

Adolor has retained commercial rights to all other ADL 2-1294 based products including a long acting local analgesic to be used following arthroscopic or laparoscopic surgery.

Peripheral opioid analgesics are designed to reduce patient dependence on opioid narcotics.

Product	Research	Preclinical	Phase 1	Phase 2	Phase 3
ADL 2-1294					
Ophthalmic Pain	•	•	•	•	•
Dermal Itch	•	•	•	•	•
Dermal Pain	•	•	•	•	•
Joint Pain	•	•	•	•	•

Adolor's family of peripheral mu and kappa opioid analgesics are designed to provide strong analgesic activity under conditions of inflammatory or visceral pain, but not enter the brain so as to avoid many of the side effects typical of current opioid narcotic analgesic drugs.





Adolor Management Team



Peripheral Kappa Analgesics – Systemic Product Candidates

Adolor also has an extensive program in the discovery and development of analgesics based on the stimulation of peripheral *kappa* opioid pain relief receptors. Unlike the ADL 2-1294 topical products, for the most part, the peripheral *kappa* analgesics are designed to be administered systemically, either by injection or orally. Peripheral *kappa* based product candidates are designed to be as potent as opioid narcotics in the relief of pain yet without the adverse side effects of opioid narcotics. In addition to having activity in the inflammatory pain and itch preclinical models as described above, the peripheral *kappa* analgesics have also

ADL 10-0101, 10-0116, 1-0398

been shown to have the advantage of being active in at least two preclinical models of visceral pain. Visceral pain is the pain associated with the distension or inflammation of internal organs. Examples of clinical indications associated with visceral pain are irritable bowel syndrome pain, menstrual cramps, childbirth pain, and kidney and gall stone pain.

ADL 10-0101

ADL 10-0101, an injectable and potentially a topical product, is Adolor's first generation peripheral *kappa* analgesic product candidate. In 2000, a Phase 1 safety study was completed and two proof-of-concept efficacy trials were initiated; a Phase 2 trial in pancreatitis visceral pain and a Phase 1 trial in experimental poison ivy for the relief of itch. Preliminary data from the latter two clinical trials are encouraging and further Phase 2 efficacy trials are planned for 2001.

ADL 10-0116 and ADL 1-0398

ADL 10-0116 and ADL 1-0398 are Adolor's second generation proprietary peripheral *kappa* analgesics that have greater oral activity, longer duration of action and greater "peripheral restriction" in preclinical models than ADL 10-0101. With this pharmacological profile, these analgesics appear to be promising product candidates to address the chronic inflammatory and visceral pain as well as itch indications where an orally active compound will have a significant clinical and commercial advantage. These indications include arthritis, irritable bowel syndrome and eczema. In late 2000, Adolor selected ADL 10-0116 for further development and plans to file an IND for the compound in June of 2001 and enter the clinic as shortly thereafter as possible.

Product	Research	Preclinical	Phase 1	Phase 2	Phase 3
ADL 10-0101					
Visceral Pain	•	•	•	•	•
Dermal Itch	•	•	•	•	•
Ophthalmic Itch	•	•	•	•	•
ADL 10-0116					
Visceral pain and Itch	•	•	•	•	•
ADL 1-0398					
Visceral Pain and Itch	•	•	•	•	•

Stockholder Information

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Alan Maycock, Ph.D.

Vice President Discovery Research
Linda Harver, J.D.
Vice President Regulatory Affairs and Quality Assurance

Adolor's website includes summaries of the Company's technologies and product candidates. The site also contains press releases and current financial data.

Senior Management

John Farrar, Ph.D.
President and CEO
Andrew Reddick, MBA
Senior Vice President of Commercial Operations and COO
Peter Schied, MBA
Vice President and CFO
David Jackson, M.D.
Senior Vice President of Research and Development
Gwen Melincoff, MBA
Vice President Business Development
William Schmidt, Ph.D.
Vice President Technical Affairs
Deanne Garver, Ph.D.
Vice President Preclinical Development

Board of Directors

Frank Baldino, Jr., Ph.D.
John Farrar, Ph.D.
Ellen Feeney
Paul Goddard, Ph.D.
Robert Nelson
David Madden
Christopher Moller, Ph.D.
Claude Nash, Ph.D.

Common stock is traded on the Nasdaq National Market® under the symbol ADLR.

Annual Stockholders Meeting

The annual meeting of stockholders will be held at 10:00 A.M. on Tuesday, May 15, 2001 at the Wyndham Suites Valley Forge, Wayne, PA.

Registrar and Transfer Agent

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Ardmore, PA 19003

Auditors

KPMG LLP
Philadelphia, PA

Company Counsel

Dechert
Philadelphia, PA

Investor Relations

Updated information about Adolor Corporation is available by accessing the Company's home page located on the world wide web at <http://www.adolor.com>.

Form 10-K

A copy of Adolor's Annual Report on Form 10-K for the fiscal year ended December 31, 2000 is included with this Annual Report and is incorporated by reference herein.