strategicvision

Advanced Tissue Sciences, Inc.
2001 Annual Report

The mission of Advanced Tissue Sciences is to redefine tissue repair and transplantation with products developed and derived from our tissue-engineering technology. Our achievements will enhance the quality of human life and create an environment that fosters innovation and employee satisfaction while delivering sustainable value to our shareholders.

strategic purpose

Investment Highlights

- Highly versatile core technology backed by strong patent portfolio
- Three products generating revenue
- Pipeline of attractive medium- and long-term products
- Strong strategic alliances and partners
- Self-pay and reimbursement markets
- Spectrum of regulatory environments
- High-volume manufacturing capability

Dear Shareholders:

At the start of 2001, Advanced Tissue Sciences had only one product approved and on the market in the United States – **TransCyte**® for burns. Since then, **Dermagraft**® has been approved by the Food and Drug Administration (FDA) for the treatment of hard-to-heal diabetic foot ulcers and is now being sold in this country. In addition, two marketing partners have begun selling skin care products containing our **NouriCel**™ cosmetic ingredient. And we're making progress toward a fourth product on the market: our strategic partner, INAMED Corporation, is pursuing approval of the company's tissue-engineered, **human-based collagen** for wrinkle injections.

There were other major events during the year:

Dermagraft received a **reimbursement pass-through code** from the Centers for Medicare & Medicaid Services. We also began the pivotal clinical trial for Dermagraft in treating venous ulcers.

We signed a broad collaboration agreement with **Medtronic,** Inc. that included an investment by one of their subsidiaries of $20 million in our company. Michael D. Ellwein, Medtronic's vice president and chief development officer, also joined our board of directors.

We completed a **private placement** of stock that raised net proceeds of approximately $13.5 million.

In last year's annual report we outlined our revised **corporate strategy,** which can be boiled down to three key principles. The **first** is to focus development and manufacturing efforts on commercializing short- and medium-term, fibroblast-based products, since we have developed extensive internal expertise and know-how about dermal fibroblast cells.

The **second** is to market, distribute and sell products through strategic partners or directly where the opportunity is compelling.

Corporate Strategy

Leverage our technology and intellectual property

Invest in broad innovative research and development, internally and through collaborations, to drive our product pipeline to achieve our mission

Focus development and manufacturing efforts on commercializing off-the-shelf fibroblast-based products

Diversify the risks and the opportunities across a broad array of opportunities and products

Market, distribute and sell products through strategic partners or directly where the opportunity is compelling

Create new initiatives to unlock shareholder value

The **third** is to create new strategic alliances and initiatives to unlock longer-term product opportunities.

The events of the past year are indicators of how we have been **implementing that strategy** to build shareholder value.

Advanced Tissue Sciences is developing products for health care that enhance the field of **regenerative medicine.** While the technology is based on tissue engineering, the ultimate goal is to develop products that rejuvenate, repair, regenerate, or replace what the body cannot heal itself.

What we're doing is guided by a **strategic vision:** a product portfolio that addresses various medical needs and builds from our core technology. As illustrated on page three, generating multiple, off-the-shelf products from a core technology can have a significant benefit on product development costs and leads to a value creation model that is a **key differentiator** between Advanced Tissue Sciences and other biotechnology companies.

We and our investors are not staking everything on just one product or a single approach to the marketplace. Instead, we are working to apply our technology to **multiple applications with commercial potential** that meet a variety of needs.

An example of this is the way we are broadening the potential applications of Dermagraft from foot ulcers to include venous ulcers, other wounds and skin conditions, and the possibility of periodontal and cardiovascular uses.

In addition, our products cover a **spectrum of regulatory environments** from the highly regulated biologics to cosmetic ingredients. That allows us to bring some new products to market much faster and with significantly lower regulatory costs.

The payment environment for our products also covers the full range from **insurance**

Value Creation Model

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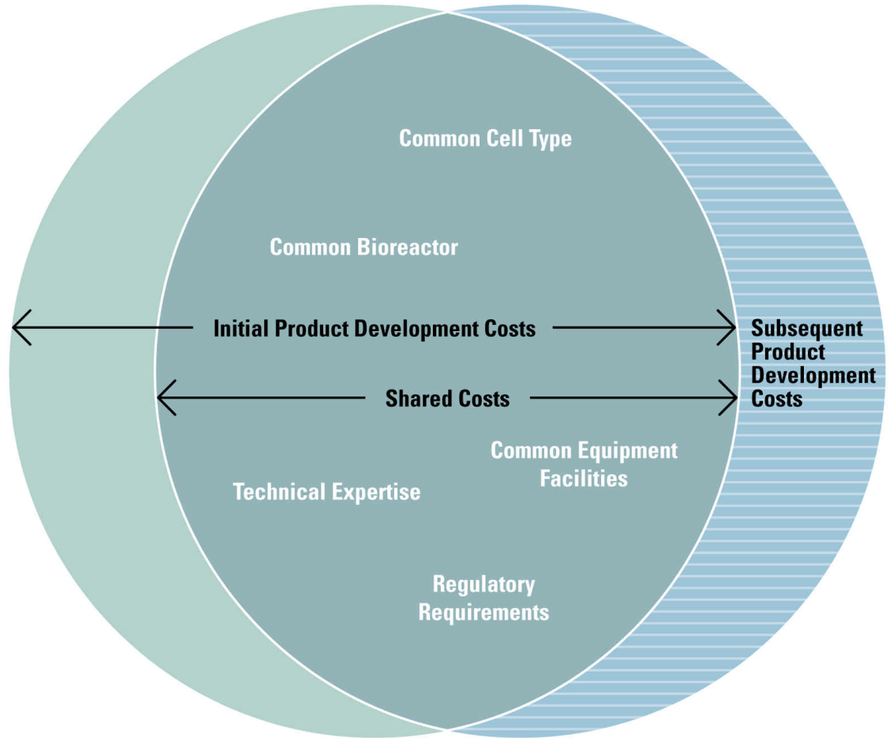
The company's strategic vision is to use our core technology to build a portfolio of off-the-shelf products that address a variety of medical needs. Most of the products in our pipeline share the same dermal fibroblast cell type, bioreactor technology, and facilities, and require related technical expertise. A major benefit of this approach is that development and other costs incurred for early products can be reduced or avoided with later products, as suggested by the diagram on this page.

For example, it took a significant investment to develop, get approval for, and begin production of TransCyte and Dermagraft. Subsequent applications of that same dermal fibroblast technology will not have to carry the development cost of learning how to work with the cells, designing and validating bioreactor technology to grow the tissue, or building a manufacturing facility. Information developed to meet regulatory requirements for earlier products can potentially be applied to future needs.

As a result, future products have the potential for higher margins to drive growing shareholder value. Current and future products that should benefit from this include NouriCel, collagen, the potential use of our dermal fibroblast technology for periodontal indications and possible future products such as Anginera™.



In October 2001, we entered into a collaboration with Medtronic, Inc. (NYSE: MDT) to explore the application of our technology in areas of therapeutic interest to Medtronic, including cardiovascular, neurological, endocrine and spinal. An affiliate of Medtronic invested $20 million in shares of our common stock in return for specified rights including a right of first refusal to participate in the further development and commercialization of Anginera, our epicardial angiogenesis therapy. As a part of this collaboration, a Medtronic representative joined our board of directors.

Smith+Nephew

The company has two joint ventures with Smith & Nephew (NYSE: SNN). The first covers the application of Advanced Tissue Sciences' tissue-engineering technology for skin wounds. This includes Dermagraft, TransCyte and possible future developments for venous ulcers, pressure ulcers, burns and other non-aesthetic wound care treatments. The second joint venture covers tissue-engineered orthopedic cartilage, initially focusing on the repair of cartilage in knee joints.

INAMED

The company has a strategic alliance with INAMED Corporation (NASDAQ: IMDC) through which Advanced Tissue Sciences and INAMED have been collaborating in the development of human-based collagen for wrinkle treatment. In the future, the companies expect that the use of human-based collagen could expand to other aesthetic and reconstructive applications.

Strategic Alliances

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reimbursement to self-pay. That means we have current and future products whose market potential is not limited by insurance reimbursement issues.

This **balanced approach allows us to manage the risks** more effectively through all stages of the process, from development through regulatory, scale-up, manufacturing and marketing. All of this improves the probability of positive outcomes for these products and for our shareholders.

Strategic alliances, with partners who are industry leaders, play an important role in our strategy. Our joint ventures with **Smith & Nephew,** alliance with **INAMED** and new collaboration with **Medtronic** help us to further manage the risks across the entire product cycle.

We continue to look for various **creative vehicles to unlock shareholder value** as we develop additional products and uses from the multiple applications of our technology. Depending on the opportunity, some of these will be in the form of new subsidiaries.

With the accomplishments made during 2001, here are the **milestones to watch for** during 2002:

Anginera – We plan to begin the **pivotal animal trial** using our dermal fibroblast technology to treat hearts compromised by insufficient blood flow. These trials could become the basis for future clinical trials.

Collagen – Our partner, INAMED, had hoped to have approval for use of our human-based collagen in wrinkle injections – without requiring patients to take a skin test – before the end of 2001. They now expect to submit additional data to the FDA by mid-year. We will be working to develop additional uses for this product.

Dermagraft – With Dermagraft approved in the United States, Smith & Nephew is working

deliberately and systematically to educate doctors about its benefits and use. Now that we have the reimbursement code, we, along with Smith & Nephew, will be working to secure actual **reimbursement coverage.** However, growth in sales will depend in part on how quickly that progresses. Our goal is to have coverage in the hospital out-patient setting in most of the United States by the end of the year.

At the same time, we are continuing to explore the use of Dermagraft for other medical indications. It is currently being evaluated for the treatment of venous ulcers in a **pivotal clinical trial.**

Periodontal – We expect to initiate **pivotal clinical trials** for use of our dermal fibroblast technology in certain periodontal indications.

Underlying everything we do is the commitment to **bring this company to profitability.** That's why the determined execution of our strategic vision is so important. It helps us generate and pursue both near- and long-term opportunities which we believe will lead the market compared to our competitors.

One of the realities of the marketplace is that the adoption of new medical technologies by doctors and hospitals can be slow, especially with new products that are revolutionary and require a fundamental change in the treatment regimen. We've seen this in the adoption rate of TransCyte.

Unexpected delays in the regulatory review process can disrupt plans for a product launch as we saw in 2001 with collagen.

These are among the reasons that, in the near term, we believe **our best revenue-generating opportunities** should come from applying our products and technology to the cosmetic and aesthetics markets. They tend to be less regulated, insurance reimbursement is not a factor, and adoption of new products is typically faster than in wound care.

Product Pipeline

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TransCyte®

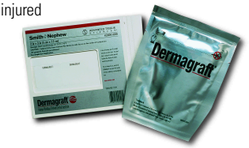
Research | Preclinical Development | Clinical Development | Marketed

TransCyte is a human fibroblast-derived temporary skin substitute, designed as a temporary wound covering for the treatment of burns. It is the first human fibroblast-derived temporary skin substitute for the treatment of burns to be approved by the FDA for use on third-degree and second-degree burns. TransCyte is available in the United States, Canada and several other countries.

Dermagraft®

Research | Preclinical Development | Clinical Development | Marketed

Dermagraft, a human fibroblast-derived dermal substitute, is designed for the treatment of conditions where skin has been injured or destroyed. It is cryopreserved, giving it an extended shelf life. In September 2001, the company received a Pre-Market Approval from the U.S. Food and Drug Administration for the use of Dermagraft in the treatment of chronic foot ulcers in patients with diabetes. In Canada and Australia, Dermagraft has been approved for the treatment of all chronic wounds.



NouriCel™

Research | Preclinical Development | Clinical Development | Marketed

NouriCel is derived from the company's patented process for growing bioengineered human tissue products. As they grow, they produce an array of natural growth factors and other compounds produced by healthy new skin. After the tissue is collected, a nutrient solution enriched with these compounds remains. This solution, which does not contain any cells or tissue, is NouriCel. It has been clinically shown to reduce the appearance and depth of fine lines and wrinkles while improving skin texture and elasticity. The company believes NouriCel has market potential as a cosmetic ingredient for rejuvenating aging and sun-damaged skin. We are also exploring other health and beauty-related applications for NouriCel.

Human-Based Collagen

Research | Preclinical Development | Clinical Development

Collagen is a family of naturally occurring proteins that serve as the basic structural building blocks of many tissues of the body. We have applied our existing technology to manufacture human-based collagen. The objective has been to develop a product which, after its purification, can be sterilized and easily injected or implanted into the human body. Injections of collagen are already used in the marketplace to help eliminate wrinkles, enhance lips and for reconstructive purposes. We plan to commercialize our human-based collagen for soft tissue augmentation, such as wrinkle revision, subject to regulatory approval, through our strategic alliance with INAMED Corporation. Other possible applications may include medical device coatings, as an additive to cosmetics, or use as a natural vehicle for drug delivery.

Dermagraft® Venous Ulcers

Research | Preclinical Development | Clinical Development

The company continues to explore the use of Dermagraft for other medical indications. The product is currently in a pivotal clinical trial for the treatment of venous ulcers.

Periodontal

Research | Preclinical Development | Clinical Development

Assuring that there is adequate hard and soft tissue around teeth is critical to periodontal health. Periodontal surgeries often require the harvesting of donor tissue from another location in the patient's mouth. Significant morbidity is often associated with both the harvesting of donor tissue as well as the healing of the donor site. In addition, there is often insufficient donor tissue available to cover all sites requiring treatment at the same time, thus necessitating repeated surgeries. The company is evaluating a fibroblast-based tissue to determine if it can be used as a substitute for an autologous connective tissue graft. Pivotal clinical trials evaluating periodontal indications are expected to begin this year.

Anginera™

Research | Preclinical Development

Improving circulation to regions of the heart that have insufficient blood flow is critical to the treatment of coronary artery disease. The company is currently evaluating the ability of a tissue-engineered, fibroblast-based tissue, Anginera, to stimulate blood vessel formation in the heart. This human-based tissue secretes multiple angiogenic growth factors which may present an advantage over other products that are based on only a single growth factor. Research has demonstrated that Anginera can induce microvessel formation with maturation into arterioles and venules. Additional preclinical studies are underway to determine if these vascular changes lead to improved ventricular function.

Other Development Work

Research | Preclinical Development

The company is doing additional development work in the following areas:

- Small diameter vascular grafts. These could ultimately be used for peripheral bypass, coronary bypass, A-V fistula and other clinical situations that require vascular grafts. This potential product is in the preclinical stage of development. Other coronary work includes efforts to develop an ischemic repair device and heart muscle.
- Tissue-engineered human cartilage for orthopedic applications such as repair of damaged joints. This potential product is in the preclinical stage of development. We are also working on cartilage for craniofacial applications.
- We also hope to develop other applications for human-based collagen and extracellular matrix in soft tissue augmentation.

Because of this, we will be working to develop the **revenue and profit potential of NouriCel.** Just before this annual report was printed, we announced the formation of **BioNuvia, Inc.,** a science-driven subsidiary, to give better focus to this effort. Its mission is to develop and market bioengineered products for enhancing appearance and rejuvenating the body. Milestones to look for during 2002 include the national launch by our existing partners of their skin care products containing NouriCel. We hope to sign agreements with **additional partners** to sell other products containing this ingredient.

In presentations we give at investor conferences, the company overview contains a summary we call **"Investment Highlights,"** which you will find printed inside the front cover of this annual report. It is a snapshot of where the company is right now. As you read this year's report, we hope you'll readily see our accomplishments and how those investment highlights are a base from which the company can grow and continue to **build shareholder value.**

We thank you for your support.

Arthur J. Benvenuto
Chairman, President and Chief Executive Officer

Gail K. Naughton, Ph.D.
Vice Chairman

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Statements in this annual report that are not strictly historical may be "forward-looking" statements, which involve risks and uncertainties. No assurances can be given, for example, that the company will successfully implement its business strategy, retain key members of management, develop its current products or any new products it may pursue, complete clinical trials, or be able to manufacture or successfully commercialize such products. Risks and uncertainties exist in the company's operations, including, without limitation, uncertainties related to clinical trials, the ability to obtain the appropriate regulatory approvals, the ability to obtain additional milestones and financing to continue operations when needed, a history of operating losses and accumulated deficits, the company's reliance on collaborative relationships, market acceptance of products, the company's ability to obtain and retain patent protection, as well as other risks detailed from time to time in publicly available filings with the Securities and Exchange Commission including, without limitation, Advanced Tissue Sciences' Annual Report on Form 10-K for the year ended December 31, 2001. The company undertakes no obligation to release publicly the results of any revision to these forward-looking statements to reflect events or circumstances arising after the date hereof.

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