

October 27, 2008

Dear Senetek Shareholder:

Calendar year 2008 brought about many changes at Senetek, the most significant being a strategic shift in our business model. Historically we have been purely a development company depending on commercial partners for revenues through licensing arrangements, but now we have accumulated the necessary financial resources to build our internal sales and marketing infrastructure. This will serve us well in the coming years as we will begin to receive 100% of revenues instead of the fractional share offered up by out licensing.

Our first entree into self-marketing is Pyratine-6™, which has been clinically proven in the treatment of photodamaged skin and acne rosacea. In 2008, Pyratine-6™ clinical data was published in the February issue of the *Journal of Drugs in Dermatology* and recently Pyratine-XR™, an advanced formulation for the treatment of acne rosacea, was accepted for publication during the first quarter of 2009. Pyratine-XR™ will be launched at the upcoming American Academy of Dermatology Annual Meeting in March of 2009.

Pyratine-6™ acceptance amongst the medical community is high with many physicians reporting successes and new indications for the product. Based on this extremely positive feedback regarding the performance of Pyratine-6™, we plan to further explore the clinical development of Pyratine-6™ in 2009 to maximize its market potential. Senetek will initiate new clinical trials to support the use of Pyratine-6™ for these novel uses to include improving outcomes and decreasing side effects with the use of Intense Pulse Light Therapy and Ablative Laser Resurfacing procedures.

Pyratine-6™ is available to consumers in the North American market only through Physicians. Distribution capabilities have been established through a collaboration with Delasco, the largest supplier of dermatological products in the world. We are working towards the build out of an outside sales force, targeting major population centers; in addition, we have contracted with TMS Health, a well known pharmaceutical provider, for the development of a Senetek inside sales organization dedicated to the promotion of Pyratine-6™. Most importantly, a Pyratine-6™ public relations campaign is currently underway targeting beauty editors at national magazines for editorial coverage and placement of print media advertising in select publications such as *New Beauty* and *Allure* is being pursued.

The current state of the economy will certainly come into play in the short term. Many of our competitors have scaled back projections and physicians report a marked slowdown in office visits and procedures. Despite this downward trend, we have optimistic expectations based on the initial market response to Pyratine-6™ and project to end 2009 with product revenues tracking at an annual pace in excess of \$10 million.

Our pipeline of skincare and dermatological products is strong. Procura™ (4HBAP), the first of a new class of cytokinins, has been successfully studied in human trials with differentiating effects from Pyratine-6™ and is ready for commercialization. AK801, another robust cytokinin, is nearing completion of the scale up of the synthesis process required for commercial feasibility and human safety testing has been successfully completed. Histological mice studies and cell culture work have demonstrated exceptional biological activity, suggesting positive therapeutic benefits for the treatment of various skin conditions including atopic dermatitis. PA100, a novel non-cytokinin, derived from the apple was developed in collaboration with the Institute of Bioorganic Chemistry of the Polish Academy of Sciences. PA100 is advancing through screening and cellular testing for wound healing, demonstrating promising results.

Invicorp® is a remarkably safe and effective treatment for erectile dysfunction. Our partner for North America, Plethora Solutions, continues to report that they remain on course for marketing authorization in the United States during the fourth quarter of 2009. Upon approval of this marketing authorization, a major milestone will have been met, triggering a seven figure payment that will mark the beginning of the most significant revenue stream to Senetek in the form of royalties on net product sales. The European marketing and distribution rights to Invicorp® were recently returned to us when our former partner, Ardana BioSciences, entered into insolvency proceedings. We are currently reviewing options for commercialization of Invicorp® in the European Union as well as the rest of the world, to include greater involvement in the regulatory process.

Reliaject®, our proprietary drug delivery system was sold to Ranbaxy in 2006 in exchange for an upfront payment, future milestone payments and royalties on all products delivered through Reliaject® for a period of 15 years from the date of first commercial sale. Ranbaxy is fully committed to Reliaject® and has made a multi-million dollar investment in their Cranbury, New Jersey manufacturing facility to house the automated equipment required for manufacturing finished products. Ranbaxy is currently seeking FDA approval for delivering epinephrine for treatment of anaphylactic shock, a market currently served by King Pharmaceutical's Epipen™ and generating \$250 million in product sales in North America. We conservatively estimate that we will begin to realize royalty income and future milestone payments for Reliaject® in mid to late 2010.

Our in-licensed RNAi-based therapy for brain cancer continues to show marked improvement in human survival rates for those individuals undergoing treatment for glioblastoma multiforme, a deadly form of brain cancer. To date, more than 45 patients have received treatment at the University of Medical Sciences in Poznan, Poland. Several of these individuals are still alive two years after treatment, a significant advancement over the six to eight month median survival rate of patients treated with conventional therapy. Just recently we reached agreement on terms for a new RNAi-based therapy from the Institute of Bioorganic Chemistry at the Polish Academy of Sciences in Poznan, with potential applications to treat a broader range of cancers. Our strategy remains to identify and partner with a major pharma company to undertake further testing and development of these potentially blockbuster therapies.

Proposal Four in the enclosed Proxy Statement requests shareholder approval of a resolution to reclassify components of the Company's capital accounts. This reclassification, which has no net financial impact on the Company, will allow Senetek, at the discretion and approval of the Board of Directors, to pay dividends or repurchase stock up to the level of the positive balance in adjusted accumulated earnings. If the resolution is approved, the reclassification is subject to English Court approval which can typically be obtained within two months. In absence of the approval of this resolution by shareholders and the Court, the Company cannot repurchase stock or pay dividends.

Over time, companies that repurchase shares have beaten the market by about 3 percentage points a year. Share repurchase programs offer a simple and structured exit program for many investors and do not result in tax liability for ongoing shareholders. Repurchase programs are particularly attractive where stocks are significantly undervalued in the market. Management believes this to be currently true for Senetek.

Dividends offer the opportunity for a cash return to all investors. Dividends are not currently being considered but may be in the future depending on cash position and business strategy.

The Board of Directors and Senetek management favor the proposed equity reclassification and urge all shareholders to vote "yes" on Proposal Four.

As I write this letter, we are experiencing very turbulent economic times. The market for microcap stocks, of which Senetek is one, has been particularly volatile with a substantial diminution of value across all industry sectors. I assure you that we are diligently managing your resources and making the necessary strategic and tactical decisions that will deliver value to Senetek shareholders over time. Thank you for your continued support.

Very truly yours,

A handwritten signature in cursive script, appearing to read "Frank J. Massino".

Frank J. Massino  
Chairman and Chief Executive Officer  
Senetek PLC