

## Convoy Therapeutics, Inc.

**Closely Held** 

## EXECUTIVE INFORMATIONAL OVERVIEW<sup>®</sup>

June 17, 2013



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### **Company Description**

Convoy Therapeutics, Inc. ("Convoy" or "the Company") is a late-stage biotechnology company developing a next-generation drug delivery technology. Convoy's innovative Skin-Penetrating-And-Cell-Entering (SPACE) Peptide Technology uses a family of proprietary peptide<sup>†</sup> sequences to transport topical drug and cosmetic compounds into the skin. A key competitive advantage of the SPACE technology is that it can be used to administer both small and large molecules. Many biologic drugs and therapeutic proteins, among other macromolecules, cannot be effectively delivered through the skin with current technologies due to the size of the active molecule. The SPACE Peptide not only facilitates skin penetration of large molecules but has also been shown to retain small compounds in the skin, potentiating a longer-lasting treatment effect. The technology is non-invasive and has been found to be non-toxic. Convoy's pipeline includes using the SPACE platform to reformulate a well-known oral and injectable therapeutic, cyclosporine A, into a topical treatment for psoriasis called CycloPsorb<sup>™</sup>, as well as creating a topical hyaluronic acid cosmetic compound to reduce fine lines/wrinkles as a supplement to **dermal filler** and Botox<sup>®</sup> injections.

### **Key Points**

- Convoy's topical hyaluronic acid for fine lines and wrinkles could reach the market in early 2014, followed by CycloPsorb<sup>™</sup> in 2015. The pipeline further includes several preclinical-stage candidates.
- The SPACE platform is adaptable to a range of molecules, and its use could enable new treatments in dermatology, immunology (vaccines), oncology and pain, and cosmetics/cosmeceuticals. Convoy seeks strategic partners interested in using the SPACE platform with their compounds or in co-development of the Company's two lead candidates.
- Medicines applied to the skin account for more than 12% of the global drug delivery market—which could expand with the advent of technologies such as Convoy's that enable topical delivery of existing oral and injectable macromolecules.
- Convoy holds an exclusive global license to the SPACE Peptide Technology, with patent applications filed in the U.S. and other worldwide territories under the Patent Cooperation Treaty (PCT).
- The Company is led by management experienced in biomedical, biotechnology, and financial markets as well as a Scientific Advisory Board chaired by Professor Samir Mitragotri, who is Director of the University of California, Santa Barbara's Center for Bioengineering and a leading researcher in the field of drug delivery. Professor Mitragotri is an inventor of the SPACE technology.
- Convoy is a closely held company. As such, information regarding its cash and financial position has not been made publicly available.



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### **Executive Overview**

Convoy Therapeutics, Inc. ("Convoy" or "the Company") is a late-stage biotechnology company working to commercialize a new drug delivery technology for administering medications into the skin and cells. This technology, termed "SPACE" for its demonstrated ability to be **S**kin **P**ermeating **A**nd **C**ell **E**ntering, is designed to overcome limitations of existing drug delivery technologies. It has been the subject of over four years of research, and could reach the market as early as the first quarter 2014.

### A New Drug Delivery Solution

The first drug delivery system applied to the skin—a patch coated with **scopolamine** to prevent motion sickness was introduced over 30 years ago. Since then, there have been many developments in this field, such as better adhesives for patches, new gels and creams that do not require a patch, and methods for reducing skin irritation at the application site, among other innovations. However, many critical medications are still given as injections, infusions, or pills to swallow simply because the size of the active drug molecule is too large to pass through the skin's dense upper layer. This top layer of skin, called the **stratum corneum**, serves as a natural barrier to foreign molecules, and without passing through it, medications cannot reach their target cellular and **capillary** destinations in the deeper layers of the skin.

To this end, scientific research published in 2011 in the *Proceedings of the National Academy of Sciences* validated the ability of Convoy's SPACE Peptide Technology to overcome the stratum corneum barrier in order to deliver large and small therapeutic molecules into the epidermis and superficial dermis. With the SPACE Peptide Technology, the active drug molecule is passively transported through the stratum corneum to arrive at living cells in the epidermis and dermis, where the technology has shown to be capable of entering the cells. To Convoy's knowledge, the SPACE Peptide Technology is the first to non-invasively deliver large molecules into the skin and cells.

Furthermore, the Company's SPACE technology has been shown to improve another area of drug delivery to the skin: namely retention of a therapeutic molecule (either small or large) within the skin's layers to achieve a longerlasting treatment effect. This is important because if the therapy is not capable of maintaining a sustained concentration of the active compound within the skin, then the patient must frequently reapply the compound creating an inconvenient treatment regimen that could result in patient non-compliance or dissatisfaction. In addition, several topical drugs possess systemic toxicity, where dermal retention may offer an effective way of mitigating toxicity. This attribute of the SPACE Peptide Technology may enable its use not solely for creating topical versions of previously injected or swallowed medicines but also for reformulating existing small-molecule topical agents to have a greater therapeutic effect or more convenient administration.

The potential of the SPACE technology to transmit large molecules into the skin and create a reservoir of small molecules within the skin for an extended period represent core competitive advantages of this drug delivery mechanism. Of note, the technology is also non-invasive, and according to Convoy, studies have shown that it is non-toxic and capable of delivering an active compound into the skin without impacting the compound's therapeutic function. Figure 1 (page 4) summarizes the technology's key benefits in comparison to existing forms of skin-based drug delivery.



Other Technologies (e.g., TAT1, poly-Lysine, poly-Arginine, meganin, TD-1)	SPACE Peptide Technology
Poor penetration, inconsistent delivery	Improved skin penetration (molecular weight up to 1.6 mDa
Low or no cell permeation	Penetrates cells via macropinocytosis
Highly polar in charge, oxidative, and toxic to cells	Net neutral, non-toxic, non-immunogenic
May alter biochemical activity of attached drugs	Does not affect function of drug cargo
Require skin substructures to effect transit	Does not require skin substructures to penetrate
Affects or alters skin or skin lipid structure	No affect on skin structure
Conjugation to active ingredient required	Adaptable liposomal system/ Conjugation to the active not required

### Figure 1 SPACE PEPTIDE TECHNOLOGY MAY OVERCOME PERCEIVED LIMITATIONS OF EXISTING TECHNIQUES

Source: Convoy Therapeutics, Inc.

### A Platform Technology

Convoy's SPACE technology capitalizes on a proprietary chain of 11 amino acids (known as a peptide sequence) that has an important capability of being able to penetrate the skin, cross cell membranes, and accumulate in the cytoplasm of most types of cells. Researchers identified this peptide sequence—the "SPACE" peptide for its skinpenetrating and cell-entering abilities—after screening over one billion possible peptide sequences for their skin penetration characteristics. The most recent U.S. and global patent applications for the technology were filed in February 2013, with patent applications also filed in 2011 that were published by the relevant patent authorities in May 2012.

One of the ways Convoy is currently employing the SPACE Peptide is via a SPACE-Ethosome, which entails the creation of a lipid vesicle that holds the active compound to be administered and then attaching the SPACE Peptide to the surface of the vesicle. In this manner, the peptide does not have to be conjugated or attached directly to the drug itself yet the vesicle can still benefit from the enhanced skin penetration attributes of the peptide on its surface. After passing through the stratum corneum, the active compound is deposited into the epidermis and dermis. Greater details of the SPACE-Ethosome and its proof-of-concept data is provided on pages 22-23.

The SPACE Peptide Technology has shown to be a versatile platform technology that is adaptable to a range of applications. Convoy has conducted proof-of-concept studies with several drug agents, including cyclosporine A, hyaluronic acid, and **silencing RNAs (siRNAs)**, among others. Details of these results are provided on pages 18-21.

### **Product Pipeline**

Convoy's lead candidates in development are topical treatments for psoriasis and wrinkles. Both of these products entail the combination of an existing therapeutic drug with the Company's peptide-dependent proprietary delivery system. Included below and on page 5 is a brief description of the Company's candidates closest to market launch—cyclosporine to treat psoriasis and a hyaluronic acid-based cosmetic to reduce wrinkles and fine lines— with greater details of the product pipeline for the SPACE Peptide Technology provided on page 26-31.

■ <u>CycloPsorb™ (Cyclosporine A for Psoriasis)</u>. Cyclosporine slows the growth of skin cells and has been approved by the FDA for severe psoriasis indications since 1997. However, as a large molecule with limited skin permeation on its own, there is not yet an approved topical cyclosporine formulation. Patients must swallow or inject currently available cyclosporine products for psoriasis, and oral administration of the compound has been associated with severe side effects, including suppression of the immune system, kidney problems, high blood pressure, and cancer. Convoy aims to seek regulatory approval for a topical cyclosporine product to treat psoriasis during 2014/2015.



As one of the most common inflammatory **dermatoses** in the U.S., psoriasis affects approximately 7.5 million people, which accounts for over 2% of the domestic population (Source: National Psoriasis Foundation). Globally, psoriasis afflicts over 125 million people. For these people, psoriasis is a chronic condition for which there is no cure—simply treatments for its flare-ups. Collectively, the National Psoriasis Foundation reports that healthcare costs related to psoriasis in the U.S. are roughly \$11.25 billion annually.

HA-202PH (Topical Hyaluronic Acid to Minimize Wrinkles). One of Convoy's chief market opportunities is in the area of cosmetics and cosmeceuticals, where products that either work on the skin or are absorbed through the skin are widely accepted. To this end, Convoy has paired its SPACE platform with hyaluronic acid (HA), a natural lubricating substance found in the joints and skin. Hyaluronic acid, which is widely used as a cosmeceutical, has been credited for giving skin its volume and fullness. Convoy's HA-202PH product candidate is an evidence-based topical wrinkle reducer to address the needs of the world's aging population. The target market for the HA-202PH cosmetic includes individuals seeking a convenient way to maintain therapeutic effect at reducing wrinkles in between dermal filler injections as well as those individuals who desire to minimize the visible effects of aging but who think they may be too young for injectable fillers. Convoy plans to file regulatory applications during 2013/2014 to market HA-202PH as a cosmetic in the U.S.

The global aesthetics industry represents an expanding market driven by an aging global population, an emerging middle class worldwide, and increasing consumer awareness of new cosmetic treatments and technologies. Accordingly, in 2012, the U.S. market for cosmetic surgery, facial aesthetics, and medical laser devices grew 10% from 2011, to top \$3 billion (Source: iData Research's *U.S. Cosmetic Surgery, Facial Aesthetics and Medical Laser Devices Market*, January 2013). Moreover, younger populations (in their 20s and 30s) are increasingly seeking preventative solutions to aging, which is likely to help drive demand for Convoy's hyaluronic acid products. In 2010, the American Society for Aesthetic Plastic Surgery (ASAPS) reported that people aged 31 to 45 accounted for 43% of all cosmetic procedures.

In addition, the Company is actively pursuing strategic relationships as a central part of its strategy for expanding the adoption of the SPACE platform beyond the current pipeline. There are a large number of possible drug targets for drug delivery with the SPACE technology, comprising existing, off-patent compounds as well as new compounds in development at other companies.

Ultimately, the SPACE platform may be suitable for the delivery of dermatology medications, vaccines, treatments for skin disorders/cancers, eye and nail diseases, pain medications, antibodies, and cosmetics/cosmeceuticals, such as dermal fillers and anti-wrinkle treatments, among other fields of medicine and skin health. If successfully commercialized, such an approach could considerably expand the market for drug delivery to the skin, which thus far has been largely limited to pain/wound management and products for women's health.

### **Corporate Information**

Convoy is a subsidiary of Nevada-based ACTUS Biotechnologies, Inc. (<u>www.actusbiotech.com</u>), which identifies technologies with high potential for commercialization. ACTUS provides initial support and infrastructure to accelerate the company from idea to commercialization, providing initial funding, management teams, product development, business development, and other necessary resources. After reviewing roughly 3,000 technologies, ACTUS Biotechnologies founded Convoy in 2011 to develop and commercialize the SPACE Peptide Technology, exclusively licensed from the University of California, Santa Barbara (UCSB). Convoy was incorporated in Delaware and is headquartered in Nevada.

Currently, Convoy's day-to-day operations are overseen by the management of ACTUS Biotechnologies and Convoy has no direct employees. Business development, strategic partnering, marketing, administration, and other functions are performed by the ACTUS Biotechnologies management team or are outsourced to third-party consultants, and R&D activities are performed by the laboratory of Professor Samir Mitragotri, Ph.D. at UCSB as well as other third-party contract laboratories under research agreements. A biography for Professor Mitragotri, chairman of Convoy's Scientific Advisory Board and inventor of the SPACE technology, is provided on pages 12-13.



### **Growth Strategy**

Convoy's primary objective is to provide a platform for the effective and efficient delivery of drugs, cosmeceuticals, or other active ingredients into the skin—for which the Company is advancing its SPACE Peptide Technology through the research and development process. To date, Convoy has received funding from its parent company, ACTUS Biotechnologies, and an unaffiliated third party to accelerate the commercialization of the SPACE technology.

Testing and commercialization of the SPACE Peptide Technology is occurring along several routes:

- (1) reformulating drugs with established safety and efficacy profiles into improved topical products;
- (2) reformulating drugs facing patent cliffs into topical products, which may enable patent extensions to cover the new formulation; and
- (3) working with partners to develop their proprietary molecules using the system (as described on pages 8-9).

### Pursuing Accelerated FDA Approval Through the 505(b)(2) Pathway

While Convoy's platform can be used with approved or novel therapeutics and cosmetics, the Company's internal development strategy is initially focused on reformulating previously approved generic compounds for use with the SPACE Peptide Technology. This allows Convoy to capitalize on the generic molecules' existing safety and efficacy data, which can be used to advance internal development as well as pursue streamlined regulatory approvals under the FDA's 505(b)(2) pathway. Over the long term, the Company also has plans for siRNA components for various skin conditions, which would likely be considered new therapeutics and thus would have a different regulatory procedure than the 505(b)(2) pathway described below.

Traditional pharmaceuticals—for which the active ingredient has not already been investigated and cleared by the FDA—are approved by the FDA under Section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act. Due to the extensive clinical studies required for these medications, new drug approval under 505(b)(1) can take up to 15 years and hundreds of millions of dollars in investment (Source: *Drug Discovery & Development*, August 9, 2012). In contrast, Section 505(b)(2) of the Act allows manufacturers to submit a New Drug Application (NDA) incorporating previous data from existing reference drugs—a feature that can greatly speed up time to market as well as reduce the costs required for development.

Based on information provided to the FDA by Convoy as of January 2013, the FDA informed Convoy in writing that a 505(b)(2) application would be acceptable for the Company to file for its CycloPsorb<sup>M</sup> candidate. Accordingly, Convoy currently plans to file an NDA under Section 505(b)(2) for CycloPsorb<sup>M</sup> as well as concurrent filings in the EU. CycloPsorb<sup>M</sup> is the Company's topical cyclosporine product candidate, which is detailed on pages 26-28.

### Development of HA Products

Convoy's most advanced hyaluronic acid formulation (HA-202PH) is projected to be launched as a cosmetic by early 2014. Convoy reports that it is presently in negotiations with a potential strategic partner for the compound's use as a maintenance product in between dermal filler or toxin injections (e.g., Botox<sup>®</sup>). Convoy is also developing a new formulation of higher-molecular-weight hyaluronic acid as a medical device for the prescription market, which is at an early preclinical stage. For this HA product, Convoy could pursue a standard regulatory route for certain medical devices—a Premarket Approval (PMA) application—for the use of topical hyaluronic acid as a prescription dermal filler replacement. A PMA is the FDA's application for approval of Class III devices, which are defined as those that "support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury" (Source: FDA). In the PMA application, the manufacturer must substantiate the device's safety and effectiveness for its intended use. The FDA states its review time for a PMA is 180 days, though it varies on a case-by-case basis.

### **Development Timeline**

Figure 2 depicts a detailed view of Convoy's planned development timeline for its two lead candidates as well as lists several possible indications where the Company expects that future development and growth could take place. As shown in the Figure, the Company could consider an initial public offering (IPO) during 2015. Additional exit strategies may include mergers or acquisitions (M&A) enabled by strategic partnership activity.





### **Strategic Partnerships**

Convoy is actively seeking out strategic partnerships with, or licenses to, other biopharmaceutical or cosmetic companies for co-development opportunities that could expand the use of the SPACE Peptide Technology in cosmetic and biopharmaceutical preparations. For example, while Convoy is internally developing treatments for psoriasis and wrinkles, the Company is actively seeking partnership opportunities for the development of future treatments for skin cancers, other dermatological diseases, and additional aesthetic products, among other indications (as summarized in Figure 3).

# Figure 3 POTENTIAL USES FOR THE SPACE PEPTIDE TECHNOLOGY/AREAS FOR STRATEGIC PARTNERSHIPS

- Dermatology
- Cosmetics/cosmeceuticals
- Immunology/vaccines
- Cancer
- Pain medications (e.g., steroids)
- Delivery of therapeutics to the eye
- Delivery of therapeutics to the nail bed
- Reformulation of third-party molecules that have poor penetration
- Reformulation of third-party molecules that could benefit from increased retention in skin

#### Source: Convoy Therapeutics, Inc.

Possible alliances could take several forms for Convoy: (1) a capital investment in the Company in exchange for an equity stake; (2) a strategic partner funds the remaining co-development and marketing for Convoy's CycloPsorb<sup>™</sup> or HA-202PH; (3) licenses or research collaborations for development of a partner's programs, Convoy's planned programs (e.g., tacrolimus, siRNAs, or other programs listed in Figure 2 [page 7]), or new indications; (4) a joint venture pursuant to which Convoy contributes the SPACE Peptide Technology and the partner supplies funding; or (5) a sale of the Company.

Figure 4 (page 9) lists several recent transactions within the dermatology and drug delivery fields, as examples of the type of value that is possible through strategic licenses or acquisitions.



Figure 4				
A SELECTION OF RECENT BIOTECHNOLOGY TRANSACTIONS Company Date Value Activity				
Kythera Biopharmaceuticals	August 2010	\$373 M (includes \$43 M upfront)	Bayer AG licensed rights to Kythera's Phase II drug to reduce chin fat	
Vicept Therapeutics	July 2011	up to \$200 M milestone payments + \$75 M upfront payment	Allergan acquired Vicept, maker of topical dermatology treatments	
Stelmi Group	May 2012	\$207 M	AptarGroup acquired the Stelmi Group, an injectable drug delivery company	
Medicis Pharmaceutical	September 2012	\$2.6 B	Valeant acquired dermatology portfolio and pipeline from Medicis	
SkinMedica Inc.	December 2012	~ \$350 M	Allergan acquired SkinMedica, maker of prescription and nonprescription topical aesthetics skin care products	

Sources: KYTHERA Biopharmaceuticals, Inc.; Reuters; AptarGroup, Inc.; and Valeant Pharmaceuticals International, Inc.



### **Intellectual Property**

Convoy's proprietary SPACE Peptide Technology was invented in part by Professor Samir Mitragotri at the University of California, Santa Barbara (UCSB). It was exclusively licensed to Convoy in October 2011.

A **freedom-to-operate (FTO)** patent investigation and analysis has been conducted for the SPACE Peptide variations by a law firm engaged by the Company.

### Pending U.S. Patent Applications

In October 2011, the Company filed a patent application with the U.S. Patent and Trademark Office, which describes an array of peptide and peptide compositions that could be used to deliver an active agent or active agent carrier in a manner capable of penetrating the stratum corneum and/or cellular membranes of viable cells. The application includes the particular peptide composition currently being developed by Convoy as the key SPACE Peptide for enabling improved drug delivery to the skin. This patent application, titled "Skin Permeating and Cell Entering (SPACE) Peptides and Methods of Use Thereof," was published in May 2012 and is undergoing active examination at the U.S. Patent and Trademark Office (USPTO). For reference, the publication number is US 2012/0128756 A1.

### **Pending PCT Applications**

In 2011 and 2013, Convoy also filed patent applications for its SPACE Peptide compositions under the Patent Cooperation Treaty (PCT). The PCT entails a unified procedure for simultaneously filing the same patent application in 146 countries (as of January 2013). Under the PCT structure, the single international patent application is examined for its patentability, which includes a search of other published documents that might affect the patentability of the application. The PCT application is then published by the International Bureau of the World Intellectual Property Organization (WIPO), after which examination and issuance procedures are handled by the relevant national or regional authorities. The PCT process greatly facilitates filing patent applications in multiple jurisdictions worldwide; however, it does not grant an "international patent," which does not exist.

Convoy's 2011 PCT application was published by WIPO in May 2012. For reference, the publication number is WO/2012/064429. The Company reports that regional filings for the application are currently underway in the European Patent Office, Japan, Canada, Australia, India, China, Brazil, and South Korea.

The 2013 PCT application has an application number of PCT/US2013/025543, and like its U.S. application counterpart, is intended to cover the composition of matter and method of use for the Company's liposomal systems.



### **Company Leadership**

Convoy Therapeutics' executive leadership team is composed of the executive management team of ACTUS Biotechnologies, which is Convoy's parent company. ACTUS's officers are serving as the management team of Convoy in order to guide the Company during the early stages of its development. Figure 5 summarizes the Company's executive leadership, followed by brief biographies.

	Figure 5
	EXECUTIVE MANAGEMENT
John Muraski, Ph.D.	President and Chief Executive Officer
James E. Carmichael, CPA	Chairman and Chief Financial Officer
Robert Davis, M.D.	Secretary and Chief Business Officer

### John Muraski, Ph.D., President and Chief Executive Officer

Dr. Muraski has more than two decades of experience in the biomedical sector with major medical research centers and biotechnology and pharmaceutical companies. His passion for the development of nascent technologies grew out of his business acumen and understanding of the commercialization process. He has revitalized struggling business units, established new business models, and led large efforts in the corporate and academic sectors. Dr. Muraski serves on the Board of Directors of ACTUS Biotechnologies, Inc. and its subsidiaries and is the vice president of these companies. Dr. Muraski currently acts as managing director of ACTUS, serves as scientific advisor to several companies, and is a San Diego CONNECT Entrepreneur in Residence. In addition, he serves in the role of stem cell and genomics moderator and scientific advisor for LabRoots, Inc. He is also a senior regulatory consultant with EMERGO Group. Dr. Muraski's contributions to the field have been recognized by Sigma Xi where has been elected to full membership. He is also an active member of several scientific and quality organizations. In his previous roles, he has assisted numerous companies and clients in R&D, manufacturing, quality system management, and compliance and regulatory submissions. He has published more than a dozen peer-reviewed manuscripts and holds a patent for the use of the cell signaling protein Pim-1 in cardiac stem cells. This patented research led to the founding of a biotechnology company in San Diego focused on cardiac regeneration using this protein in cardiac stem cells. Dr. Muraski received a Ph.D. in biology with a cellular and molecular biology focus from University of California at San Diego and was a fellow at Harvard Medical School's Brigham and Women's Hospital.

### James E. Carmichael, CPA, Chairman and Chief Financial Officer

Mr. Carmichael is a certified public accountant (CPA) with over 35 years of business experience. He is a graduate of the University of Texas at Austin. He was with Arthur Andersen & Co. for over 11 years in the commercial section of the audit division. He is licensed to practice as a CPA in Arizona, Texas, and New Jersey. Since leaving public accounting, he has been a chief executive officer and chief operations officer of corporations, both public and private, mainly in the construction materials industry. He has also consulted as a turn-around expert within this industry sector. He has testified before congressional hearings and practiced extensively before the U.S. Securities and Exchange Commission (SEC), being responsible and associated with over \$1 billion in public capital offerings and initial public filings. He currently operates a privately held exploration and development company in addition to his duties at ACTUS and its subsidiaries, and resides in Scottsdale, Arizona. Mr. Carmichael serves on the Board of Directors of ACTUS and its subsidiaries and is the president of these companies.



### Robert Davis, M.D., Secretary and Chief Business Officer

Dr. Davis's passion is to capitalize on unique market opportunities in medical and biotechnology markets. Dr. Davis and his team at Horizon View Partners work to provide capital resources for the technology under development at ACTUS. He and his partners at Horizon View invest their own money in transactions and/or team up with family offices, private equity, venture capital, hedge funds, pension funds, endowments, and wealth advisors. His deep institutional relationships allow him to provide substantial investment resources to developing technologies. According to Convoy Therapeutics, some of Dr. Davis's notable recent financings arranged have included \$82 million for MGM Resorts International (MGM-NYSE), a \$40 million credit facility for an orthotics/orthopedics medical device company roll-up, \$15 million for a well servicing and oil drilling company, and \$5 million for Brown Field Municipal Airport (San Diego airport development to supplement San Diego's current International Airport), among others. Dr. Davis has been the managing partner of QuestStar Capital Partners, where he gained experience in medical device financing with Sutura, a Fountain Valley, California, medical device company. Sutura designed, developed, and manufactured a family of suture-mediated stitching devices for vascular tissue approximation. Dr. Davis received a B.S. from the University of Michigan with a minor in creative writing. He graduated Phi Beta Kappa with High Honors, third in his class, and was a James B. Angel Scholar and member of the University of Michigan's President's Advisory Committee, a seat he held for over a year. His medical school training occurred at the University of Miami, with internal medicine residency training at the University of Nevada, Las Vegas. Dr. Davis is Board Eligible in emergency medicine, and has worked on an MBA with the University of Phoenix. Dr. Davis serves on the Board of Directors of ACTUS and its subsidiaries and is the secretary and treasurer of these companies.

### Scientific Advisory Board

In support of its management team and corporate objectives, Convoy has established a Scientific Advisory Board led by the individuals profiled below. These members have expertise in the area of drug delivery and are intended to assist Convoy in the strategic development of its platform. In addition, the Company seeks to add to the Board several additional clinicians who have significant expertise in the psoriasis and skin care fields.

	Figure 6
SCIENTIFIC ADVISORY BOARD	
amir Mitragotri, Ph.D.	Chairman of the Scientific Advisory Board
Erkki Ruoslahti, M.D., Ph.D.	Scientific Advisor

### Samir Mitragotri, Ph.D., Chairman of the Scientific Advisory Board

Professor Mitragotri is a professor of chemical engineering at the University of California, Santa Barbara (UCSB). He is also the director of the Center for Bioengineering at UCSB. He received a Ph.D. in chemical engineering from the Massachusetts Institute of Technology (MIT) and completed a fellowship with Dr. Robert Langer. Professor Mitragotri is a leading researcher in the field of drug delivery. His research interests include the development of novel methods of drug delivery, including transdermal, oral, and particle-based methods. His scientific contributions have provided much-needed fundamental insights in the field of drug delivery. At the same time, his technological innovations as well as entrepreneurial initiatives have led the way for translating laboratory discoveries into useful products. Professor Mitragotri has a strong publication record (over 150 publications). He has published in prominent journals, including *Science, Nature Medicine, Nature Biotechnology, Nature Materials, Proceedings of the National Academy of Sciences, Nature Reviews Drug Discovery, Nature Reviews Immunology, and Advanced Materials.* His work has been highlighted in numerous popular and news media, including *Scientific American, Popular Science, New York Times, USA Today,* and *Discover* magazine. His work is also highly cited, with over 10,000 citations and an **h-index** of 55 per Google scholar.



Professor Mitragotri has further received numerous awards for his contributions. Some of his awards include the Ebert Prize by the American Pharmacists Association (1996), *MIT Technology Review's* Young Innovator ("Innovators Under 35") award (1999), the CRS-Dow Corning award for outstanding research (2000), the 3M Young Faculty award (2001), the Global Indus Technovators Award (2003), the Pfizer-Capsugel award for innovative work in oral drug delivery (2004), the Hendrick C. Van Ness Lecturer at RPI (2004), the Allan P. Colburn award from American Institute of Chemical Engineering (2005), and the Young Investigator award from CRS (2008). He is an elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE). His teaching honors include an outstanding faculty award (2001) and the Chancellor's award for excellence in undergraduate research (2003). He also serves on several editorial boards including for the *Journal of Pharmaceutical Sciences, Journal of Controlled Release, European Journal of Pharmaceutical Sciences, Experimental Biology and Medicine,* and Cancer Nanotechnology. He further serves as an associate editor of *Therapeutic Delivery* and section editor on drug delivery in *Current Opinion on Colloids* and *Interfacial Science.* 

### Erkki Ruoslahti, M.D., Ph.D., Scientific Advisor

Dr. Ruoslahti earned an M.D. and Ph.D. from the University of Helsinki in Finland in 1967. After postdoctoral training at the California Institute of Technology, he held various academic appointments with the University of Helsinki and the University of Turku in Finland and the City of Hope National Medical Center in Duarte, California. He joined the Sanford-Burnham Medical Research Institute in 1979 and served as its president from 1989 to 2002. He has been a distinguished professor at UCSB in biological sciences since 2005. His honors include elected membership to the U.S. National Academy of Sciences, Institute of Medicine, American Academy of Arts and Sciences, and the European Molecular Biology Organization. He is the recipient of the G.H.A. Clowes Award, Robert J. and Claire Pasarow Foundation Award, Jacobaeus International Prize, and the Jubilee Award given by the British Biomedical Society. He was a Nobel Fellow at the Karolinska Institute in Stockholm in 1995, and is an Honorary Doctor of Medicine from the University of Lund, as well as a Knight of the Order of the White Rose of Finland. Dr. Ruoslahti is the recipient of the 2005 Japan Prize in cell biology.

Dr. Ruoslahti is also a distinguished professor at the Ruoslahti Research Laboratory at the Sanford-Burnham Medical Research Institute at UCSB. The underlying themes of his work are tumor vasculature, metastasis, and the use of targeted nanoparticles in cancer diagnosis and treatment. Dr. Ruoslahti is currently on three Editorial Boards and six Academic Advisory Boards. He has published over 400 scientific articles.



### **Core Story**

Biotechnology company Convoy Therapeutics, Inc. ("Convoy" or "the Company") is capitalizing upon a proprietary drug delivery system to improve the administration of a wide variety of topical ("applied to the skin") medications. Through its technology, Convoy seeks to create new topical treatments as well as reformulate existing treatments to be more effective and easier to use.

Medicines applied to the skin are estimated to account for between 12% and 15% of the global drug delivery market. Worldwide, drug delivery was a \$101 billion market as of 2009, believed to be expanding at a 10.3% annual rate to reach \$199 billion by 2016 (Source: GBI Research and in-PharmaTechnologist.com, November 15, 2010).

Development of the Company's skin delivery technology, termed "Skin-Penetrating-And-Cell-Entering (SPACE) Peptide Technology," is focused on enhancing the ability of large molecules to penetrate the skin as well as improving the retention of small molecules within the skin and cells. To this end, Convoy screened over one billion peptide sequences specifically for their skin-penetrating characteristics in order to identify the optimal peptide family, and is currently moving two topical formulations through product development using the novel SPACE Peptide Technology.

Figure 7 overviews Convoy's product pipeline, followed by a description of the Company's SPACE Peptide Technology platform on pages 15-25 and greater details of each of the Company's drug candidates and market opportunities on pages 26-31.

		PRODUC	Figure 7 T CANDIDATE PI	PELINE		
	Formulation Development	Proof of Concept	Formulation Optimization	Toxicology	Submission	Commercialization
<b>CycloPsorb™</b> Topical Cyclosporine for Treatment of Psoriasis						
HA-202PH Topical for Wrinkle Reduction Source: Convoy Therape	utics, Inc.					



### CONVOY'S TECHNOLOGY PLATFORM AND SCIENTIFIC BACKGROUND

The **S**kin-**P**enetrating-**a**nd-**C**ell-Entering ("SPACE") Peptide Technology upon which Convoy has based its product development was created by Professor Samir Mitragotri, Ph.D., and his laboratory at the University of California, Santa Barbara (UCSB). Professor Mitragotri (biography on pages 12-13) is director of UCSB's Center for Bioengineering and is chairman of Convoy's Scientific Advisory Board. His UCSB laboratory specializes in drug delivery research emphasizing improved treatment of skin diseases, such as psoriasis, dermatitis, and cancer.

To date, the SPACE Peptide Technology has been the subject of over four years of research and study, and Convoy states that its development has been funded by roughly \$1.5 million in grants and \$4.5 million in cash and cash equivalents from investors.

Essentially, the SPACE Peptide Technology is a method for delivering large and small therapeutic molecules into patients' skin and cells that is believed to offer several improvements over current technologies. It works by using a specific chain of 11 amino acids that have an important capability of being able to penetrate the skin, cross cell membranes, and accumulate in the cytoplasm of key cells. Because of its skin-penetrating and cell-entering attributes, this amino acid group has been termed the SPACE Peptide. (A peptide is a chain of two or more amino acids.) Research and development of the SPACE Peptide has found that it can be attached to the surface of a lipid carrier, within which Convoy can encapsulate drug molecules. The presence of the SPACE Peptide on the surface of the carrier enhances its penetration through the skin and enables the deposition of the target drug molecule inside the body. The Company has already demonstrated the validity of this approach for several drug agents, including cyclosporine, hyaluronic acid, and silencing RNAs (siRNAs).

### **Drug Delivery to the Skin**

The art of administering a medication through the unbroken skin has been available for roughly 30 years and has become an accepted route for drug delivery. There are many benefits to employing topical products versus oral medicines (taken by mouth) or injections. For one, many patients dislike injections, swallowing pills, and the bad tastes often associated with chewable medications. As well, when a drug is taken orally, it is subject to first-pass metabolism in the body. This effect occurs as the drug is absorbed by the digestive system and is carried into the liver, which metabolizes the compound. In some cases, treatments are so extensively broken down by the liver that only a small amount of medication actually enters systemic (whole body) circulation, reducing the bioavailability of the drug. As a result, patients must consume larger or more frequent doses of medication in order for the required amount to reach the affected area.

Alternatively, topical delivery allows drug makers to deposit a medicine directly on the affected area—offering a more direct path to the cells than going through the digestive system. As a result, products applied to the skin may be safer and more convenient for patients to use, as they often require less frequent dosing, have fewer side effects (because less medication is needed), and allow patients to quickly discontinue treatment by simply removing the delivery system (Source: Kalorama Information's *World Markets for Transdermal Drug Delivery*, September 2012).

Topical medicines may further offer improved therapy, as they can enable the continuous, controlled release of a therapeutic agent into the body for more uniform plasma levels (Source: PharmaLive Special Report, *Transdermal Medicine Review and Outlook 2011*). Both oral and intravenous (injection) routes are subject to delivering large initial doses of medicine into the patient's bloodstream, which then decreases in concentration over time and potentially leaves the patient without treatment until the next dose. In contrast, some transdermal patches have been developed to effectively deliver sustained doses of medication for several days.

erapy,	Figure 8
ise of	POTENTIAL ADVANTAGES OF DRUG DELIVERY TO THE SKIN
iform eport,	<ul> <li>Improved bioavailability</li> </ul>
Both	<ul> <li>More uniform plasma levels</li> </ul>
ct to	<ul> <li>Longer duration of action, reducing dosing frequency</li> </ul>
the	<ul> <li>Reduced side effects</li> </ul>
s in 5 the	<ul> <li>Greater convenience and comfort for patients</li> </ul>
e. In	<ul> <li>Improved therapy due to maintenance of plasma levels</li> </ul>
been	up to the end of the dosing interval versus a decline in
es of	plasma levels with conventional oral dosage forms

Source: Transdermal Medicine Review and Outlook 2011.



### Need for New Macromolecule Drug Delivery Technologies

Despite their benefits, medicines applied to the skin are still believed to account for less than 15% of the global drug delivery market (Source: *Transdermal Medicine Review and Outlook 2011*). Their uses are primarily concentrated within the fields of pain management/wound care and women's health, but have not been greatly expanded into other therapeutic areas. Today, more than half of medications are still orally delivered; however, employing gels, patches, and creams to deliver molecules through the skin is one of the most effective alternatives to oral administration (Source: *Transdermal Medicine Review and Outlook 2011*).

With the SPACE Peptide Technology, Convoy may be able to overcome some of the limitations that have kept the medical community from developing more medicines in a topical formulation. The skin is the body's largest organ and is very complex. Its function is to protect the body and keep foreign molecules out—which has made this organ a challenging barrier to cross in terms of drug delivery.

As shown in Figure 9, the body's top layer of skin is known as the stratum corneum, which is the outermost layer of epidermis. The depth of the stratum corneum varies but it is generally only approximately 20 µm thick. Historically, scientists viewed the stratum corneum as the barrier layer to the skin. It was thought that by simply penetrating this level, the drug could reach the dermis and systemic delivery (circulation of the medication) would occur. However, delivery in this manner has not proved to be too successful, because rather than being distributed throughout the body, many medications have remained locked in the skin, where they can cause irritation. This is because the stratum corneum is made of multiple layers of dead, flattened skin cells called corneocytes, embedded within a **hydrophobic** lipid matrix (as illustrated on the right side of Figure 9), that prevents many molecules from passing through.



Sources: MedicineNet, Inc., Convoy Therapeutics, Inc., and Crystal Research Associates, LLC.

Below the stratum corneum and epidermis is the dermis, which is the thickest region of the skin. Depending on a molecule's target, the molecule must be able to pass into the epidermis and potentially into the dermis. However, only small, hydrophobic drugs are easily able to diffuse into the skin and cross the stratum corneum via the transcellular or intracellular routes (shown in Figure 9) in order to penetrate the epidermis and dermis. Large or water-soluble compounds have a very difficult time penetrating the skin, leading medical companies to develop new delivery technologies that overcome this constraint as the vast majority of drugs fall into this category.



Over time, scientists have sought to develop more complex and aggressive liposomes, solvents, and penetration agents that encapsulate and transport drugs through the skin, many of which are still less than optimal in terms of safety and delivery efficiency. Convoy's SPACE Peptide has been studied as a next-generation penetration agent for delivering both new therapies and reformulations of existing compounds to cells via the skin.

### Identifying the SPACE Peptide Using Phage Display

Peptides are made from biocompatible building blocks called amino acids, which can be arranged in many different ways. Different amino acid sequences have varying characteristics, which scientists can study in order to identify which sequence (or peptide) is best suited for a particular purpose. In order to determine that the SPACE Peptide was beneficial for skin penetration, Professor Mitragotri's laboratory at UCSB used a technique called phage display (as illustrated in Figure 10). This involved placing a large library of bacteriophages (a virus that reproduces in bacteria) in a **Franz diffusion cell**. The bacteriophages are placed in the top of the Franz chamber on a piece of skin, which is positioned in the middle of the two glass compartments. Porcine (pig) skin was used for the initial peptide screening due to its resemblance to human skin. The phage incubates with the skin for 24 hours. At the end of the incubation period, researchers collect the sample from the bottom of the Franz diffusion cell, which contains the bacteriophages that were able to successfully penetrate and pass through the skin sample. These bacteriophages are then evaluated to see what sequence of peptide is present on their surface.



During research to identify the SPACE Peptide, this phage display process was repeated multiple times, with over one billion peptide sequences ultimately screened. At the end, researchers were able to determine which particular phage (and thus, peptide) was able to best permeate the skin and travel from the surface of the skin into the receiver compartment of the Franz diffusion cell. In the course of these experiments, scientists found that there was one peptide—the SPACE Peptide—that exhibited favorable skin penetration characteristics.



### About the SPACE Peptide Sequence

Fig	ure 12	
RELEVANT AMINC	ACID DESCRIPTIONS	
SPACE Peptide Sequence: ACTGSTQHQCG		
One Letter Code	Amino Acid	
А	Alanine	
С	Cysteine	
G	Glycine	
Н	Histidine	
Q	Glutamine	
S	Serine	
т	Threonine	
Source: Human Genome V	/ariation Society.	

The SPACE Peptide is made up of a primary sequence of 11 amino acids—ACTGSTQHQCG. Amino acids are the basic ingredients of proteins and are necessary components in all cells. Proteins are long chains of amino acids linked together, while peptides are short amino acid chains linked together with peptide bonds.

As listed in Figure 12, the SPACE amino acid sequence used by Convoy is ACTGSTQHQCG, for which the Company filed a U.S. patent application in October 2011. The patent application covers this peptide and other key amino acid sequences identified through this research as it relates to facilitating the delivery of an active agent or active agent carrier in order to penetrate the stratum corneum and/or cellular membranes of viable cells (Source: U.S. Patent Application, US 2012/0128756 A1).

Because of its composition, the SPACE Peptide is hydrophilic (water soluble) and has a neutral charge, which Convoy believes may increase its safety for drug delivery. Convoy reports that studies to date using its SPACE Peptide Technology have found the platform to be non-toxic, and its use has not impacted the biochemical activity of the therapeutic agent being administered into the skin. Toxicology studies performed in mice by an independent third-party research organization found that, at 50mg/kg, there was no acute systemic toxicity and no detectable immunogenicity.

### **Proof-of-Concept Studies**

Once the SPACE Peptide was identified and isolated through the phage display process described on page 17, it was removed from the phage and studied independently to see if it was able to penetrate the skin on its own. Researchers labeled the SPACE Peptide fluorescently and incubated it with a pig skin sample. Figure 13 depicts an image of the skin after contact with the fluorescently labeled peptide. As visible in Figure 13, SPACE Peptide was able to cross the stratum corneum and into the epidermis. Similar results were obtained in *in vitro* tests with human skin samples, as shown in Figure 14 (page 19).



Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.







Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.

Figure 15 illustrates the results of another study visually confirming that the SPACE Peptide binds to the stratum corneum. In the Figure, the stratum corneum is shown under visible light conditions in three scenarios: (1) with fluorescently labeled SPACE Peptide; (2) with a control peptide (not SPACE); and (3) with no peptide. Notably, the peptide has not been found to disrupt the structure of the stratum corneum.



Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.

One of the competitive features of the SPACE Peptide is that it is not only able to penetrate the skin, but it has also shown that it can enter cells. Figure 16 (page 20) illustrates that the SPACE Peptide was able to cross the cell membrane and accumulate in the cytoplasm of three key skin cell types: human keratinocytes, human fibroblasts, and human endothelial cells. The peptide can penetrate most cell types via macropinocytosis, which is one of the methods by which cells actively absorb important molecules by engulfing them since many large molecules cannot pass through the cell membrane on their own.



### Figure 16 SPACE PEPTIDE HAS SHOWN IT CAN ENTER A VARIETY OF HUMAN CELLS

(In color) Blue = cell nucleus; Green = fluorescently tagged SPACE peptide accumulated in the cell cytoplasm (Grayscale) Dark gray = cell nucleus; Medium gray to white = SPACE peptide

Scale bar: 100 µm



Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.

### Streptavidin

Based on the characteristics of the SPACE Peptide Technology, Convoy believes that this technique has potential as a delivery technology for a wide array of agents, including macromolecules, proteins, silencing ribonucleic acid (siRNA), and other targets. Figure 17 illustrates the results of a study using the SPACE Peptide Technology to deliver the protein **streptavidin** (a large molecule) into pig skin in the laboratory. Convoy reports that these experiments have been validated by an independent third-party pharmaceutical company.



Laboratory Experiment Using Pig Skin In Vitro (Scale bar: 200 μm)



Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.



### Silencing Ribonucleic Acid (siRNA)

SiRNA is a new class of therapeutics composed of nucleic acids, which must be able to cross the stratum corneum and enter the cells because the target of this class of therapeutics is within the cells. By combining siRNAs with the SPACE Peptide, researchers have demonstrated that Convoy's SPACE Peptide Technology is able to deliver therapeutic quantities of siRNA into the skin and maintain its activity.

This was tested by Professor Mitragotri and his colleagues, who studied a combination of the SPACE Peptide with Interleukin 10 (IL-10) siRNA and GAPDH siRNA in mice in order to assess the level of skin penetration and the level of siRNA activity after penetration. The goal of IL-10 siRNA is to reduce the activity of—or silence—the IL-10 anti-inflammatory cytokine in cells. SPACE-IL-10 (which is IL-10 siRNA combined with the SPACE Peptide) penetrated the skin and localized in the dermis within one hour. As shown in Figure 18, siRNA activity was maintained 24 hours after treatment, at which point local IL-10 protein levels were decreased by approximately 30%.

Investigators also studied GAPDH siRNA conjugated to the SPACE Peptide. GAPDH (or Glyceraldehyde 3-Phosphate Dehydrogenase) is an enzyme in the body that serves to break down glucose for energy and carbon molecules as well as mediate a number of other processes, such as initiating apoptosis (programmed cell death). SPACE-GAPDH siRNA was found to penetrate the mouse epidermis *in vivo* and induced knockdown of the GAPDH protein targets, as illustrated in Figure 19. SPACE-GAPDH siRNA was shown to decrease GAPDH expression by more than 40% within 72 hours in a dose-dependent manner.



Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.



Source: Proceedings of the National Academy of Sciences, 2011 September 20; 108(38): 15816-15821.



### **Creating a Carrier Using the SPACE Peptide**

As described on pages 18-21, Convoy's SPACE Peptide Technology has been able to demonstrate extensive skin penetration with large molecules as well as the ability to retain small molecules in the skin, thereby creating a reservoir of the active therapeutic agent in the skin cells. Consequently, the SPACE Peptide has become the center of Convoy's drug delivery technology for carrying its product candidates into the skin.

There are a variety of ways to employ the SPACE Peptide Technology for drug delivery. One of the techniques Convoy is using entails a "lipid vesicle," or SPACE-conjugated phospholipids suspended in an ethanol-water mixture. The technique involves making a carrier composed of lipids that is conjugated to the SPACE Peptide (as represented in Figure 20). Lipids are naturally occurring molecules that are essential to cells. Researchers have been able to attach the SPACE Peptide to the surface of a lipid vesicle known as a liposome. The liposome is a manmade, microscopic vesicle that has an aqueous center surrounded by a lipid membrane. Both the aqueous center and the membrane components of the liposome are capable of transporting drug molecules. With the SPACE Peptide added to the liposome's surface, the vesicle is able to have enhanced penetration into the skin and cells. As well, naked SPACE Peptide can be used in the interior of the ethosome (the liposomal mixture with ethyl alcohol and lipids attached to SPACE Peptide) to enhance transit.



Source: Convoy Therapeutics, Inc.

Researchers have found that a variety of drug agents can be encapsulated within the liposome. If the drug or medicine is hydrophobic (water-repelling), it is encapsulated in the hydrophobic region of the vesicle (as shown in Figure 20). Alternatively, if the medicine to be delivered is hydrophilic (dissolves in water), then it can be carried in the central core of the vesicle. In this way, the system is adaptable to a multitude of drug molecules, and does not require that the SPACE Peptide be conjugated or attached directly to the active drug itself. Because it is not conjugated, the SPACE Peptide is not believed to have any impact on the function of the encapsulated agent, which is key to Convoy's initial regulatory strategies for CycloPsorb<sup>™</sup> and HA-202PH.

Convoy has already tested the delivery of several molecules, including cyclosporine A, hyaluronic acid, and siRNA, in this manner. The tests summarized below were conducted in porcine skin, although comparable results for both cyclosporine and hyaluronic acid have been observed in human skin samples.

### SPACE-Ethosomes Proof of Concept

- CycloPsorb<sup>™</sup>. Researchers used a non-conjugated SPACE-Ethosome where the SPACE Peptide was not attached to the active cyclosporine A molecule. The formulation included the SPACE-Ethosome (2 mg/ml) with cyclosporine A as the active cargo as well as free (or naked) SPACE Peptide (50 mg/ml). This formulation is being developed by Convoy as CycloPsorb<sup>™</sup> (detailed on pages 26-28). According to Convoy, results showed that nearly 11% of the applied dose penetrated the skin and 3.7% penetrated the epidermis, which the Company states represents a roughly 12-fold enhancement of epidermal delivery versus the control. The control entailed cyclosporine A (5 mg/ml) alone in ethanol. Data is illustrated in Figure 21 (page 23).
- HA-202PH. Similar to CycloPsorb<sup>™</sup>, the hyaluronic acid candidate entails a non-conjugated formulation of a SPACE-Ethosome with hyaluronic acid. The Company uses a 200,000 to 300,000 Daltons (the molecular weight) hyaluronic acid molecule, and has tested it at a range of pH levels. As illustrated in Figure 21 (page 23), over 9% of the applied dose penetrated the skin, with over 3% penetrating the epidermis. Convoy states that this represents an 11-fold enhancement of epidermal delivery versus the control. Additionally, the Company has shown that the formulation is stable for at least 28 days. Current work seeks to optimize the candidate for room temperature stability.



- SiRNA. Studies in porcine skin of a conjugated siRNA-SPACE formulation found that roughly 18.5% of the total applied dose penetrated the skin, with nearly 5% of the total applied dose reaching the epidermis. In this scenario, skin penetration appears to have been enhanced by DOTAP Ethosomes and SPACE conjugation to the siRNA. This formulation, called "SI-102c+" by Convoy, is stated to represent approximately a 10-fold enhancement of epidermal delivery versus the control of siRNA (25nmol/ml) alone in a buffer solution. SI-102c+ is composed of a SPACE-DOTAP-Ethosome with siRNA-SPACE (25nmol/ml) and free SPACE (50mg/ml).
- Fluorescein Isothiocyanate (FITC). Using a small molecule, FITC, researchers have shown that infinite dosing of a conjugated formulation of SPACE-Ethosomes, FITC-SPACE, and free SPACE demonstrated significant penetration and the formation of an FITC reservoir in different skin layers. Skin penetration data is as follows: nearly 8% of the total applied dose penetrated the skin and nearly 2% of the total applied dose penetrated the epidermis—which Convoy has stated shows a 10-fold improvement of epidermal delivery versus the control.



Figure 21 PACE-ETHOSOMES PROOF OF CONCEPT: DELIVERY INTO SKIN



Source: Convoy Therapeutics, Inc.



### Potential Competitive Advantages Using a SPACE Peptide Enhancer for Drug Delivery

Convoy believes that it can capitalize on the unique attributes of the SPACE platform for developing new topical compounds as well as for improving the performance of existing topical products. To the Company's knowledge, its SPACE Peptide Technology may be the first to effectively deliver large molecules into the skin and cells. The benefits of being able to offer a delivery option capable of transporting small or large, hydrophobic or hydrophilic compounds through the skin are numerous, but chiefly include the following:

- Enhancing the patient experience by creating topical formulations that are easier to use, safer, and more effective;
- Improving patient compliance by offering treatments that have less frequent dosing regimens than existing options as a result of being able to retain small molecules in the skin for a longer period of time;
- Reducing Convoy's time to market by leveraging the established safety and efficacy profiles of well-known existing compounds (the Company aims to seek expedited regulatory approval pathways for existing compounds in its new topical formulations); and
- Continued development of the SPACE platform is elucidating a number of opportunities for new topical products in growing markets.

Figure 22 summarizes the key attributes of the SPACE Peptide Technology that make it suitable for Convoy's product development.

Figure 22	
KEY ATTRIBUTES OF CONVOY'S DRUG DELIVERY PLATFORM	
<ul> <li>The technology is net neutral in charge.</li> </ul>	

- It is believed to be non-toxic to cells.
- It is water soluble and non-invasive.
- It does not require the presence of skin substructures (such as hair follicles) in order to penetrate the skin.
- It does not require conjugation to the active compound.
- SPACE Peptide Technology is an adaptable system, essentially a "plug and play" technology for active compounds.
- It does not disrupt the stratum corneum.
- The SPACE peptide has an affinity for keratin, which is found in all three layers of the skin.
- The technology has demonstrated the delivery of small molecules and large molecules.
- The technology has shown improved penetration and retention kinetics versus competing approaches.
- New data has shown that the technology creates a reservoir of drug in the skin for longer-lasting treatment.

Source: Convoy Therapeutics, Inc.



### Applications

When Professor Mitragotri's UCSB laboratory identified the SPACE Peptide as a method for the topical delivery of molecules, the university actively began looking for a licensor for the technology. In parallel, Convoy's parent company, ACTUS Biotechnologies, was looking to acquire rights to technologies that could have a potentially transformative impact on medicine. After evaluating the technology at UCSB, the Company entered into an exclusive license agreement with the university in October 2011 for use of the SPACE Peptide Technology. Since then, Professor Mitragotri has continued to work with Convoy to commercialize the SPACE platform through development of the product candidates described on pages 26-31, which seek to improve treatments for problematic skin conditions including psoriasis and wrinkles.

Beyond Convoy's current pipeline, the Company believes that there are a large number of possible drug targets for this technology, comprising compounds that are already approved as well as those under development at other companies (which could eventually become strategic partners). Moreover, as the Company demonstrates that its delivery system can enable decreased dosages with greater efficacy (due to medications being better received and retained in the body), it is possible that some of today's oral and injected medications can move to a topical administration instead.

The Company's primary demonstration of reformulating an oral/injectable medicine into a topical form is with cyclosporine A for psoriasis. To date, there is no approved topical cyclosporine formulation for skin application, although the drug is available in both oral tablets and intravenous injections and as a topical ophthalmic emulsion for dry eye (Restasis<sup>®</sup>). Convoy aims to seek regulatory approval for its topical cyclosporine product to treat psoriasis during 2014/2015. The platform may also be beneficial for medications nearing patent expiry, where combination with a new delivery system could help extend patent protection.

Ultimately, the SPACE platform may be suitable for the topical delivery of dermatological medications, vaccines, treatments for skin disorders/cancers, eye diseases, delivery to the nail bed, pain drugs, various antibodies, and cosmetics/cosmeceuticals, such as dermal fillers and anti-wrinkle treatments, among other fields of medicine and skin health.



### PRODUCT CANDIDATE PIPELINE

Convoy is initially exploring the application of SPACE Peptide Technology in three fields—(1) inflammatory dermatoses (e.g., psoriasis and eczema); (2) skin cancers; and (3) cosmetics and cosmeceuticals—although the Company is actively seeking pharmaceutical or cosmetic strategic partners capable of developing the technology in any of its applicable arenas.

The first two candidates being developed at Convoy are topical treatments for psoriasis and wrinkles. Both of these products entail the combination of an existing therapeutic drug with the Company's peptide-dependent proprietary drug delivery system.

### CycloPsorb<sup>™</sup> (Topical Cyclosporine A)

In the CycloPsorb<sup>™</sup> program, Convoy has paired the SPACE Peptide Technology with cyclosporine, a well-known immunosuppressant compound to treat severe psoriasis and rheumatoid arthritis as well as to prevent organ rejection after a transplant. Cyclosporine, which works to slow the growth of skin cells, has been approved by the FDA for severe psoriasis indications since 1997. However, as a large molecule with limited skin permeation on its own, the drug is currently administered either orally or as an injection.

In an attempt to bridge this gap and ease the administration of cyclosporine for patients, Convoy has worked to optimize its CycloPsorb<sup>™</sup> formulation in a manner that enables a topical cyclosporine psoriasis treatment. To date, the Company reports that it has already demonstrated that, without conjugation or attachment directly to the active molecule, its cyclosporine A product candidate enabled the delivery of more than 10% of the applied dose into the skin. Convoy considers this to be an important development in cyclosporine's topical delivery, especially considering that to the Company's knowledge only 0.1% of oral cyclosporine is able to reach the skin. The CycloPsorb<sup>™</sup> data is described on page 22 and illustrated in Figure 21 (page 23), which also shows how Convoy's formulation does not carry cyclosporine past the dermis (into the "receptor"), suggesting the possibility for fewer side effects given that far less cyclosporine may be circulated systemically.

Following optimization of the formulation and initial scale-up, the Company expects to commence toxicology studies on the SPACE Peptide and product formulation in late 2013 and to file regulatory applications for approval of CycloPsorb<sup>™</sup> in both the U.S. and Europe in late 2014, noting that in some jurisdictions the path to market may be managed by a strategic partner. Based on information provided to the FDA by Convoy as of January 2013, the FDA has confirmed in writing that a 505(b)(2) application would be an acceptable regulatory pathway for CycloPsorb<sup>™</sup> in the U.S. The 505(b)(2) route may facilitate a rapid time to market for Convoy.

Convoy states that it has already identified reimbursement codes with a price component for CycloPsorb™.

### Psoriasis Market

Psoriasis is a genetic autoimmune disease affecting the skin and joints. The condition most commonly manifests as raised, red lesions on the skin covered by whitish scales, as shown in Figure 23 (page 27), but can also progress to psoriatic arthritis in the joints. It often begins appearing between the ages of 15 and 25 but can affect people of all ages. The severity of psoriasis typically depends on the extent of skin affected by the disease; more than 10% of skin showing lesions is considered to be a severe case. As one of the most common inflammatory dermatoses in the U.S., psoriasis affects approximately 7.5 million people, which accounts for over 2% of the domestic population (Source: National Psoriasis Foundation). Globally, this skin condition is estimated to afflict over 125 million people. For these people, psoriasis is a chronic condition for which there is no cure to date—simply treatments for its flare-ups.



### Limitations of Existing Treatment Options

For people suffering from psoriasis, there are a wide range of possible treatments, which vary in administration, effectiveness, and side effects. The National Psoriasis Foundation reports that direct and indirect healthcare costs related to psoriasis in the U.S. alone are roughly \$11.25 billion annually, based on a 2008 study published in the *Journal of the American Academy of Dermatology*. Lost time from work accounts for 40% of these costs, as the majority of psoriasis patients miss an average of 26 days of work a year due to their disease.



Sources: A.D.A.M., Inc. and Wikimedia Commons (by user: The Wednesday Island [of the English Wikipedia]).

Today, topical treatments are typically the first line of defense for psoriasis patients. Available topical products range from over-the-counter creams (such as salicylic acid, which promotes shedding of skin in order to help remove psoriasis scales) to prescription steroids, which can be used as anti-inflammatory agents to reduce the swelling and redness of mild psoriasis lesions. There are also a number of non-steroidal Vitamin A- and Vitamin D3-based products that can be applied to mild psoriasis lesions. These too can be used to slow skin cell growth and reduce inflammation.

Phototherapy (light therapy) alone or in combination with medications can be used to improve skin appearance in the midst of a psoriatic outbreak. There are many different forms of phototherapy being performed by dermatologists, aestheticians, and other clinicians, but most typically entail exposing the skin to artificial ultraviolet A (UVA) or ultraviolet B (UVB) light. Controlled exposure to natural sunlight may also help mitigate symptoms.

### Systemic Medications, Including Cyclosporine

However, for many patients, currently available topical products are not enough to treat their disease. For moderate to severe psoriasis and psoriatic arthritis cases, physicians may prescribe systemic medications that are given by mouth, injection, or intravenous infusion. One of these products is cyclosporine—the compound being redeveloped by Convoy as a topical formulation. Today's cyclosporine medications are given either orally or intravenously, and have shown effective in clearing psoriatic lesions as early as two weeks after the start of medication. Cyclosporine may also help prevent future flare-ups (Source: WebMD's "Cyclosporine for Psoriasis," January 6, 2010). Yet, when given as an oral medication, cyclosporine can be associated with erratic absorption by the body. For example, prescribing information for Novartis AG's (NVS-NYSE) Sandimmune® Soft Gelatin Capsules and Oral Solution (cyclosporine) warns physicians to closely monitor the levels of cyclosporine in the blood of patients taking the capsules or oral solution, as absorption by the body is inconsistent. Too much cyclosporine can cause toxicity, cancer, and severe side effects while too little may not achieve a therapeutic effect.



Additional concerns with oral forms of cyclosporine include the medicine's foul taste and strict guidelines for use. Liquid formulations must be diluted with room temperature orange or apple juice or milk (but not grapefruit juice as it raises blood levels of cyclosporine too much) and must be taken in the same way and at the same time every day due to the ease at which food or other liquids can alter cyclosporine's absorption by the body. Glass cups are preferable, though a hard plastic cup may be used but a foam cup should not (Source: WebMD<sup>®</sup>). Accordingly, Convoy seeks to improve the administration of cyclosporine for psoriasis patients, who could benefit from an easily applied topical cream that may be safer and more effective than current cyclosporine products.

There are multiple manufacturers of FDA-approved cyclosporine products, though none that have been able to successfully develop the compound in a topical form. Figure 24 summarizes the FDA's database of approved cyclosporine products, which include generic cyclosporine approved under the **Abbreviated New Drug Application** (ANDA) pathway.

Product Name	Administration	Manufacturer
Neoral®	Soft Gelatin Capsules; Oral Solution	Novartis AG
Sandimmune®	Soft Gelatin Capsules; Oral Solution; Injection	Novartis AG
Gengraf <sup>®</sup>	Oral Solution	AbbVie Inc. (formerly part of Abbott Laboratories)
Restasis <sup>®</sup> *	Ophthalmic Emulsion	Allergan, Inc.
"Cyclosporine" *Used for chronic dry	Capsule (100 mg, 25 mg, or 50 mg); Injection (50 mg/ml); or Oral solution (100 mg/ml)	Multiple: Boehringer Ingelheim's Bedford Laboratories Novartis's Sandoz Inc. Apotex Inc. Watson Laboratories, Inc. Teva Pharmaceuticals USA Daiichi Sankyo's Luitpold Pharmaceuticals, Inc. Wockhardt USA LLC Novex

Listed below are other oral or injectable systemic medications (non-cyclosporine) that are used to treat severe or resistant psoriasis cases, though many of these are only used for brief periods or are alternated with other treatment modalities due to the risk of side effects (Source: the Mayo Foundation for Medical Education and Research).

- Retinoids: (e.g., Stiefel Laboratories, Inc.'s Soriatane®) Alleviates psoriasis symptoms but does not prevent recurrences after therapy is discontinued. Like many compounds on this list, retinoids are known to cause severe birth defects.
- Methotrexate: A disease-modifying anti-rheumatic drug (DMARD) that may slow the progression of psoriatic arthritis.
- *Hydroxyurea:* Not as effective as cyclosporine or methotrexate but can be combined with phototherapy.
- Biologics: A new class of psoriasis drugs given mainly by intravenous infusion, intramuscular injection, or subcutaneous injection to block inflammatory pathways and interaction between certain immune cells. While family members or patients can administer these drugs in some cases, others require administration by a healthcare provider. Common products include Amgen, Inc.'s (AMGN-NASDAQ) Enbrel®, Abbott Laboratories' (ABT-NYSE) Humira®, and Janssen Biotech, Inc.'s Remicade®.



### HA-202PH Topical Wrinkle Reducer

One of Convoy's chief market opportunities is in the area of cosmetics and cosmeceuticals, for which topically applied products are common. The aesthetics industry is already well-acquainted with products that either work on the skin or are absorbed through the skin. Moreover, it is also an expanding field driven by an aging global population, an emerging middle class worldwide, and increased consumer awareness of new cosmetic treatments and technologies.

Convoy's first product to address the needs of the world's aging population is a topical wrinkle reducer. This candidate, HA-202PH, is a reformulation of an existing molecule—hyaluronic acid (HA)—used to minimize wrinkles. Convoy has paired hyaluronic acid with its next-generation drug delivery system in the development of HA-202PH, which is designed to fill in wrinkles, thus smoothing the skin's fine lines and wrinkles and creating a younger-looking profile. According to the Company, studies have shown that, without conjugation or attachment, Convoy's SPACE Peptide Technology can deliver approximately 10% of the applied hyaluronic acid dose into the skin (as described on page 22 and shown in Figure 21 [page 23]). In comparison, to Convoy's knowledge, alternative hyaluronic acid topical agents at the same molecular weight have a maximum delivery of only 0.1% HA. Convoy's formulation uses 200 to 300kDa molecular weight HA, which is a much higher weight than is currently found in cosmetic preparations (which typically range from 10 to 20kDa) and which Convoy expects can have a tangible effect on wrinkle reduction and smoothing of fine lines. Convoy plans to launch its topical wrinkle reducer as a cosmetic in both the U.S. and Europe, noting that in some jurisdictions the path to market may be managed by a strategic partner.

Convoy's hyaluronic acid cosmetics will likely include an entire line of products, such as an eye serum, night serum, and moisturizer, containing the HA-202PH formulation. These products are expected to be sold via two channels: (1) directly by dermatologists/clinicians to their clientele; and (2) via top-shelf over-the-counter retail. The target market for HA-202PH-containing cosmetics includes individuals seeking a convenient way to maintain therapeutic effect at reducing wrinkles in between dermal filler injections as well as those individuals who desire to minimize the visible effects of aging but who think they may be too young for injectable fillers.

Going forward, Convoy also plans to develop additional hyaluronic acid product candidates, including one using hyaluronic acid as a prescription-based dermal filler regulated as a medical device.

### Hyaluronic Acid

Hyaluronic acid is a molecule naturally found within the synovial fluid in joints. It is a protective gel-like substance that is known to cushion and lubricate joints, and has also been credited for giving skin its volume and fullness due to the concentrations of hyaluronic acid present in both the epidermis and deeper dermal layers of the skin. Hyaluronic acid also occurs in the aqueous humor of the eye, where it helps retain the shape of the eyeball.

Due to hyaluronic acid's numerous possible benefits, scientists have long since discovered how to make synthetic or animalderived versions for use in a wide variety of orthopedic and cosmetic products. Today, the substance is sold in many forms, from injections that treat joint disorders to prescription and over-the-counter anti-aging supplements. Figure 25 summarizes many of the more commonly accepted uses of hyaluronic acid today, noting that the substance's effectiveness for these indications may vary based on a wide range of factors, including product manufacturer, formulation, administration, and intended use.

Figure 25	
A SELECTION OF USES OF HYALURONIC ACID	

Joint disorders (e.g., osteoarthritis)

- Eye injuries, cataract removal, cornea transplant, detached retina repair, and other eye surgeries
- Plastic surgery (e.g., lip filler)
- Healing wounds, burns, and skin ulcers
- Healing mouth sores
- Moisturizers
- Facial wrinkles and folds
- Anti-aging supplements, creams, and serums
- Cosmetics

Sources: WebMD<sup>®</sup> and the Los Angeles Times.



### Opportunity for a Topical Dermal Filler/Cosmetic

Over time, damage from the sun, stress, toxins (e.g., smoking), disease, and general aging can cause skin to lose its youthful appearance as well as begin to develop fine lines and wrinkles, which is further impacted by a depletion of hyaluronic acid in the body that occurs with age. Hyaluronic acid alone cannot overcome all of the skin damage that occurs over the years; however, it is a key molecule for nourishing and hydrating the skin and maintaining its structural integrity. To this end, hyaluronic acid injections have been proven to be clinically effective at reducing wrinkles (Source: *New York Times*, August 18, 2008). As the hyaluronic acid reaches the dermis layer of the skin, the skin's fibroblast cells respond by producing more collagen—which is responsible for giving the skin its shape and elasticity. Collagen production naturally deteriorates due to age and UV exposure, and its absence means the skin lacks structural support and consequently begins to wrinkle. Hyaluronic acid injections have been shown to stimulate increased collagen production within a month after treatment, for an anti-wrinkle benefit that lasts from six months to a year.

However, the hyaluronic acid molecule is too large to be effectively applied to the skin with available technologies, as the molecule cannot effectively penetrate the skin's top layer (Source: *Los Angeles Times*, June 7, 2010). What often occurs with conventional topical hyaluronic acid solutions is that they have a soothing, moisturizing effect on top of the skin but are unable to actually eliminate wrinkles because the product does not penetrate into the skin layers.

Convoy has already shown that its SPACE Peptide Technology is able to deliver large molecules past the stratum corneum and into the epidermis and dermis. Importantly, Convoy has also demonstrated the uptake of its peptide sequence by fibroblast cells, which may be a key advantage for the Company in terms of developing an effective topical hyaluronic acid product, and has shown proof of concept using its SPACE-Ethosome for improved delivery of hyaluronic acid into the skin.

### Injectable Hyaluronic Acid for Wrinkle Reduction

Existing products for wrinkle reduction typically function by changing the nature of the skin's structure (as in hyaluronic acid products), stretching the skin, filling in the depressions in the skin, or paralyzing the muscles that cause the skin to crease (e.g., Botox<sup>®</sup>). The leading hyaluronic acid dermal fillers for wrinkles are listed below. At present, each of these solutions must be injected into the skin and requires patients to visit an authorized treatment center or clinic to receive the injections, which can be an inconvenient and sometimes painful process. Moreover, injections must be continued for a lasting effect. An effective topical hyaluronic acid product to reduce wrinkles, such as that which Convoy expects to launch, could present a novel supplement to the injectable dermal filler marketplace. Convoy's cosmetics are targeted to help individuals maintain anti-wrinkle effects in between injections. In the future, the Company's technology may ultimately be able to replace current injectable dermal fillers, such as those below and other anti-aging injections (e.g., Botox<sup>®</sup>).

- Restylane<sup>®</sup> from Medicis Pharmaceuticals Corp. (acquired by Valeant Pharmaceuticals International, Inc. [VRX-NYSE] in December 2012)
- Juvéderm<sup>®</sup> from Allergan, Inc. (AGN-NYSE)

Overseas, a third major dermal filler for facial wrinkles is available: Emervel<sup>®</sup> from pharmaceutical company Galderma. Like Restylane<sup>®</sup> and Juvéderm<sup>®</sup>, Emervel<sup>®</sup> is an injectable system of clinically proven hyaluronic acid dermal fillers indicated for the treatment of facial lines, contouring, and volume loss (Source: Galderma). Emervel<sup>®</sup> injections have held a **CE Mark** since 2011 and are available in many countries across Europe and South America.

In addition to the above procedures, other non-hyaluronic acid-based cosmetics to reduce the appearance of fine lines and wrinkles include topical Vitamin A prescriptions (e.g., **retinol**) and creams that moisturize or replenish the skin's antioxidants as well as invasive techniques such as deep peels, microdermabrasion, dermabrasion, and **laser resurfacing**.



### Market for Anti-aging Products

By 2050, nearly two billion people over age 60 are expected to be alive, which is almost triple the 700 million people over 60 who were alive in 2009 (Source: United Nations' Department of Economic and Social Affairs, Population Division). Aging baby boomers with disposable income are increasingly seeking products and services to improve their appearance, including treatments and technologies to reduce the appearance of wrinkles and other external signs of aging-stimulating growth in the aesthetic market. Accordingly, in 2012, the U.S. market for cosmetic surgery, facial aesthetics, and medical laser devices was estimated at over \$3 billion, representing approximately a 10% increase over 2011 (Source: iData Research's U.S. Cosmetic Surgery, Facial Aesthetics and Medical Laser Devices Market, January 2013). Within this market, dermal fillers are one of the contributors together with Botox<sup>®</sup> top and



augmentation/reconstructive implants.

In addition, baby boomers are not the only population group desiring to maintain a youthful appearance. Younger populations (in their 20s and 30s) are increasingly seeking preventative solutions to aging, which may expand the market for products such as Convoy's hyaluronic acid-based cosmetics designed as a topical option for people who feel that they are too young for dermal filler injections. In 2010, the American Society for Aesthetic Plastic Surgery (ASAPS) reported that people aged 31 to 45 accounted for 43% of all cosmetic procedures and baby boomers, aged 51 to 64, accounted for 28% of such procedures (Source: FOXBusiness's Generation X Leads Boomers in Cosmetic Surgery Procedures, November 21, 2011). It is thought that younger individuals are attempting to use Botox<sup>®</sup> as a preventative technique against wrinkles. According to ASAPS, individuals between the ages of 19 and 34 represented 15.2% of the Botox<sup>®</sup> injection market in 2010.

As such, wrinkle treatments are expected to continue to be an expanding market going forward due to consumer demand for products that can reduce the appearance of fine lines, wrinkles, and age spots. As well, a growing acceptance of aesthetic procedures worldwide will likely broaden the pool of individuals considering cosmetic treatments to address the signs of aging (Source: Millennium Research Group's [a Decision Resources Group company] European Markets for Facial Injectables 2013, January 2013).

Major trends identified within the global aesthetic industry include a shift toward less invasive procedures as well as giving patients greater accessibility to products and services. One impetus for these changes has been recent economic fluctuations and uncertainties, which have led consumers to cut back on spending. Thus, many buyers are now opting for less expensive versions of professional aesthetic treatments that can be performed at home rather than in the clinic.



### Competition

The following summaries are not intended to be an exhaustive collection of other skin-based drug delivery technologies. Yet, they are believed to represent the type of competitive techniques that Convoy may encounter as it seeks to further develop and commercialize its SPACE Peptide Technology. Additionally, Figure 27 (page 34) summarizes many of the psoriasis treatments currently in development (as identified by the National Psoriasis Foundation). Convoy aims to launch a topical psoriasis therapy in 2014/2015.

### Massachusetts Institute of Technology (MIT)

http://web.mit.edu/newsoffice/2012/ultrasound-waves-and-drug-delivery-0914.html

Engineers from MIT have been working to refine the use of ultrasound waves as a method of drug delivery. In this technique, ultrasound is used to enhance the permeability of skin to medicines by delivering ultrasound waves to a section of skin and then applying the topical medicine to the treated part of the skin. Studies at MIT have shown that applying both low-frequency and high-frequency beams of ultrasound to the skin lightly wears away the top layer of skin (reported to be a pain-free and temporary effect), thus making the skin more permeable. The technology expands upon existing ultrasound drug delivery in that it employs both low- and high-frequency waves, versus only the low-frequency waves commonly used. Tests with pig skin found that the engineers' approach boosted the skin's absorption of both glucose and the inulin carbohydrate more than a single-frequency system. It is reported that ultrasound could be useful for improving the administration of topical steroids, systemic drugs, proteins (e.g., insulin), vaccines, acne treatments, psoriasis medications, and nicotine patches, among other molecules and patches already in use (Source: MIT News' "Getting (drugs) under your skin," September 13, 2012). Research is now focused on identifying additional ways to increase skin permeability even more, as well as on developing a prototype handheld ultrasound device that could enable practical use of the technology by physicians and consumers. Single-frequency ultrasound systems based on the work of MIT researchers have previously received FDA approval, although studies for a dual-frequency system have not yet been completed (Source: "Getting (drugs) under your skin").

### Zosano Pharma<sup>™</sup>, Inc.

http://www.zosanopharma.com/

Closely-held biopharmaceutical company Zosano Pharma (formerly known as the Macroflux Company) has developed a microneedle patch technology, called the ZP Patch Technology, which Zosano expected could be used to improve the delivery of a number of therapeutic molecules into the skin. The company has previously studied its ZP Patch Technology in combination with 30 compounds, including new chemical entities (NCEs) as well as reformulations of existing large molecules, small molecules, and vaccines. Among other molecules, Zosano's research included preclinical studies using the ZP Patch to administer cyclosporine A. However, the company's lead indication is a rapid delivery microneedle patch to treat severe osteoporosis, called ZP-PTH, which has shown safety and efficacy in Phase II clinical studies (Source: Zosano Pharma's *Pharmaceutical Development of Microneedle Patch Delivery Systems – Challenges and Process Development*, May 24, 2012). When applied to the skin using a special applicator, the drug-coated microneedle tips of the ZP-PTH patch reach past the stratum corneum and into the epidermis, where the osteoporosis therapy is deposited. Daily and weekly controlled-dose formulations are under development as an alternative to today's injectable treatments for osteoporosis. The company reports that its technology, while minimally invasive, is pain-free and simple to use, with reduced skin irritation since it passes the stratum corneum.

California-based Zosano was spun out of Johnson & Johnson's ALZA Corp. in 2006. The company reports that it holds more than 19 patent families in the U.S., 12 in the EU, and 20 pending patent applications. In October 2011, Zosano licensed the use of its ZP Patch technology to Japanese company, Asahi Kasei Pharma Corp., for the transdermal delivery of parathyroid hormone (PTH) to treat osteoporosis.



#### Pantec Biosolutions AG http://www.pantec-biosolutions.com/

Headquartered in Liechtenstein, Pantec is a biopharmaceutical company commercializing laser microporationbased transdermal drug delivery. In developing its technology, Pantec sought to create an alternative to injections for administering large-weight biopharmaceuticals. In order to deliver these medicines past the stratum corneum, the company uses its **P**recise **L**aser **E**piderm**al System** (P.L.E.A.S.E.<sup>®</sup>) microporation technology to pre-treat skin before administering a transdermal patch. The laser creates up to 5,000 micropores on the skin, through which medication can be delivered. The number of micropores generated allows for control over the dose administered. The company reports that its method improves drug absorption and reduces treatment duration without thermal damage of surrounding tissue.

The P.L.E.A.S.E.<sup>®</sup> system can also be used independently as an ablative laser in aesthetic dermatology. To this end, a CE-marked P.L.E.A.S.E.<sup>®</sup> Professional system is currently marketed in Europe as a medical device for dermatologists' use. An at-home system and combination systems of the laser with drug delivery are in development. Primary initial indications are for fertility drugs. Beyond infertility and in-office aesthetic dermatology, additional applications where Pantec may seek to commercialize its technology include non-melanoma skin cancers, asthma, skin rejuvenation, wrinkle reduction, and scar treatment. (Wrinkle treatments, melasma, and other pigmentation issues can already be treated by the technology at clinics in Europe.)

### Nitto Denko Corporation (6988-Tokyo)

http://www.nitto.com/product/industry/health/index.html

In May 2012, Nitto Denko, a diversified materials manufacturer in Japan, acquired Atlanta, Georgia-based Altea Therapeutics Corp. and Altea's active transdermal therapeutic system, the PassPort<sup>™</sup> system. Like the aforementioned P.L.E.A.S.E. technology, PassPort<sup>™</sup> combines microporation to generate pores on the skin with the subsequent application of a transdermal patch. With this approach, higher molecular weight molecules can be administered. Nitto Denko acquired this technology specifically to broaden the application of its own patch technologies, which had been limited to small molecule drugs. The company believes that it holds the highest global market share for conventional transdermal drug delivery patches for asthma and angina (Source: Nitto Denko's May 9, 2012, Press Release).



	Topi	cal Treatments in the Pipeline		
Drug Name	Company	Mechanism of Action	Phase	Indication
Calcipotriene foam	GSK	vitamin D3 analog		Psoriasis (pediatric
STF 115469)		U U		ages 2-11)
ofacitinib (CP-690,550)	Pfizer Inc.	anti-inflammatory (JAK kinase inhibitor)	Ш	Psoriasis
AN2728	Anacor Pharmaceuticals	anti-inflammatory (phosphodiesterase-4 inhibitor)	П	Psoriasis
A\$101	BioMAS Ltd.	anti-inflammatory (integrin inhibitor)	Ш	Psoriasis
CT 327	Creabilis Therapeutics	skin cell inhibitor (Trk kinase blocker)	П	Psoriasis
DPIV/CD26 (IP10.C8)	Immunotech	immune suppressant	Ш	Psoriasis
6201	Eisai Ltd.	anti-inflammatory (MEK kinase inhibitor)		Psoriasis
NCB18424 (ruxolintinib)	Incyte	anti-inflammatory (JAK kinase inhibitor)		Psoriasis
AS41004	Almirall, S.A.	anti-inflammatory/skin cell inhibitor (proprietary)		Psoriasis
.EO 80185 (Taclonex)	LEO Pharma	anti-inflammatory/skin cell inhibitor		Psoriasis
		(vitamin D/steroid)	"	(adolescents)
EO 90100	LEO Pharma	proprietary	П	Psoriasis
M518101	Maruho Co. Ltd.	anti-inflammatory/skin cell inhibitor (proprietary)	Ш	Psoriasis
РН-10	Provectus Pharmaceuticals	skin cell inhibitor (Rose Bengal)	II	Psoriasis
WBI-1001	Welichem Biotech Inc.	anti-inflammatory (proprietary)	Ш	Psoriasis
	Ora	al Treatments in the Pipeline		
Drug Name	Company	Mechanism of Action	Phase	Indication
Apremilast CC-10004)	Celgene Corporation	anti-inflammatory (phosphodiesterase-4 inhibitor)	Ш	Psoriasis and Psoriatic arthritis
CF101	Can-Fite BioPharma	anti-inflammatory (adenosine A3 receptor inhibitor)		Psoriasis
ofacitinib	Pfizer Inc.	anti-inflammatory (JAK kinase inhibitor)		Psoriasis and
CP-690,550)				Psoriatic arthritis
/oclosporin (ISA247)	Isotecknika	immune suppressant (calcineurin blocker)	111	Psoriasis
ACT-128800	Actelion	immune suppressant (S1P1 receptor agonist)		Psoriasis
AEB071	Novartis	anti-inflammatory (protein kinase C blocker)		Psoriasis
	Basilea Pharmaceutica			
Alitretinoin		skin cell inhibitor (retinoid)		Psoriasis (pustular
ASP015K	Astellas Pharma Inc.	anti-inflammatory (JAK kinase inhibitor)		Psoriasis
Apo805K1	ApoPharma	proprietary		Psoriasis
3MS-582949	Bristol-Myers Squibb	anti-inflammatory (p38 MAP kinase blocker)	II	Psoriasis
P187	Forward-Pharma GmbH	anti-inflammatory (fumaric acid)	П	Psoriasis
lectoral (Doxercalciferol)	Genzyme	skin cell inhibitor (vitamin D derivative)	Ш	Psoriasis
EO 22811	LEO Pharma	anti-inflammatory (proprietary)	П	Psoriasis
y3009104 (INCB28050)	Eli Lilly & Co.	JAK1 and JAK2 inhibitor	Ш	Psoriasis
SRT2104	GlaxoSmithKline	anti-inflammatory (sirtuin activator)	Ш	Psoriasis
/B-201	VBL Therapeutics	anti-inflammatory (oxidized phospholipid)	II	Psoriasis
		able Treatments in the Pipeline		
Drug Name	Company	Mechanism of Action	Phase	Indication
Brodalumab (AMG 827)	Amgen	anti-inflammatory (IL-17 receptor blocker)	III	Psoriasis
Cimzia (Certolizumab Pegol)		anti-inflammatory (TNF blocker)	III	Psoriatic arthritis
xekizumab (LY2439821)	Eli Lilly & Co.	anti-inflammatory (IL-17 blocker)	III	Psoriasis
/K-3222/SCH 900222	Merck	anti-inflammatory (IL-23 blocker)	III	Psoriasis
Secukinumab (AIN457)	Novartis	anti-inflammatory (IL-17 blocker)	Ш	Psoriasis and
				Description of a state of the
Jstekinumab (Stelara)	Janssen	anti-inflammatory (IL-12/-23 blocker)	III	Psoriatic arthritis

# Figure 27



### Milestones

### **Recent Milestones**

### 2013

Convoy launched a newly designed website to include information about its technologies in skin-penetrating treatments. The website contains detailed backgrounds on the Company's scientists, directors, officers, and technology, including how the technology can be applied in a variety of cosmetic and therapeutic uses.

Among other notable recent conferences, the Company attended the EBD Group AG's 7<sup>th</sup> Annual International Partnering Conference—"BIO-Europe Spring<sup>®</sup>"—held during March 2013 in Barcelona, Spain; the EBD Group's ChinaBio<sup>®</sup> Partnering Forum in May 2013 in Beijing, China; and the 15<sup>th</sup> Annual TIDES: Oligonucleotide and Peptide<sup>®</sup> Therapeutics From Research Through Commercialization, hosted by IBC Life Sciences (a part of Informa plc [INF-LON]) in Boston during May 2013.

### 2012

Convoy attended the Partnership Opportunities in Drug Delivery (PODD) conference in Boston, Massachusetts, where Company management presented its research to date on the SPACE Peptide and detailed its plans for this platform technology as a delivery system to transport macromolecules into the skin. The presentation included a discussion of Convoy's expedited development timeline and anticipated upcoming launch of two products: CycloPsorb<sup>™</sup> and HA-202PH (described in this report on pages 26-31).

Convoy raised approximately \$3 million to further develop its SPACE Peptide Technology.

Convoy's patent applications covering the SPACE Peptide Technology and its use as a drug delivery platform were published by the U.S. Patent and Trademark Office (USPTO) as well as the International Bureau of the World Intellectual Property Organization (WIPO). Greater details are provided on page 10.

### 2011

Scientific research was published in the *Proceedings of the National Academy of Sciences* journal that illustrated and validated the potential of the Company's SPACE Peptide sequence. The journal article, titled "Delivery of siRNA and other macromolecules into skin and cells using a peptide enhancer," is available at the following link: http://www.pnas.org/content/early/2011/09/07/1016152108.

### **Potential Milestones**

- Convoy is working toward multiple product launches over the next 12 to 24 months: (1) HA-202PH, a topical hyaluronic acid product to treat wrinkles, which could be launched as a cosmetic in the first quarter 2014; and (2) CycloPsorb™, a topical formulation of cyclosporine A to treat psoriasis, which may be on the market by 2015. Development timelines specific to each of these candidates are provided in Figure 2 (page 7).
- The Company is working to enter into strategic development partnerships, including potential co-development opportunities for HA-202PH and CycloPsorb<sup>™</sup>, as well as for a number of future and third-party therapeutic targets.
- The Company may consider an IPO in the first quarter 2015. In preparation for a possible IPO, Convoy aims to recruit a full-time CEO, CBO, CSO, and vice president of regulatory affairs along with certain key project management, logistics, R&D, and administrative and secretarial staff.



- Convoy has scheduled a number of events over the next several months in order to keep the medical and investment community updated on its technology development as well as to continuously seek out potential partnership or licensing opportunities. A selection of the upcoming events that Convoy is scheduled to attend include those listed below.
  - October 2013–3<sup>rd</sup> Annual Partnerships in Drug Delivery event in Boston
  - October 2013—BioJapan 2013 World Business Forum in Yokohama, Japan
  - o November 2013—BioEurope 2013 in Vienna, Austria


### **Key Points**

- The SPACE Peptide Technology is potentially a transformative method of drug delivery, as it may enable the conversion of many oral or intravenous dermatology medicines into more convenient topical forms. In addition to avoiding painful injections, effective topical compounds may be dosed less frequently as they avoid being metabolized too quickly by the gastrointestinal system (an issue with oral medicines) and may offer better efficacy through controlled-release administration and improved patient compliance.
  - The technology appears to have utility in the delivery of new compounds as well as established compounds that could benefit from improved skin penetration or more convenient administration.
  - To date, more than four years of research and millions of dollars in investment have gone into studying the SPACE technology. The technology's inventor, Professor Samir Mitragotri, director of the University of California, Santa Barbara's Center for Bioengineering, is chairman of Convoy's Scientific Advisory Board.
- To Convoy's knowledge, its SPACE Peptide Technology may be the first to effectively deliver large molecules into the skin and into the cytoplasm of cells. Consequently, continued development of the SPACE platform is elucidating a number of new opportunities in growing markets.
- The Company is initially exploring the application of SPACE Peptide Technology in three fields—(1) inflammatory dermatoses (e.g., psoriasis); (2) skin cancers; and (3) cosmetics and cosmeceuticals—although the Company actively seeks pharmaceutical or cosmetic strategic partners capable of developing the technology in any of its applicable arenas.
- Convoy's topical hyaluronic acid-based cosmetic line, HA-202PH, could achieve a market launch during 2014. The Company's HA-202PH cosmetic line of products, targeted to reduce wrinkles and minimize the signs of aging, will likely include an eye serum, night serum, moisturizer, and other products, sold via two channels: (1) directly by dermatologists/clinicians to their clientele; and (2) via top-shelf over-the-counter retail.
  - Aging baby boomers are increasingly seeking products to improve their appearance, primarily including treatments and technologies that reduce the appearance of wrinkles and other external signs of aging stimulating rapid growth in a more than \$3 billion U.S. cosmetic surgery and facial aesthetics market.
- Subsequently, Convoy plans to market a topical treatment for psoriasis, a chronic skin disease, by early 2015. The Company is studying the combination of its SPACE Peptide Technology with cyclosporine, a highmolecular-weight immunosuppressant compound that is known to be effective in severe psoriasis but that is only available as an injection or oral medicine for psoriasis patients today.
  - Results to date have demonstrated that the SPACE Peptide Technology can deliver more than 10% of the applied dose into the skin, which Convoy considers to be a key development in cyclosporine's topical delivery. Importantly, this was achieved without the need to attach the SPACE Peptide directly to the cyclosporine molecule—which Convoy believes is another competitive advantage of its technology.
- Worldwide, drug delivery was a \$101 billion market as of 2009, believed to be expanding at a 10.3% annual rate to reach \$199 billion by 2016 (Source: GBI Research and in-PharmaTechnologist.com, November 15, 2010). Medicines applied to the skin are estimated to account for between 12% and 15% of the global drug delivery market.
- Convoy holds an exclusive license to the SPACE Peptide Technology, and has filed patent applications for the technology in both the U.S. and under the global Patent Cooperation Treaty (PCT). A Freedom-to-Operate opinion has also been conducted by a patent attorney.



### **Historical Financial Results**

Convoy is a closely held company. As such, its financial statements have not been made publicly available. For further information regarding the Company's financial position, please contact Convoy directly as this data is only available under a Confidential Disclosure Agreement (CDA) from the Company.

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### **Risks and Disclosures**

This Executive Informational Overview<sup>®</sup> (EIO) has been prepared by Convoy Therapeutics Inc. ("Convoy" or "the Company") with the assistance of Crystal Research Associates, LLC ("CRA") based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in Convoy's public documents as well as other forms and materials released from time to time.

The content of this report with respect to Convoy has been compiled primarily from information available to the public released by the Company through news releases and its website and presentations. Convoy is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Convoy or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated by the Company in cash of forty-two thousand, five hundred U.S. dollars and forty-two thousand, five hundred warrants.

Readers of this EIO should carefully consider the risks and information about Convoy's business, as described below. Readers should not interpret the order in which considerations are presented in this or other documents as an indication of their relative importance. The risks and uncertainties overviewed in Convoy's materials may not be the only risks that the Company faces. Additional risks and uncertainties not presently known to Convoy or that it currently believes to be immaterial may also adversely affect the Company's business. If any of such risks and uncertainties develops into an actual event, Convoy's business, financial condition, and results of operations could be materially and adversely affected.

This report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. More complete information about the risks involved in an investment in the Company and additional information about Convoy is available on the Company's website at <a href="http://www.convoytx.com">www.convoytx.com</a>.

### **RISKS RELATING TO CONVOY**

### Convoy has a limited operating history and there is no assurance that it will achieve profitability.

Convoy was formed on September 21, 2011, and has had a very limited operating history. Convoy has not made any sales of its products or entered into any commercialization licenses thereto. Consequently, Convoy's proposed operations are subject to all of the risks inherent in a new business enterprise. Convoy has had no revenues to date on which to base an evaluation of its business and prospects. The likelihood of the success of Convoy must be considered in light of the delays, uncertainties, problems, expenses, difficulties, complications, and risks inherent in any new business, many of which may be beyond Convoy's control. There can be no assurance that Convoy will successfully develop and market its technology or achieve profitability.



### Convoy will be subject to extensive regulation.

The pharmaceutical, dermatological, and cosmetics industries are subject to extensive regulation; any or all of which may affect the regulatory and commercial potential of a contemplated product. The preclinical studies and clinical trials of any product incorporating Convoy's technology which may be developed by Convoy and its collaborators and the manufacturing, labeling, sale, distribution, export or import, marketing, advertising, and promotion of any of those products are subject to regulation by federal, provincial, state, and local governmental authorities, principally by the U.S. Food and Drug Administration (FDA) and by other similar agencies in other countries. Convoy's products must receive all relevant regulatory approvals or clearances before it may be marketed and sold in a particular country.

Convoy is planning to seek approval for its products in a new drug application (NDA) to be filed under Section 505(b)(2) of the Federal Food Drug and Cosmetic Act (the "Act"). These applications differ from a typical NDA (described under Section 505(b)(1) of the Act), in that they allow an applicant to rely, at least in part, on the FDA's findings of safety and/or effectiveness for a previously approved drug (the "referenced drug"). An applicant is permitted to submit reports of clinical investigations not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

However, Convoy still must provide certain additional preclinical or clinical data necessary to ensure that any differences of a SPACE-peptide containing product and a reference drug, as applicable, do not compromise safety and effectiveness. The scope and extent of testing under a 505(b)(2) application is highly variable and determined on a case-by-case basis. There is a risk that the FDA may require more extensive preclinical or clinical testing than originally contemplated under this approval pathway. The FDA also may decide that one or more products incorporating Convoy's technology is not eligible for 505(b)(2) approval, and that an NDA must be filed under a 505(b)(1), which would require further testing and likely result in additional uncertainty and costs.

There also are some regulatory challenges that are unique to 505(b)(2) applications. Unlike a 505(b)(1) NDA, wherein the applicant owns all the data necessary for approval (or has obtained the right to reference), the filing or approval of a 505(b)(2) application may be delayed due to patent or exclusivity protection on the reference drug. Applicants filing 505(b)(2) applications must include patent certifications in their applications relating to any patents pertaining to the reference drug, and must also provide notice of such certifications to the NDA holders of the reference drug. Such notice can provoke a legal challenge by such NDA holders.

### Convoy's product development programs are based on novel technologies, are at early stages of development, and are inherently risky.

Convoy is subject to the risks of failure inherent in the development of products based on new technologies. The novel nature of Convoy's technology creates significant challenges in regard to product development and optimization, manufacturing, government regulation, possible third-party reimbursement, and market acceptance. These challenges may prevent Convoy from developing and commercializing products on a timely or profitable basis or at all.

Convoy's technologies are at early stages of discovery and development, and the Company may fail to develop any commercially acceptable or profitable products. No product has yet been developed using Convoy's technology nor has Convoy entered into any collaborative commercialization and/or development agreement for any such prospective product. Convoy has not begun the process for obtaining approval to market any product incorporating its technologies and the Company does not generate revenues from the sale of any such products for human use or otherwise. Products using Convoy's technology will require significant additional clinical testing, additional development, and investment prior to commercialization. Such product development efforts may not be successfully completed, Convoy or its prospective collaborators may not be able to obtain required regulatory approvals, and Convoy is uncertain that any products, if developed and introduced, will be successfully marketed or achieve market acceptance.



The data obtained from preclinical and clinical activities are susceptible to varying interpretations and the successful completion of the regulatory process is uncertain. Convoy or its collaborators may encounter delays or have limits imposed on it or its collaborators or on Convoy's products, and Convoy or its collaborators may fail to obtain the regulatory approval or clearance required to commercialize its products. In addition, delays or rejections may be encountered based upon changes in regulatory policy during the period of product development and/or the period of review of any application for regulatory approval or clearance for a product. Delays in obtaining regulatory approvals or clearances would adversely affect the marketing of any products developed by Convoy or its collaborators, if any; impose significant additional costs on Convoy's expenditures and investment of time and effort, Convoy or its collaborators may never receive any required regulatory approvals or clearances for any of its products, which may be developed by Convoy or its collaborators may never receive any required regulatory approvals or clearances for any of its products, which may be developed by Convoy or its collaborators may never receive any required regulatory approvals or clearances for any of its products, which may be developed by Convoy or its collaborators may never receive any required regulatory approvals or clearances for any of its products, which may be developed by Convoy or its collaborators directly.

Moreover, if regulatory approval of a product is granted, such approval may entail limitations of the indicated uses for which it may be marketed. Further, even if such regulatory approval is obtained, a marketed product, its manufacturer, and its manufacturing facilities are subject to continual review and periodic inspections, and late discovery of previously unknown problems with a product, manufacturer, or facility may result in restrictions on such product or manufacturer, including withdrawal of the product from the market. Failure to comply with the applicable regulatory requirements can, among other things, result in fines, suspension of regulatory approvals, product recalls, operating restrictions, and criminal prosecution. Further, additional government regulation may be established, which could prevent or delay regulatory approval of Convoy's products.

Additionally, Convoy or its prospective collaborators are or may become subject to various federal, state, and local laws, regulations, and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, and the use, generation, manufacture, storage, air emission, effluent discharge, handling, and disposal of certain materials, including animal waste, used in connection with research and development work and the manufacturing operations. Convoy is unable to predict the effect of these rules and future government regulation on introduction of any of Convoy's potential products, Convoy's financial condition, or results of operations.

## Convoy is reliant on licensed intellectual property and must comply with third-party license agreements to maintain its rights.

The Company relies on licensed proprietary technology. Convoy has acquired worldwide exclusive rights to a portfolio of patented skin-permeating and cell-entering peptides (also referred to as the "SPACE" peptide) from the University of California, Santa Barbara (UCSB), through a certain Exclusive License Agreement, dated October 14, 2011 (the "License"). This License grants certain exclusive, royalty-bearing worldwide rights to make, have made, use, sell, offer for sale, import, and sublicense products and services, and practice methods, covered by certain Licensed Patents described in the License. As a condition to any sublicense, the License requires, in part, that Convoy pay to UCSB a percentage of any sublicense payments received by Convoy, excluding payments to be used for future research and development of the products and services, or debt or equity investments at fair market value rates.

Like any other conventional license, this License provides for various obligations of the parties. The failure to meet or otherwise cure deficiencies with respect to certain failed obligations may lead to termination of the License or a change in the license from exclusive to non-exclusive, and thus the potential loss of all or a substantial number of rights granted therein to Convoy. For example, Convoy is required to make certain minimum payments to UCSB to maintain its exclusive rights under the License. In addition, Convoy could also lose its rights to the License if it became bankrupt or insolvent, or if Convoy defaults on any of its obligations and fails to cure within a certain notice period. Finally, Convoy is required to meet certain development milestones in order to maintain its exclusive rights under the License.



### Convoy must pursue patent prosecution of its licensed technology and protect its confidential information.

Convoy pursues patent protection for its core technologies. Under the License Agreement, UCSB must diligently prosecute and maintain the licensed patents, and Convoy is required to reimburse UCSB for its documented costs in preparing, filing, prosecuting, and maintaining the licensed patents. If UCSB elects to relinquish control over such prosecution, Convoy would have the option and right to pursue such prosecution on its own.

The patent positions of pharmaceutical and biotechnology companies, including Convoy's and those of UCSB granted under the License, are generally uncertain and involve complex legal and factual questions. For example, there is always a risk that any licensed patents may be successfully challenged. While Convoy believes it has received sufficient assurances from UCSB under the License that they will take all steps necessary to protect Convoy's licensed intellectual property rights, there is no assurance that any such protection will be sufficient, or that any patents will not be challenged or replaced by superseding technology.

In addition to patent protection, Convoy also relies upon keeping information confidential and upon obtaining contractual non-disclosure agreements from various parties who may obtain access to Convoy's intellectual property. Nonetheless, Convoy may not be able to keep such information confidential and, should competitors or other interested parties obtain such information, Convoy's biotechnology rights and competitive advantage could be severely compromised.

### Convoy's business model exposes it to third-party intellectual property rights.

There is also a risk that Convoy's potential and its potential partners' products that incorporate Convoy's technology might infringe the patent, trademark, or other intellectual property rights of third parties. A freedom-to-operate patent investigation and analysis has been conducted for Convoy's SPACE peptides. To Convoy's knowledge, there have not been any recent claims or threats of litigation made against it based on any third-party patent, trademark, or other intellectual property rights. If the use of any of Convoy's technology and/or any prospective products based on Convoy's technology infringe the patents of others, Convoy may be required to design around such patents, potentially causing increased costs and delays in product development and introduction, or precluding Convoy and its collaborators from developing, manufacturing, or selling any of these planned products. Further, there is no assurance that technology developed by Convoy can be used in any of a number of potential applications without the use of other proprietary technology not owned or controlled by Convoy, which may not be available to Convoy on license terms acceptable to it or at all.

## Convoy's business plan calls for collaborative development of its products. If third parties with whom Convoy collaborates do not perform, Convoy may not be able to develop and market products as anticipated.

Convoy anticipates entering into collaborative arrangements with third parties to develop and market some or all of its products. Convoy cannot make assurances that these collaborations will be successful, lead to additional sales of Convoy's products, or lead to the creation of additional products. Dependence on collaborative arrangements with third parties subjects Convoy to a number of risks, including the following:

- Convoy's inability to fully control the amount and timing of resources its collaborative partners may devote to
  products based on the collaboration, and Convoy's partners may choose to pursue alternative products to the
  detriment of Convoy's collaboration;
- collaborative partners may not perform their obligations as expected;
- Convoy could become involved in disputes with collaborative partners, which could lead to delays or termination of the collaborations and time-consuming and expensive litigation or arbitration;
- collaborative partners may choose to terminate the applicable collaboration under various permitted and prohibited circumstances;



- Convoy's inability to fully control the sharing of Convoy's confidential information with third parties in furtherance of the collaborative development thereby potentially exposing critical and proprietary trade secrets relating to Convoy's technology; and
- potential misappropriation of sensitive intellectual property rights.

### Convoy has a history of losses and anticipates that it will continue to incur losses for the foreseeable future.

Convoy's efforts to date are focused on securing additional equity funding and/or collaborative arrangements to develop and commercialize its technology. If Convoy is unable to secure additional equity investments and/or collaborative arrangements with other biotechnology companies allowing them to develop and/or commercialize Convoy's technology, the Company will not be able to achieve profitable operations. Convoy incurred losses of \$119,742 for the fiscal year ended December 31, 2011. Until Convoy is able to generate substantial sales of its products or licenses of any rights thereto, it will continue to incur operating losses. Convoy currently does not receive any revenue from operations and does not expect to earn any significant revenues from operations until such time as the Company receives FDA approval and successfully commercializes its technology, secures a development license with a partner company, or is acquired by such a company. Either event is expected to take several years.

There is no assurance that Convoy will be able to secure additional financing or collaborative arrangements providing for the payment of royalties or other milestone payments on favorable terms or in amounts sufficient to cover Convoy's anticipated operating expenses or which provide for payment of such amounts on favorable terms and conditions. Even if Convoy does secure such collaborative arrangements, there is no assurance that Convoy will be able to meet the milestone conditions for any such milestone payments, or that a product utilizing Convoy's technology platform will ever be successfully commercialized. Even if one or more of Convoy's products are profitably commercialized, the initial losses incurred by Convoy may never be recovered.

## Convoy has limited capital resources and may not be able to obtain the significant additional capital needed to sustain its research and development efforts, bring its products to market, or to continue as a going concern.

Convoy has limited liquidity and capital resources and must obtain significant additional capital resources in order to sustain product development efforts and acquire technologies and intellectual property rights that may be important to Convoy's business, continue preclinical and clinical testing of Convoy's products, pursue regulatory approvals, acquire capital equipment, laboratory and office facilities, establish production capabilities, maintain and enforce Convoy's intellectual property portfolio, and support Convoy's general and administrative expenses and other working capital requirements. Convoy may not be able to obtain adequate financing or financing on acceptable terms to meet its capital requirements and obligations, which may require it to delay, curtail, or cancel further development of its technology. Given Convoy's history of losses and Convoy's business strategy, there is reasonable doubt that Convoy will be able to continue as going concern.

# Convoy needs to enter into and subsequently successfully manage corporate partnerships with third parties in connection with research, development, and commercialization of its products. There is no assurance that any of Convoy's efforts will be successful.

Convoy plans to enter into several essential relationships to develop and commercialize its potential drug targets. The success of Convoy's business strategy is therefore largely dependent on Convoy's ability to enter into corporate collaborations for matters such as the development of, clinical testing of, seeking regulatory approval for, and commercialization of Convoy's products, and to effectively manage the relationships that may come to exist as a result of this strategy. Convoy may be unable to establish any such corporate collaboration on favorable terms, or at all, which will require the Company to fund its own development of, clinical testing of, seeking regulatory approval for, and/or commercialization of Convoy's products, which it may not have sufficient capital to do. Even if Convoy is successful in establishing such corporate collaborations, these collaborations may not result in the successful development of products using Convoy's technology or the generation of significant revenues.



Since the success of Convoy's business is largely dependent upon its ability to enter into corporate collaborations and to effectively manage issues that arise from such collaborations, management of these relationships will require significant time and effort from Convoy's management team and effective allocation of Convoy's resources. Convoy also expects to dedicate substantial resources in identifying and developing relationships with potential collaborative partners.

## Convoy could be exposed to significant liability claims if it is unable to obtain insurance at acceptable costs and adequate levels or otherwise protect against product liability claims.

The testing, marketing, sale, and use of prospective products using Convoy's technology may entail risk of product liability. While Convoy does not anticipate engaging in direct product development within the foreseeable future, there may be instances where Convoy faces significant liability directly, particularly where liability can be linked to the product features created by the use of Convoy's technology. Such risk exists in human clinical trials and even with respect to those products that receive regulatory approval for commercial sale. Convoy can make no assurance that the Company can avoid significant product liability exposure. Convoy can make no assurance that it will be able to obtain appropriate levels of product liability insurance prior to any sale of these products. An inability to obtain insurance on economically feasible terms or to otherwise protect against potential product liability claims could inhibit or prevent the commercialization of these products.

Various testing, development, commercialization, and other agreements contemplated by the Company could require it to indemnify certain third-party activity and claims, and certain third-party activities (e.g., collaborator activities) may otherwise subject the Company to certain liability, whether or not the Company is otherwise insured against such claims by counterpart indemnification provisions in such contemplated agreements.

## Convoy is dependent upon its key personnel, who are necessary for the Company to achieve its scientific and business objectives. The loss of some or all of Convoy's key personnel would make it extremely difficult to manage business operations, and in such a situation, Convoy may not be able to develop new products.

As a technology-driven company, intellectual input from key management and scientists is critical to achieve the Company's scientific and business objectives. Specifically, Convoy depends on the continued services of John Muraski, Ph.D., Convoy's CEO, and Samir Mitragotri, Ph.D., Convoy's scientific advisory and other members of Convoy's Board of Directors. Consequently, Convoy's ability to retain these individuals, and attract other qualified individuals, is critical to the Company's success. The loss of the services of key individuals might significantly delay or prevent achievement of Convoy's scientific or business objectives. In addition, because of a relative scarcity of individuals with the high degree of education and scientific achievement required for Convoy's business, competition among biotechnology companies for qualified employees is intense, and as a result, Convoy may not be able to attract and retain such individuals on acceptable terms, or at all. In addition, because Convoy does not maintain "key person" life insurance on any of Convoy's directors, officers, employees, or consultants, any delay in replacing such persons, or an inability to replace them with persons of similar expertise, could have a material adverse effect on Convoy's business, financial condition, and results of operation.

Convoy does not have employment agreements in place for any key members of management at the present time. Instead, Convoy's key officers are made available pursuant to a Management Agreement between Convoy and ACTUS. Convoy has an equity incentive plan in place to attract and/or retain key individuals to stay with Convoy; however, there is no certainty that Convoy will sufficiently progress its development programs and/or market conditions will be sufficient to render such equity incentives as motivating to Convoy's key team members. As a result, such an incentive could be perceived to have little value to Convoy's employees and advisors. In such event, Convoy's key executives or advisors could be susceptible to being hired away by Convoy's competitors which may be able to offer a better compensation package.



### Convoy may have difficulties managing anticipated growth.

Convoy's anticipated growth may place significant demands on its management, capital, and other resources. If Convoy and its management team are unable to manage such anticipated growth effectively, this inability could have a material adverse effect on Convoy's business, financial condition, and results of operations. Convoy's ability to manage such anticipated growth effectively will require it to continue to develop and improve its operational, financial, and other internal systems, as well as its business development capabilities, and to train, motivate, and manage its employees.

### **RISKS RELATING TO THE INDUSTRY**

There are inherent risks in pharmaceutical and dermatological research and development. The marketability of any product developed by Convoy and Convoy's collaborators will be affected by numerous factors beyond the Company's control. Failure to obtain market acceptance for some or all of these products would have a negative impact on Convoy's revenue and ability to operate profitably.

Pharmaceutical, dermatological, biological, and cosmetics-based research and development is highly speculative and involves a high and significant degree of risk. The marketability of any of Convoy's products will be affected by numerous factors beyond Convoy's control, including the following:

- the discovery of unexpected toxicities or lack of sufficient efficacy of products, which make them unattractive or unsuitable for human use;
- preliminary results as seen in animal and/or limited human testing may not be substantiated in larger controlled clinical trials;
- manufacturing costs or other factors may make manufacturing of products impractical and non-competitive;
- proprietary rights of third parties or competing products or technologies may preclude commercialization;
- requisite regulatory pathways may prove more difficult than anticipated, and final approval for the commercial sale distribution of products may not be obtained; and
- other factors may become apparent during the course of research, up-scaling, or manufacturing, which may result in the discontinuation of research and other critical projects.

Convoy plans to conduct preclinical and clinical trials for its products and its other clinical product candidates, and it plans to commence additional trials of its product candidates in the future. Each of these trials, particularly clinical trials, requires the investment of substantial expense and time. The timing of the commencement, continuation, and completion of clinical trials may be subject to significant delays relating to various causes, including scheduling conflicts with participating clinicians and clinical institutions, difficulties in identifying and enrolling patients who meet trial eligibility criteria, failure of patients to complete the clinical trial, delay or failure to obtain Institutional Review Board (IRB) approval to conduct a clinical trial at a prospective site, and shortages of available drug supply. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the existence of competing clinical trials, and the availability of alternative or new treatments.



Clinical trials must be conducted in accordance with FDA or other applicable government guidelines and are subject to oversight by the FDA and IRBs at the medical institutions where the clinical trials are conducted. Convoy, the FDA, or other governmental agencies could delay, suspend, or halt Convoy's clinical trials or any of Convoy's product candidates for numerous reasons, including the following:

- deficiencies in the conduct of the clinical trial, including failure to conduct the clinical trial in accordance with regulatory requirements, or clinical protocols;
- deficiencies in the clinical trial operations or trial sites resulting in the imposition of a clinical hold;
- Convoy's products or product candidates may have unforeseen adverse side effects, including fatalities, or a
  determination may be made that a clinical trial presents unacceptable health risks;
- the time required to determine whether Convoy's products or product candidates are effective may be longer than expected;
- fatalities or other adverse events arising during a clinical trial due to medical problems that may not be related to clinical trial treatments;
- Convoy's products or product candidates may not appear to be more effective than current therapies or treatments;
- the quality or stability of Convoy's products or product candidates may fall below acceptable standards;
- Convoy's inability to produce or obtain sufficient quantities of the Company products or product candidates to complete the trials;
- Convoy's inability to reach agreement on acceptable terms with prospective contract research organizations and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different contract research organizations and trial sites;
- Convoy's inability to obtain IRB approval to conduct a clinical trial at a prospective site;
- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies, and increased expenses associated with the services of Convoy's contract research organizations and other third parties;
- Convoy's inability to recruit and enroll patients to participate in clinical trials for reasons including competition from other clinical trial programs for the same or similar indications; or
- Convoy's inability to retain patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy, personal issues, or who are lost to further follow-up.

In addition, Convoy may experience significant setbacks in advanced clinical trials (e.g., Phase III trials), even after promising results in earlier trials (e.g., Phase II trials). Setbacks could include unexpected adverse events, including events that occur when its product candidates are combined with other therapies, which often occur in later-stage clinical trials. In addition, clinical results are frequently susceptible to varying interpretations that may delay, limit, or prevent regulatory approvals. Negative or inconclusive results or adverse medical events, including patient fatalities that may be attributable to Convoy's products or product candidates, during a clinical trial could cause it to be redone or terminated or negatively affect Convoy's ability to market its technology or expand into other indications. Further, some of Convoy's clinical trials may be overseen by an Independent Data Monitoring Committee (IDMC), and an IDMC may determine to delay or suspend one or more of these trials due to safety or futility findings based on events occurring during a clinical trial.



## The commercial success of any products that Convoy may develop will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Any products that Convoy ultimately brings to the market, even if they receive marketing approval, may not gain market acceptance by physicians, patients, third-party payors, or others in the medical community. If these products do not achieve an adequate level of acceptance, Convoy may not generate significant product revenue and it may not become profitable. The degree of market acceptance of Convoy's drug candidates, if approved for commercial sale, will depend on a number of factors, including the following:

- the prevalence and severity of any side effects, including any limitations or warnings contained in the product's approved labeling;
- the efficacy and potential advantages over alternative treatments;
- the ability to offer Convoy's product for sale at competitive prices;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and the timing of market introduction of competitive products; and
- publicity concerning Convoy's products or competing products and treatments.

Even if a potential product displays a favorable efficacy and safety profile, market acceptance of the product will not be known until after it is launched. Convoy's efforts to educate patients, physicians, third-party payors, and the medical community on the benefits of Convoy's products may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by conventional technologies marketed by Convoy's competitors.

### Convoy will face intense competition. Many of Convoy's competitors have significantly greater resources than Convoy. Convoy may not be able to compete successfully based on many factors, including product price or performance characteristics. An inability to successfully compete could lead to the Company having limited prospects for establishing market share or generating revenues.

The market for Convoy's technology is large and competition is intense. Convoy's competitors includes major pharmacuetical and biotechnology companies, such as Nitto Denko Corporation (Japan), Pantec Biosolutions AG (Liechtenstein), Regeron, Inc. (Korea), Zosano Pharma<sup>™</sup>, Inc. (U.S.), Advancell (Spain), Phosphagenics (U.S.), and Revance Therapeutics, Inc. (U.S.). Many of these competitors are established companies that have the advantages of larger financial resources, extensive research and development capabilities, established distribution channels, broad name recognition, and significant market penetration. These competitors could use their resources to compete with Convoy by, among other ways, developing new and innovative products, conducting broad marketing campaigns, and lowering the prices of their products. Also, future competitors that are not currently serving Convoy's market area may enter at any time. These and other factors may limit Convoy's ability to generate commercial interest in its technology. Convoy cannot predict the effect of competition on its ability to gain market acceptance and operate profitably.

Convoy's competitors also compete with it in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to Convoy's technology. Convoy or its collaborators will face competition with respect to product efficacy and safety, ease of use and adaptability to various modes of administration, acceptance by physicians and customers, the timing and scope of regulatory approvals, availability of resources, reimbursement coverage, price, and patent position, including potentially dominant patent positions of others. An inability to successfully compete could lead to Convoy having limited prospects for establishing market share or generating revenues from its technology.



Convoy's technologies may become obsolete and it may not be able to meet the industry's evolving requirements. Failure to keep up with the technological advances and obtain market acceptance for some or all of the products using Convoy's technology would have a negative impact on Convoy's revenue and ability to operate profitably.

The pharmaceutical, dermatological, biological, and cosmetic industries are characterized by rapidly changing markets, technology, emerging industry standards, and frequent introduction of new products. The introduction of new products embodying new technologies, including new manufacturing processes, and the emergence of new industry standards may render any products using Convoy's technology obsolete, less competitive, or less marketable. The process of developing Convoy's technology is extremely complex and requires significant continuing development efforts and third-party commitments. Convoy's success will depend, in part, on its ability to continue to enhance Convoy's existing technology, develop new technological advances and emerging industry standards and practices on a timely and cost-effective basis. Convoy may not be successful in commercializing its technologies or exploiting its niche markets effectively or adapting its businesses to evolving customer or medical requirements or preferences or emerging industry standards.

### There are risks for potential changes in FDA regulatory requirements.

New pharmaceutical and biopharmaceutical products, and diagnostic agents and tests are subject to strict regulation by the FDA in the U.S. and by national and regional agencies abroad. Approval for new products can take up to 15 years and cost hundreds of millions of dollars. It is estimated that only one molecule in 10,000 is finally proven to be safe and effective, and is approved. Each year of delay in approval increases costs dramatically and reduces the remaining time before the expiration of relevant patents on the products. Should new legislation, political pressures, or administrative policies increase even more the time to approval, it could be very adverse for the pharmaceutical and biotechnology industries.

### Convoy's performance is affected by general economic and political conditions and taxation policies.

Consumer demand for Convoy's products may be impacted by financial and credit market disruptions, or other economic downturns in the U.S. or other nations. Convoy's results may be materially affected by changes in general economic and political conditions in the U.S. and other countries, the financial markets through which Convoy accesses capital, political unrest, and terrorist acts in the U.S. or other countries in which Convoy intends to carry on business.

The enactment of or increases in tariffs, including value added tax, or other changes in the application of existing taxes, in markets in which Convoy may be active in the future, or on prospective products that Convoy sells or with which Convoy's prospective products may compete, may have a material adverse effect on Convoy's business, results of operations, and financial condition.

## There has been no independent verification of the factual statements, and no independent due diligence of the forward-looking statements, made in the EIO (including these Risk Factors).

The factual statements made in the EIO (including these Risk Factors) are based upon information from various sources believed by Convoy to be reliable. Convoy has not independently verified any of such information and will have no liability for any inaccuracy or inadequacy thereof.

Furthermore, no independent party (including legal counsel to Convoy) has been engaged to verify the accuracy or adequacy of any of the factual statements contained in the EIO (including these Risk Factors) or to conduct due diligence with respect to the forward-looking statements contained in the EIO (including these Risk Factors). In particular, neither legal counsel nor any other party has been engaged to verify or conduct any due diligence regarding any statements relating to the experience, track record, skills, contacts or other attributes of the directors or executive officers of Convoy or to the anticipated future performance of Convoy.

THE FOREGOING LIST OF RISK FACTORS DOES NOT PURPORT TO BE A COMPLETE ENUMERATION OR EXPLANATION OF THE RISKS RELATING TO THE COMPANY.



### Glossary

**Abbreviated New Drug Application (ANDA)**—An application to the U.S. Food and Drug Administration (FDA) for a generic drug approval based on an existing licensed medication or approved drug.

**Capillary**—(Capillaries) Tiny blood vessels between arteries and veins that distribute oxygen-rich blood and nutrients to the body's tissues.

**CE Mark**—French for "Conformité Européene." A CE Mark on a product indicates that the product/medical device conforms to relevant EU directives.

**Cosmeceuticals**—Cosmetics that have or are purported to have medicinal properties.

**Cyclosporine A**—One of the immunosuppressant medications given after a transplant to prevent rejection. It has also been used to treat severe psoriasis.

**Dermal Filler**—A substance injected into the skin to restore volume to the skin and smooth out facial wrinkles. The dermal filler market comprises a variety of products prescribed to treat fine lines and wrinkles, plump lips, and improve other facial imperfections, such as scars.

**Dermatoses**—A disease of the skin, especially one that does not cause inflammation.

**Franz Diffusion Cell**—One of the most important methods for researching transdermal drug administration. This system is used to study the permeation of a drug on a certain type of membrane. A Franz Diffusion Cell system is composed of a receptor and a donor cell.

**Freedom to Operate (FTO)**—The ability of a company to develop, make, and market products without legal liabilities to third parties.

**H-Index**—An index that attempts to measure both the productivity and impact of the published work of a scientist or scholar. The index is based on the set of the scientist's most cited papers and the number of citations that they have received in other publications. The index can also be applied to the productivity and impact of a group of scientists, such as a department or university or country, as well as a scholarly journal.

**Hyaluronic Acid**—A polysaccharide found in large amounts in connective tissue, in the synovial fluid of the joints and the aqueous humors of the eye; a cementing and protective substance.

**Hydrophobic**—Tending to repel or fails to mix with water.

**Laser Resurfacing**—The laser removes thin layers of skin without damaging surrounding tissue. As the wound heals, new collagen is produced. The procedure is also used for removing scars, warts and birthmarks.

**Macromolecules**—Very large molecules, such as a polymer or protein, consisting of many smaller structural units linked together.

**Patent Cooperation Treaty (PCT)**—A unified procedure for simultaneously filing the same patent application in 146 countries (as of January 2013). The PCT process greatly facilitates filing patent applications in multiple jurisdictions worldwide; however, it does not grant an "international patent," which does not exist.

**Peptide**—A compound containing two or more amino acids where the carboxyl group of one acid is linked to the amino group of the other.

**Retinol**—A fat-soluble carotenoid vitamin (vitamin A) present in fish oils and green vegetables that is essential to normal vision and bone development, and that has been used to treat fine wrinkles and acne.



**Scopolamine**—A poisonous plant alkaloid used as an antiemetic in motion sickness, as a preoperative medication for examination of the eye, and formerly as a sedative and hypnotic.

**Silencing RNA (siRNA)**—SiRNA is a new class of therapeutics composed of nucleic acids, which must be able to cross the stratum corneum and enter the cells because the target of this class of therapeutics is within the cells. By combining siRNAs with the SPACE Peptide, researchers have demonstrated that Convoy's technology is able to deliver therapeutic quantities of siRNA into the skin and maintain its activity.

**Stratum Corneum**—The horny outer layer of the epidermis, consisting mainly of dead or peeling cells.

**Streptavidin**—A 60 kDa protein purified from the bacterium *Streptomyces avidinii*. Streptavidin is used for protein purification, protein detection, DNA hybridization, and immunological assays.



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### **EXECUTIVE INFORMATIONAL OVERVIEW<sup>®</sup>**

About Our Firm: Crystal Research Associates. (www.crystalra.com) is an independent research firm that has provided institutional-quality research on small- and mid-cap companies for the past decade. Our firm's unique and novel product, the Executive Informational Overview® (EIO), is free of investment ratings, target prices, and forward-looking financial models. The EIO presents a crystal clear, detailed report on a company (public or private) in a manner that is easily understood by the Wall Street financial community. The EIO details a company's product/technology/service offerings, market size(s), key intellectual property, leadership, growth strategy, competition, risks, financial statements, key events, and other fundamental information.

Crystal Research Associates is led by veteran Wall Street sell-side analyst Jeffrey Kraws, who is well known by the international financial media for his years of work on Wall Street and for providing consistent award-winning analyses and developing longterm relationships on both the buy-side and sell-side. He has been consistently ranked on Wall Street among the Top Ten Analysts for pharmaceutical stock performance in the world for almost two decades as well as ranked as the Number One Stock Picker in the world for pharmaceuticals by Starmine and for estimates from Zacks. Additionally, Mr. Kraws has been 5-Star ranked for top biotechnology stock performance by Starmine.

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