

Aposense's Apo-Si Technology Reached Successful Completion of its Proof of Concept(POC) Program, for the Trans-Membrane Delivery of Genetic drugs, for Gene Silencing

Aposense Ltd. [TASE: [APOS](#)] ("The Company") announced that it has successfully completed the Technological Proof of Concept (POC) program of its **Apo-Si Technology**, in the field of gene therapy. The **Apo-Si Technology** is an innovative delivery platform, for the delivery of genetic drugs across biological membranes. The **Apo-Si Technology** is developed for clinical applications, for silencing the expression of genes involved in disease processes. This platform has potential applications in a wide-array of medical disorders. The POC program of the **Apo-Si Technology** was initiated in August 2014.¹

The proof of concept program was conducted by the Company, according to a pre-defined Program, that was determined by the Company's Board of Directors, with the supervision of a Scientific Advisory Board (SAB). The POC program consisted of five stages: **(1)**.The design of innovative **Molecular NanoMotors (MNM)**, for the trans-membrane delivery of macromolecule drugs; **(2)**.Organic synthesis of the MNMs; **(3)**.Conjugation of the MNMs with siRNA Duplexes (siRNA: small interfering RNA);**(4a)**.Assessment MNM-mediated delivery of the Conjugates into cells; **(4b)**. Assessment of the biological performance of the delivered Conjugates, in exerting down-regulation ("silencing") of specific gene expression of in cell cultures *in vitro*;² and **(5)**. Assessment of the performance of the technology *in vivo* in rodents that included :**(5a.)**Bio-distribution of a Conjugate in the body following its intravenous administration;and **(5b.)**Evaluation of gene silencing exerted by the Conjugates following their intravenous administration.

All these goals were accomplished successfully by the Company. Following intravenous administration, the **Apo-Si Conjugates** manifested a desired bio-distribution pattern that included reaching various organs, followed by a slow and gradual clearance thereafter. In addition, in several independent and consecutive efficacy studies, a highly statistically-significant gene silencing effect was demonstrated, following intravenous administration of the Conjugates *in vivo*, as compared to control groups that included administration of siRNA without the MNMs; or included administration of **MNM-siRNA Conjugates** that was not specific to the target gene.In both control groups, no gene silencing was observed.

These results were presented, first to the SAB, and then to the Company's Board of Directors, which decided, on 11 July 2017, based on the conclusions of the SAB, that the results of these studies indicate that the Company has successfully completed the POC program, reaching all its predefined stages, including its primary objective, *i.e.*, **Proof Of Concept of the Technology(POC)** in a pre-clinical model *in vivo*.

This completion of the **Apo-Si POC** as aforesaid, meets a significant objective, set by the Company for the year 2017. The Company intends to continue the development plan of the **Apo-Si Technology**, which will include, among others, an optimization of the technology's pharmacokinetic profile, and concurrently, striving at formation of strategic collaborations

¹For more information on the Apo-Si project in particular and on the gene therapy field in general, see, *inter alia*, Section 5, 7, 10, 13 and 21 in Chapter A (Description of the Corporation's Business) of the Company's annual statement of 30 March 2017 [[MAGNA distribution system](#), Reference No. 2017-01-033762] which is incorporated herein by reference.

²It should be noted that these stages of the project produced a platform of a series of molecular, biologically-active **Molecular NanoMotors**.

with companies active in the field, for which the **Apo-Si Technology** may fulfill their unmet need for a delivery technology, that can carry genetic drugs across biological membranes in the body.

About the Apo-Si Technology

The Apo-Si Technology is an innovative gene delivery platform, for the delivery of genetic drugs, such as siRNA, through biological membranes in the body, for clinical use in a wide-array of medical disorders. This proprietary delivery technology, developed by **Aposense**, comprises innovative **MolecularNanoMotors (MNM)**, which are small, rationally-designed chemical compounds, based on the Company's core strength in the fields of biological membranes and their related electric fields. The MNMs recruit a recently-discovered, powerful source the energy that is located internally, within the depth of every biological membrane. This utilization allows **MNM-siRNA** conjugates to overcome the large energetic barrier, associated with delivery of macromolecule drugs across biological phospholipid membranes. A major application of the **MNM-siRNA Conjugates**, is "shutting down" ("silencing" or suppressing) the expression of specific genes, encoding for proteins that play a role in disease processes.

About the field of gene therapy

Gene therapy is a new field in medicine, based on utilizing genetic material (DNA or RNA) or their derivatives, in order to halt or slow-down disease processes. An important and innovative sub-field within the realm of gene therapy, is siRNA (small-interfering RNA), a therapeutic strategy, based on the administration of short sequences of RNA, designed to utilize an inherent intracellular molecular machinery, for knocking-down ("silencing") the expression of specific disease-related genes. These genes encode for proteins, which are involved in disease processes, either being the cause of the disease, or mediators in its evolution.

One of the major current limitations of gene therapy is the hurdle of the delivery of the large and highly-charged genetic constructs, through phospholipid membranes into cells. This limitation holds-back the entire field, and prohibits the introduction of novel genetic therapies for numerous medical disorders. To the best of the Company's knowledge, to date, **Aposense** is the only company that recruits the internal membrane electric field to provide the large energetic needs of the trans-membrane delivery of genetic drugs.

Cautionary Note Regarding Forward Looking Statements – the Company's assessments as aforesaid, regarding the Company's intent to engage a potential partner for continued, future research and development activity of a medical product/s based on the technology, the adjustment of the Pre-Clinical Trials' results in the course of additional Preclinical Trials and/or future clinical trials, such additional trials as are required for continued research and development and the approval of a medical product based on the technology, such regulatory tracks as are required for the purpose of developing such products, the dates of commencement and/or completion of clinical trials of such products (including proof of safety and/or efficacy in humans), the dates of obtaining approvals for the marketing of such products and the dates of commencement of the sales of such products in the various markets, are "Forward Looking Statements", within the meaning of this term in the Securities Law, 5728-1968, which contain prospective information which is based on many

factors and variables, among them assessments, decisions and intentions of third parties over which the Company has no control. In actual fact, the Company's assessments could change and/or be realized, all or part thereof, in a significantly different manner than its aforesaid assessments. Among the other factors which could cause material changes in the Company's assessments as aforesaid, one can note, inter alia, the need and/or prolongation of performance of Preclinical Trials and additional clinical trials in products developed by the Company and which are based on the technology and/or demands to perform repeated trials and/or expand them and/or improve them so as to adjust to specific applications, the establishment of regulatory tracks for the approval of such products, lack of success in proving their clinical efficacy and/or safety on the required dates (and/or at all) in humans, a change and/or exacerbation of the approval policy of the regulatory authorities with respect to the approval and registration for marketing of the Company's products which are based on the technology, the period of time required to obtain approval to market the product (if at all), lack of success in obtaining the additional financing required for completing the development of such products and/or lack of success in engaging in agreements for strategic collaborations for completing the development of the medical product (including by means of the provision of sublicenses), the entry of additional competitors into the target markets of such products, a change in the structure of competition in the markets for which such products are intended, technological developments which would obviate the use and/or application of the Company's technology, and additional risk factors applying to the Company's operations, as provided in Section 26 of Chapter A (Description of the Corporation's Business) of the Company's Annual Report for the year 2016 (as filed with the MAGNA) (the "2016 Annual Report"). It should further be emphasized that there is no certainty that additional Preclinical Trials and/or clinical trials would be successful, and the lack of success of trials might require an update of the research and development plans, the budgets and the schedules, and that the Company is exposed to additional risk factors as set forth in Section 26 of the 2016 Annual Report, which could, jointly and severally, significantly affect the Company's assessments as aforesaid.

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