



e-therapeutics plc

("e-therapeutics" or the "Company")

RNA Therapeutics Platform

Oxford, UK, 01 February 2021 – e-therapeutics plc (AIM: ETX) today announces the addition of its RNAi platform as a therapeutic drug modality.

- *Experiments underway to characterise GalNAc-siRNA platform and corresponding patent application has been filed, with additional applications to be filed shortly*
- *New team established to identify novel hepatocyte-expressed therapeutic targets, using generated hepatocyte-specific protein interactome*
- *The Company's proprietary GAINs functional genomics capability will provide genetic validation of new targets*
- *Informatics platform highly synergistic and will provide mechanistic insights into relevant biologic networks*

The Company has recently filed a patent application related to the chemistry of novel GalNAc-conjugated siRNAs (short interfering RNA), an important element of its RNAi platform that enables specific hepatocyte targeting for liver gene silencing. In addition, a number of siRNA constructs have been designed with potentially beneficial safety and potency profiles and additional patent applications are expected to be filed shortly. We believe that the new patent applications, combined with our know-how, will provide a significant competitive advantage in RNAi. The new constructs will include features to minimise potential microRNA off-target effects, thermally destabilising regions of the siRNA for reduced toxicity and important position-specific stabilisation chemistries to improve potency. Multiple *in vitro* and *in vivo* experiments are underway to test these constructs with contract research organisations in Germany and China.

We expect to offer our proprietary platform to potential business development partners in 2021-2022 and anticipate that these constructs will demonstrate at least equivalence to competitors' platforms. In line with our stated strategy of the capital raise of July 2020, we intend to advance high confidence candidates to *in vivo* studies to realise higher value through our partnerships.

Liver Target Group and Functional Genomics

Alongside our RNAi technology platform and significant in-house know-how in the field, our ability to investigate novel biology and drug targets using our computational platform will be a key differentiator from competitors in the RNAi space. Efforts in this area include proprietary data resources in hepatocyte biology using our hepatocyte-specific interactome,

which is an important and recently completed component. By leveraging our cutting-edge informatics platform alongside our novel RNAi technology platform, we believe that we can harness the many opportunities that the liver offers which have not yet been pursued by competitors.

A highly skilled team of scientists and physicians has been formed to identify novel hepatocyte-expressed targets for complex indications such as cardiovascular and metabolic diseases. This team will conduct validation of those targets in appropriate phenotypic assay systems and animal models and assess genetic support for the therapeutic targets using our functional genomics capability. To this end, headcount has increased over the past six months, from 15 to 25 FTEs at the end of 2020 with recruitment in all key areas of the Company.

Genome-Associated Interaction Networks (GAINs) for Genetic Validation

GAINs, a proprietary network biology-based functional genomics approach that places genes identified by GWAS (Genome Wide Association Studies) into their network context will play an important role in our RNAi platform. This approach permits identification of the processes that are affected by background variations in DNA and hence impact the risk of developing a particular disease. It also reveals mechanistic insights that are not resolvable at the individual SNP (Single Nucleotide Polymorphism) or gene level and not discoverable from the lists of genes typically generated by GWAS. GAINs technology enables actionable insights to inform target- or network-driven drug discovery to be derived from GWAS data. Typically, GWAS data yields tens or even hundreds of genetic variants identified as jointly contributing to disease risk, being of limited value for novel drug discovery and development.

Chairman & CEO Ali Mortazavi said: *“In 2020, the speed and specificity of RNA-based therapies have been further demonstrated with RNA-based vaccines against SARS-CoV-2. GalNAc-conjugated siRNA is amongst the most powerful and validated technologies in the RNA field. This class of therapeutics has a safety and performance profile which is now well established with approved drugs and a large human safety and efficacy precedent.*

Our platform has the significant and added advantage of being able to leverage our expertise in network biology. In an area where many monogenic and previously validated targets are being prosecuted by multiple companies, we are confident that we can harness the potent performance of the GalNAc-siRNA platform to derive novel biology and therapeutic targets using our computational approaches, particularly in complex polygenic disease. Genetic validation is a major de-risking checkpoint in drug discovery for many biopharmaceutical companies and we believe our informatic technologies such as GAINs will give us an edge over competitors in the space.

We believe that e-therapeutics offers a unique partnering proposition in hepatocyte-associated indications, as well as in other areas of biology given the disease-agnostic computational toolkit we have developed over many years. I would like to congratulate the

team on the speed of execution since our July 2020 capital raise and we look forward to the future with great confidence. In addition, we remain in business development discussions with potential partners using our informatics platform.”

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About e-therapeutics plc

e-therapeutics plc is an Oxford, UK-based company with a powerful computer-based approach to drug discovery, founded on its industry-leading expertise in network biology to fully capture disease complexity. The Company combines network science, machine learning, artificial intelligence, statistics and big data with expertise in drug discovery and development to transform the search for new medicines and intervention strategies.

e-therapeutics has developed an *in silico* laboratory that enables the rapid screening of millions of compounds and the identification of small sub-sets that are enriched for highly active hits. Its proprietary platform also has novel applications in functional genomics, being able to analyse complex genetic datasets, provide a deep understanding of pathological mechanisms and distil actionable insights for the discovery of novel drugs, biomarkers and diagnostics.

e-therapeutics has deployed and validated its disease-agnostic drug discovery platform both in house and with partners, including Novo Nordisk, Galapagos NV and a US-based, top 5 pharmaceutical company.