Executive Summary

Period 3 (January-December 2016)

Project rationale and overall objectives of the project

The European Bank for Induced Pluripotent Stem cells (EBiSC) Consortium will establish a facility for distributing qualified human, disease representative stem cell lines for research. The EBiSC cell line repository will make future drug development more effective and provide resources for future EU-funded iPSC projects.

Key objectives of EBiSC are to establish a single European iPSC repository with the unique identifying features of a catalogue created by user demand. It will: provide sustainable supply of quality assured, research grade lines on a not for profit basis; develop procedures for engaging a wide scientific and clinical community in a network of cell line derivation centres; apply scientific excellence for standardisation of optimised methodologies for deriving iPSC, their cryopreservation, recovery and differentiation; and demonstrate standards in quality control for the routine banking, characterisation and distribution of cell lines. The cell line distribution model will be supported by a harmonized ethics and legal governance framework and information management system developed to accommodate user-generated content. It will establish mechanisms to facilitate ongoing stakeholder enhancement of the biobanking process in support of a strategic business strategy based on a phased execution to ensure self-sustainability.

Overall deliverables of the project

Demonstrating effective project management, to include both strong financial and strategic leadership, developing the banking business rationale tuned to user's needs and linking this to an EBiSC brand are key deliverables from overall project development. A key consequence of developing a better understanding of user needs will lead to the recruitment of additional EPFIA companies as integrated partners.

Procuring existing cell lines and deriving new ones commissioned by partners to build a diverse collection, demonstrating effective infrastructure for their centralized processing and storage and international distribution by harmonized protocols, are core deliverables from the bank operations. Phenotypic assay data from the use of selected cell lines and gene edited derivatives from the collection will ensure that the project delivers validation on all elements of the cell line supply chain.

The project will provide deliverables that reflect a movement beyond current art status in platforms for improved cell processing, Quality Control testing, information management and innovation in human cell line banking governance models. Deliverables related to the development of an EBiSC cell line collection that researchers are using and operations for engagement with paying customers will be key for future self-sustaining business.

Summary of progress versus plan since last period

The EBiSC iPSC Catalogue consists of the two components*:*

***Foundational Collection*:** This has a cumulative total of **521** lines registered with data into the Human Pluripotent Stem Cell Registry (https://hpscreg.eu/). Of these approximately **330** cell lines are validated, and approximately **330** are available for purchase from ECACC, nearly tripling the total number of lines being processed since Periodic Report 2. Of the 387 cell lines, **162** remain accessible in the Collection on an Expand to Order basis, available to users once distribution stock is generated. Approximately two thirds of the lines with validated entries in the Collection have been deposited by the Wellcome Trust Sanger Institute from the HiPSCi pipeline (~210) and approximately 40% of these are available on an Expand to Order basis. Since the second project year, this represents an excess of a 6 times increase in deposition rate into the Collection. By the end of the third project year, the original commitment of number of cell lines to be made available from the HiPSCi project by the Wellcome Trust Sanger Insitute had been reached.

The EBiSC consortium has continued to provide research support to new project ideas for the generation of novel cell lines to supplement the collection. The Consortium Board has approved in year 3 a further 19 new sub projects, of which all except two involve EFPIA and EBiSC project beneficiary collaboration. Fifteen of these commissioned projects specifically focus on augmenting the Catalogue via the generation of new patient derived or gene edited cell lines, in direct response to EFPIA partner interests in accessing novel lines for 11 distinct classified diseases. Almost the entire remaining grant to support New Cell Line Commissioning (NCLC) projects was expended during Period 3. The total budget committed to these new projects was €2,979,039 of which €1,685,957 consists of grant and €404,421 EFPIA contributions .

The NCLC projects plan to make 265 patient derived cell lines, using 191 new donor samples procured from 11 clinical centres. Six of these centres are EBiSC partners and the remaining 5 are third party procured clinical samples, including from collaboration with the Cure Huntington's Disease Initiative (CHDI). An additional 35 new gene edited derivative lines were initiated. *Approximately 200 new lines will enter the Foundational Collection therefore during the project extension year 4, from these NCLC projects.*

Horizon scanning identifies new technologies for cell line characterisation, such as miRNA analysis with Sistemic, with which 40 iPSC lines were analysed and results reviewed by the Consortium.

***Collaboration Collection*:** (cell lines generated in other EU funded projects). Although the EBiSC Foundational Collection made significant strides to meet the original forecast of 1,000 deposited lines by the end of year 3, this was not achieved. This was in part due to delays in deposition of cell line cohorts from other large scale iPS collaborating research projects, which had originally been forecast to be included, notably StemBANCC.

Direct deposition from StemBANCC cell line owners into EBiSC is now in progress, facilitated by approval of the StemBANCC General Assembly and modification of their Project Agreement in order for formal recognition of the StemBANCC partners of Oxford, Newcastle and Kings as the StemBANCC cell line owners (depositors). The Universities of Oxford (80 cell lines) and Newcastle (165 lines) have signed the EBiSC deposition agreement and with subsequent execution of the agreement with Kings College London (36 lines), cell line transfer is anticipated in 2017 during the IMI-JU approved EBiSC project extension.

In addition to the collaboration with StemBANCC, EBiSC proactively initiated generation of 30 lines to facilitate the 'primed' start of the IMI-JU (Call 5) projects ADAPATED and PHAGO, . EBiSC partners with gene editing expertise initiated derivation, using EBiSC EFPIA in kind support, of approximately 20 novel lines with allelic variants of the ApoE locus to support the ADAPTED project and approximately 10 lines with allelic variants of the TREM2 and CD33 loci for PHAGO. All these lines will be accessible to the wider research community via the EBiSC iPS Catalogue.*Additional capability to integrate with other collaborative networks, further ensuring sustainability, has been demonstrated through a pilot study to test data integration and QC processing between the Bavarian stem cell network ForIPS and EBiSC.*

The public launch of the catalogue took place March 23rd 2016, as a result of a greater proportion of validated lines distributed to ECACC from the Central facility (Roslin Cell Sciences). It is forecast that the EBiSC iPSC Catalogue will consist of in excess of **1100** cell lines and associated data by the end of 2017 (Period 4).

Significant achievements since last report

The Foundational Collection has increased more than 3-fold in the overall number of lines released and made available in P3. Pleasingly this included the first EBiSC NCLC projects to complete in year 3, a key internal milestone reached by the Consortium. Successful demonstration that the EBiSC platform can function in support of other IMI-JU funded projects (ADAPTED, PHAGO) is a strong endorsement of the quality and future utility of the resource for EU research.

The iPSC Catalogue officially launched in March of P3 and collaborators are able to follow the project on twitter and other social networking sites to get latest updates on new cell line releases. Now that deposition agreements have been made with StemBANCC depositors, the expectation is that this large collection of lines will be added into the EBiSC iPS Catalogue of lines. The official launch of the iPSC Catalogue and availability of lines from ECACC has demonstrated the robustness of EBiSC data management systems, harmonising data flow across multiple organisations. Fraunhofer IBMT has developed a process for expanding cell lines as they progress through the workflow from thawing to banking with only one passage in a single vessel,

Since Catalogue launch the project has continued to maintain a high international profile through presentation at key meetings such as the Annual Meeting of the International Society for Stem Cell Research (ISSCR) and the European Society for Gene and Cell Therapy (ESGCT). EBiSC has been promoted through ECACC's monthly newsletter which goes out to 12,500 registered contacts worldwide. As recommended at Interim Review, a report on the Hot Start process was prepared and submitted for publication. EBiSC now has Twitter and LinkedIn accounts and regular posts are received. In support of dissemination and ECACC activities in cell line distribution, marketing campaigns have been established. The practical training courses and workshop provided by EBiSC continued to be popular events with high attendance and represent an international hallmark of success for the project in knowledge and expertise transfer.

Executive Summary

Period 3 (January-December 2016)

Amendment 2 to the Grant Agreement (GA) in support of new partners joining was approved by the IMI-JU, as well as the submitted Report for Period 2. Pfizer announced closure of research activities in the UK at the end of Period 2, but mitigated the adverse impact of this on EBiSC by continuing to co-ordinate the project throughout P3. A successful request to extend the project for 12 months, was approved by the IMI-JU, with a new Period 4 being added to the modified GA. This required some undertaking of work as budget underspends of some partners was identified, negotiations held between public partners and reallocations of unspent budgets agreed to beneficiaries who would have additional operational and administrative costs due to the extension of the project duration. Pfizer will continue to make in kind contribution during this P4, but will transition coordination of the project to EFPIA Partner 33 (JPNV), if approved. *Co-ordinated by Pfizer for thr third project year, the consortium has been overseen and managed via weekly Executive Office calls, monthly Consortium Board calls, bi-annual WP leader face-face meetings and an annual meeting of the General Assembly which* was held at Charité in Berlin in April 2016, in conjunction with meetings of the EFPIA representatives and WP leaders, who also met in October 2016 in Grimbergen/Brussels. Both allowed discussion of not only the scientific data generated within the consortia but also critical issues to ensure long-term sustainability of the bank.

Information on EBiSC
www.ebisc.eu
Contact
ebisc@eurtd.com

Access to the EBiSC iPSC Catalogue
https://cells.ebisc.org
Follow us on Twitter
@EBiSC_cells

The EBiSC project has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115582, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.