Summary of the context and overall objectives of the project

The objective of “proLungPlasma” was the clinical validation of a lung cancer test for the assessment of methylated DNA biomarkers prepared from DNA extracted from plasma.

The Epi proLung test provides an aid in the diagnosis of lung cancer in patients at increased risk for the disease. Lung cancer risk factors include patient life history, and/or presentation with symptoms, and/or radiological findings in the lung.

Methylation of DNA is an important epigenetic process involved in fundamental biological processes as development and cell differentiation. Aberrant DNA methylation plays a major role in cancer development.

Lung cancer remains one of the world’s most common and deadliest forms of cancer. While early detection is clearly beneficial for survival, there are no recommended screening methods in many parts of the world and lung cancer patients are usually diagnosed by the appearance of suspicious symptoms or accidentally by clinical imaging performed for other indications.

Recently, based on the evidence of a 20% mortality reduction in the National Lung Screening Trial (USA), a recommendation to screen patients with an elevated risk for lung cancer based on a smoking history and age was issued in the USA, using Low-Dose Computed Tomography (LDCT). To date, similar recommendations have not been made in Europe or the rest of the world, in part because LDCT is burdened by a high positive rate. As a consequence, as screening is implemented there will be a significant need for additional methods to distinguish between true and false positives and to clarify the clinical status of indeterminate positives.

Furthermore, regardless of the method of identification, clinical evaluation of patients with suspected lung cancer usually includes a Computed Tomography scan (CT-scan) of the chest and a bronchoscopy for definitive diagnosis. The latter is often used to confirm a lung tumour by pathological assessment of a cytological specimen obtained by rinsing the affected lung area. However, definitive diagnosis following an initial bronchoscopy is often not possible because either the tissue could not be collected or the cytological assessment is inconclusive and additional invasive diagnostic procedures are necessary. In this instance, a diagnostic test with a low false positive rate could reduce the need for risky, invasive and costly follow-up procedures and dramatically facilitate early treatment.

The newly developed Epi proLung Assay may serve as a tool for reducing false positive rates.

The objective of the business innovation project was to validate an epigenetic biomarker test for lung cancer detection in plasma samples. Development and clinical validation follow the current European IVD regulation. This business innovation project prepared a valid instrument for lung cancer detection. It delivers a molecular diagnostic instrument (IVD) for complementing systematic lung cancer screening for the very first time.

The resulting standard process for validation of all further test kits of Epigenomics’ Epigenetic Biomarker Test Platform will
enable Epigenomics to grow its MDx business for the detection of relevant cancers including colorectal, lung cancer, and others based on its outstanding portfolio of proven biomarkers.

Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

The project was completed successfully by registration of the CE marked validated Epi proLung product at the responsible agency (LAGeSo, Berlin, Germany) in Dec. 2017, and submission of all remaining deliverables to EU commission’s SyGMA webportal.

During the second reporting period, project management, product and manufacturing risk management (design control), compliance with regulatory and quality assurance requirements were continued as part of several work packages. Furthermore, management of a growing scientific network was continued leading to access to key opinion leader’s clinical expertise and their perception to the clinical value of the product. Additional research agreements with clinical sites were closed such that access to well annotated clinical specimens was secured. Several additional research questions regarding a wide range of biomarkers (proteins, DNA mutations, DNA methylation, micro RNAs, autoimmune antibodies) were triggered by discussions with these scientific partners. Clinical questions included disease monitoring, chemotherapy response, risk determination and screening eligibility. For clinical validation, enrolment of patients and collection of clinical specimens was coordinated with the clinical partners. These activities were followed by testing of clinical specimens, comparison to the patients’ clinical status, data analyses, and ultimately the evaluation of the clinical performance was conducted. Finally, the clinical validation study was completed within the duration of the project.

Meanwhile, analytical studies were continued, including generation of real-time stability data on product reagents. For the purpose of this project all studies were completed, even though additional data will be generated with respect to long-term stability of reagents.

The scale up of the manufacturing capabilities was implemented during the first reporting period. Pilot lots of the Epi proLung test kits were manufactured during this reporting period. Full manufacturing process validation was completed as well. Market research studies were conducted for Germany, Italy, and the USA aiming at information gathering for successful preparation of product launch. Based on these data and further acquired information a Strategic Marketing Plan was compiled.

Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)

Development of the Epi proLung test was conducted obeying scientific principles and regulatory rules. Research work conducted as pre-requisite to the final project goal has been summarized in scientific abstracts and were presented in scientific poster sessions at international cancer conferences in Europe, USA, and Japan. These results were furthermore described in a scientific manuscript that was published in the Journal of Thoracic Oncology (Weiss, G. et al. (2016) Validation of the SHOX2 / PTGER4 DNA methylation marker panel for plasma-based discrimination between malignant and non-malignant lung disease patients, JTO).

Epigenomics proposes the Epi proLung as a necessary and suitable tool for clarifying these indeterminate radiological findings. Successful deployment will lower false positive rates, reduce unnecessary procedures and associated psychological burdens, and would result in detection at earlier stages with better prognosis. In this regard, the Epi proLung is a highly anticipated prerequisite for successful implementation of lung cancer screening by LDCT in Europe.

The Epi proLung test will be Epigenomics’ second major product in the context of cancer screening after Epi proColon. After premarket approval by US FDA in April 2016 the Epi proColon product is available in U.S.A. (as US FDA approved IVD), in Europe (as CE-marked product), as well as in China (approved by the CFDA). Therefore, three major markets are addressed with this product. With the Epi proLung test Epigenomics will offer a second high impact product to these markets and potentially additional markets (Japan) supporting the ambition of the firm to
become a market leader in molecular diagnostics.