Hummingbird Diagnostics Announces Publication of Study on the Utility of miRisk, a Blood-based microRNA Analysis, to Predict Overall Survival for Advanced Non-Small Cell Lung Cancer in *npj Precision Oncology*

- *Results describe development of analysis to uncover association of several microRNAs with overall survival following initiation of immunotherapy*
- *Blood-based test holds potential for broad applicability for the management of patients with cancer*

HEIDELBERG, Germany, March 31, 2022 – Hummingbird Diagnostics GmbH, a leader in reading blood-based microRNAs for early disease detection and characterization, today announced the publication of a study in the journal *npj Precision Oncology* that describes the discovery and validation of miRisk, a first-of-its-kind microRNA (miRNA) biomarker signature that offers the prospect of a blood-based companion diagnostic for immunotherapy in advanced non-small cell lung cancer (NSCLC). The results of the study illustrate the development of miRisk and its prognostic value for overall survival following immunotherapy. The blood-based test holds the potential for broad applicability for the management of patients with cancer.

Biomarkers have been shown to help identify patients who are most likely to benefit from treatment with immunotherapies, such as PD-1/PD-L1-targeted therapies. Still, the gold standard of tumor tissue PD-L1 staining, as well as other biomarkers, such as tumor mutational burden, do not always accurately predict the efficacy of these therapies in patients. Immune cell-derived miRNAs reflect physiological and pathophysiological processes and can be sampled from peripheral blood. miRNAs are short non-coding RNAs that act as molecular rheostats that exercise control over the expression of most human genes. miRNAs are relatively accessible yet reflect complex underlying biology, offering the prospect of a blood-based companion diagnostic to determine the best candidates for immunotherapy.

"Immunotherapy has revolutionized the treatment of non-oncogene-driven advanced cancers, yet only approximately 30 percent of patients respond favorably to these treatments. Determining which patients will respond to these powerful therapies represents one of the greatest needs in oncology," said Bruno Steinkraus, PhD, Chief Scientific Officer of Hummingbird Diagnostics and leader of the published research. "This study illustrates the potential of how miRNAs taken from peripheral whole blood can be analyzed to predict the efficacy of PD-(L)1-targeted therapies in patients with NSCLC and improve patient outcomes. We thank all of our collaborators and patients for their vital contributions to this research."

The work, led by Hummingbird, was part of a collaboration with Priv.-Doz. Petros Christopoulos, MD, and Prof. Michael Thomas, MD, of the Thoraxklinik at Heidelberg

University Hospital, as well as Prof. Martin Reck, MD, of the LungenClinic Grosshansdorf.

"Patient stratification — identifying who will benefit from treatment and who will likely fail to respond or even come to harm due to adverse events — remains challenging, and there is pressing need for more accurate biomarkers for immunotherapy response prediction," said Jochen Kohlhaas, Founder and Chief Executive Officer of Hummingbird Diagnostics. "This work could broaden our general understanding of tumor immunobiology and, if validated, offers several important opportunities to improve management and outcomes of patients with advanced NSCLC and possibly other cancers."

Based on an analysis of whole blood miRNA profiling of 3 well-characterized cohorts consisting of a total of 334 stage IV NSCLC patients, the team discovered and validated a 5-microRNA risk score (miRisk) that is prognostic of overall survival following immunotherapy of either pembrolizumab or nivolumab. In a head-to-head comparison of miRisk and the gold standard PD-L1 tumor proportion score (TPS), the authors report superior diagnostic performance of miRisk compared to PD-L1 status. Of note, the miRNA signature does not require tumor tissue and could thus be employed in an off-the-shelf manner. The identified biomarker signature was traced back to a myeloid origin, especially neutrophils and macrophages, and miRNA target prediction was performed to identify a potential direct mechanistic link to the PD-L1 signaling pathway and PD-L1 itself. One example of a potential first clinical application is the selection of PD-L1-high patients for either single agent immunotherapy or chemo-immuno combination therapy where presently both options are licensed. In addition, miRisk measurements might provide a tissue-independent way of identifying by current standards ineligible patients who may benefit from immuno-monotherapy.

The open-access article can be found online on the journal's website: https://www.nature.com/articles/s41698-022-00262-y

About Hummingbird Diagnostics GmbH

Hummingbird is harnessing the predictive power of blood-borne miRNAs to provide insights into human health and disease. Analyzing miRNAs with Hummingbird's platform holds the potential for early disease detection, disease-specific prognostics, treatment response prediction, and the development of patient-centric therapies. To learn more, visit: https://www.hummingbird-diagnostics.com

Media Contact:
MacDougall Advisors
Matthew Corcoran
mcorcoran@macdougall.bio
+1 617-866-7350