

Presse release

New Micro-Simulation Study in Cancer Medicine Finds Epi proColon® Provides Clinically Meaningful Reductions in Incidence and Mortality of Colorectal Cancer

- *Adherence rates and screening intervals recognized as decisive elements of successful screening strategies*

Berlin (Germany), 29 November, 2019 – Epigenomics AG (FSE: ECX, OTCQX: EPGNY; the “Company”), today reported on micro-simulation model results indicating that Epi proColon®, a colorectal cancer (CRC) screening test approved for patients who are unwilling or unable to be screened by the United States Preventive Services Task Force (USPSTF) recommended methods, provides clinically meaningful reductions in the incidence and mortality of CRC comparable to those of USPSTF currently recommended methods. The micro-simulation model, developed and validated at Harvard Medical School, evaluated the impact of adherence rates, testing intervals and clinical performance of different screening strategies on CRC incidence and mortality. Results show that adherence rates and screening intervals can have a profound impact on the effectiveness of screening strategies as compared to one-time sensitivity and/or specificity. The study has been published in [Cancer Medicine](#).¹

“While colonoscopy-based screening for CRC offers the highest sensitivity of all available screening strategies, the results of this micro-simulation model demonstrate that patient adherence and prescribed screening intervals heavily influence the long-term clinical effectiveness for all CRC screening strategies,” said Daniel Sussman, MD, University of Miami Miller School of Medicine and an author on the publication. “Evaluating an environment where realistic colonoscopy adherence rates are less than 70% and the recommendation exists for ten-year intervals between colonoscopy screenings for individuals with average CRC risk, the findings of this study suggest that stool- and blood-based CRC screening strategies with higher adherence and considerably shorter intervals offer competing options to patients and clinicians in an effort to reduce CRC incidence and mortality. CRC is a disease that is largely preventable when detected and treated early.”

The study was conducted using an individual-level model to simulate the natural history of CRC and enables comparison of clinical benefits, harms, and burden of alternative strategies for CRC screening. The model was validated by comparison of predicted CRC incidence and mortality, adenoma dwell times, overall dwell times and lifetime risk of developing CRC with results from two large randomized controlled trials^{2,3} and those of the National Cancer Institute’s Cancer Intervention and Surveillance Modeling Network (CISNET) models.⁴

The model used a hypothetical cohort of individuals aged 50 years or older and emulated the distribution of baseline characteristics for subjects in the landmark clinical studies. Identical

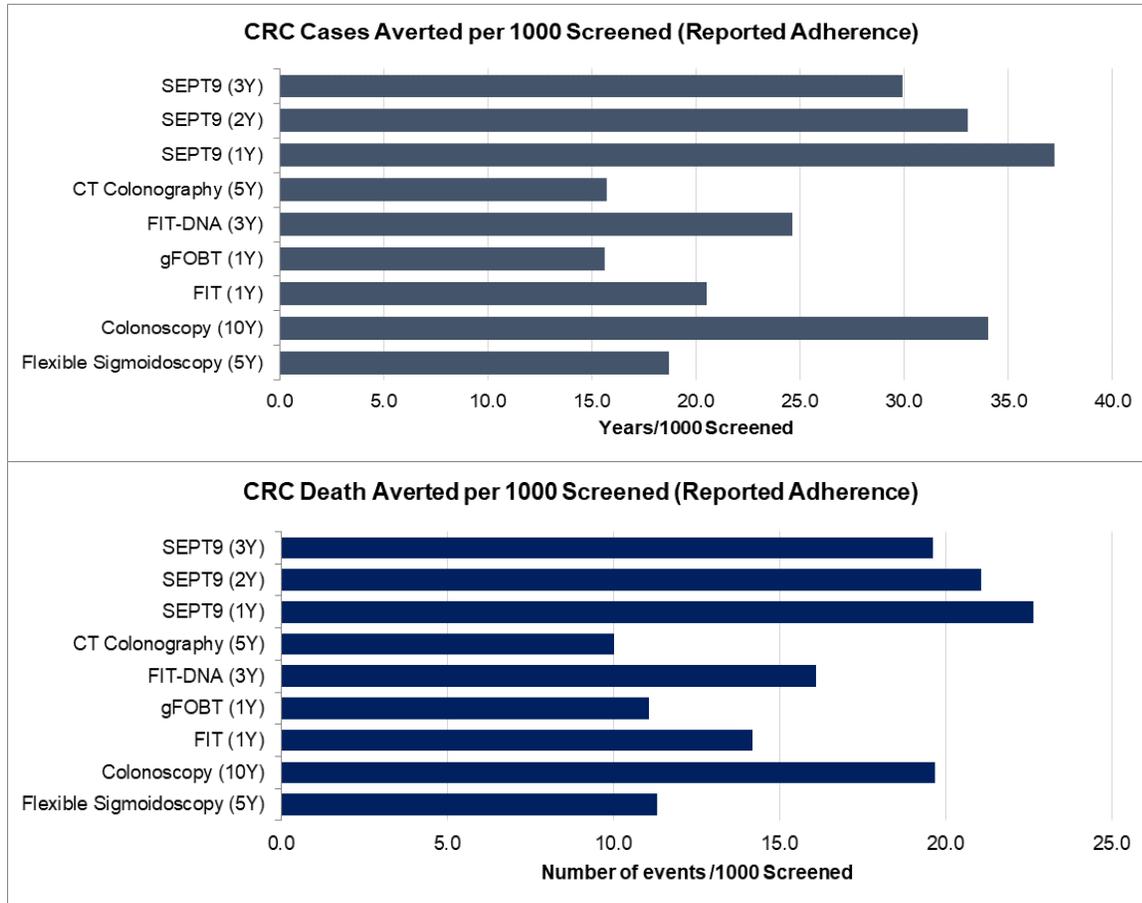
cohorts were then created and assigned to different screening strategies in order to compare intervention-related differences in outcomes. The strategies and intervals summarized in the table below were analyzed under two scenarios: 1) adherence fixed at 100%; 2) adherence based on published rates. Sensitivity analyses based on varying initial and resulting overall adherence rates were also conducted.

Screening Strategy	Screening Interval
No Screening	N/A
Flexible sigmoidoscopy (FS)	5 years
Colonoscopy (COL)	10 years
Fecal immunochemical testing (FIT)	1 year
High-sensitivity guaiac-based fecal occult blood testing (HS-gFOBT)	1 year
Multitarget stool DNA testing (FIT-DNA)	3 years
Computed tomographic colonography (CTC)	5 years
Methylated SEPT9 DNA blood test (SEPT9) (Epi proColon)	1, 2, or 3 years

Key findings from the study include:

- Assuming an adherence rate of 100%:
 - FIT-DNA, FIT, HS-gFOBT, and SEPT9 averted 42-45 CRC cases and 25-26 CRC deaths
 - COL averted 46 cases and 26 deaths
 - CTC averted 39 cases and 23 deaths and FS averted 32 cases and 19 deaths per 1,000 individuals screened
 - Estimated LYG were similar across FIT-DNA, FIT, HS-gFOBT, SEPT9, CTC, and COL strategies
- Based on reported adherence of eligible individuals to CRC screening, per 1000 individuals screened, colonoscopy produced the best outcomes unless a non-invasive method achieves a 65% - 70% or greater adherence rate
- Screening individuals with COL every ten years or SEPT9 every year (assuming reported adherence rates) resulted in more favorable outcomes compared to all other strategies (see figure below)

- The impact of analytic performance on screening outcomes is heavily influenced by adherence rates and screening interval



“The key take away from this study is that Epi proColon done annually can serve as an effective non-invasive CRC screening strategy that can provide long-term benefits similar to those of other currently recommended CRC screening methods with harms lower than those reported for colonoscopy. Most importantly, however, as stated by the authors, even for tests with the highest accuracy, such as colonoscopy, the benefit of screening could be muted by a suboptimal uptake and therefore we agree with many experts in the field in saying that the best test is the one that gets done,” said Dr. Jorge Garces, President and Chief Scientific officer at Epigenomics AG.

“We hope that this study will spur discussion within the gastroenterology community and between physicians and their patients about how to best deploy all available screening strategies to reduce CRC incidence and deaths and improve patient outcomes,” said Greg Hamilton, CEO at Epigenomics AG.

About Colorectal Cancer (CRC)

Colorectal cancer remains a leading cause of cancer death in the United States. Although screening and early detection of colorectal cancer can save lives, about 35% of eligible U.S. patients are not being screened regularly. The unscreened population disproportionately results in 43% of new colorectal cancer cases and about 76% of colorectal cancer deaths and costs. Approximately \$18 billion is spent annually on this preventable disease. Over \$13 billion is spent on cases from unscreened individuals.

By increasing screening and detecting more cancers early, the costs and deaths from this disease both can be addressed.

About Epi proColon®

Epi proColon® is indicated for colorectal cancer screening in average-risk patients who are unwilling or unable to perform colorectal cancer screening by colonoscopy and stool-based methods. It is a qualitative, in vitro diagnostic blood test for CRC that uses real-time PCR to detect methylation of a target DNA sequence within the Septin 9 gene promoter; methylation of this DNA sequence is associated with the occurrence of CRC and can be detected in cell-free DNA that circulates in the plasma.

For patients, the test only requires a simple blood sample draw as part of routine healthcare provider visits. There are no dietary restrictions or alterations in medication required for the test. The sample will be analyzed at a national or regional diagnostic laboratory.

Epi proColon is recipient of the 2019 Excellence in Molecular Diagnostics by Corporate LiveWire's Innovation and Excellence Awards.

For more information on Epi proColon, visit www.epiprocolon.com.

About Epigenomics

Epigenomics is a molecular diagnostics company focused on blood-based detection of cancers using its proprietary DNA methylation biomarker technology. The company develops and commercializes diagnostic products across multiple cancer indications with high medical need. Epigenomics' lead product, Epi proColon, is a blood-based screening test for the detection of colorectal cancer. Epi proColon has received approval from the U.S. Food and Drug Administration (FDA) and is currently marketed in the United States, Europe, and China and selected other countries. Epi proLung® and HCCBloodTest, blood-based tests for lung and liver cancer detection, has received CE mark in Europe.

For more information, visit www.epigenomics.com.

References

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⁴ Joseph DA, King JB, Richards TB, Thomas CC, Richardson LC. Peer Reviewed: Use of Colorectal Cancer Screening Tests by State. Preventing chronic disease 2018; 15.

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