

Focus → PRESEPT

ANNUAL REPORT 2008

# Highlights \_\_ 2008 / 2009

## Progressed colorectal cancer screening program

- Positive clinical data for <sup>m</sup>SEPT9 biomarker from two case-controlled studies
- Initiated PRESEPT Study for <sup>m</sup>SEPT9 validation in a screening population
- Partnered <sup>m</sup>SEPT9 with Quest Diagnostics and Sysmex Corporation
- Progressed IVD development with Abbott Molecular according to plan and expanded partnership to include PRESEPT

## Advanced pipeline development

- Presented clinical data on lung cancer biomarkers in two application areas
- Generated further feasibility data on a prostate cancer urine test
- Validated <sup>m</sup>PITX2 test for prostate cancer prognosis
- Prepared <sup>m</sup>PITX2 commercialization through “Early Access Program” and partnering
- Signed collaboration agreement with Philips for IVD platform development

## Increased focus on commercialization

- Launched first Research-Use-Only (RUO) products
- Hired Senior VP Product Development as well as Head of Marketing & Sales

## Strengthened intellectual property position

- Obtained allowance for key patents in EU
- Licensed several technologies to Philips, OncoMethylome Sciences, and DxS

## Strengthened financial position

- Raised new capital
- Reduced cash burn

» Our mission: To build a world-leading cancer molecular diagnostics company based on DNA methylation.«

Epigenomics focuses on the development and commercialization of molecular diagnostic products for the early detection and diagnosis of cancer.

Our products in development are innovative in addressing highly unmet diagnostic needs to the benefit of patients and serving the highly attractive market of molecular cancer diagnostics.

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## Group Key Figures

EUR thousand (unless stated otherwise)	2007	2008
Revenue	2,567	2,586
Research and development costs	-10,471	-10,028
Earnings before interest and taxes (EBIT)	-13,504	-12,750
Earnings before interest, taxes, depreciation and amortization (EBITDA)	-12,259	-10,242
Net loss for the year	-13,151	-12,271
Weighted-average number of shares issued (notional par value: EUR 1)	17,807,258	26,007,110
Earnings per share (basic and diluted) in EUR	-0.74	-0.47
Cash flow from operating activities	-11,516	-9,800
Cash flow from investing activities	1,049	1,468
Cash flow from financing activities	4,547	11,500
Cash flow total (incl. currency adjustments)	-5,920	3,168
EUR thousand (unless stated otherwise)	31.12.2007	31.12.2008
Liquid assets at balance sheet date (incl. marketable securities)	10,016	12,100
Total equity at balance sheet date	17,821	16,568
Equity ratio in %	77.8	81.7
Total assets at balance sheet date	22,914	20,283
Share price at balance sheet date in EUR (Xetra)	1.95	2.00
Number of employees at balance sheet date	112	90

- Successful financing through rights issue strengthened financial position
- Significant revenue through successful technology licensing
- “Epi 2010” initiative extended liquidity well into 2010 and transforms Company into commercially-driven enterprise

# Products under Development

Indications & Applications	Marker Identification	Clin. Proof-of-Concept	Clinical evaluation	Research assay & EAP**	LDT*** Dev. & launch	IVD Dev. & launch	Marketing & Sales by
<b>Colorectal cancer</b>							
Screening (blood)	mSEPT9			Q1 / 09		Q4 / 09	Epigenomics, Quest Diagnostics, Abbott, Sysmex
	OTHER BIOMARKERS						
<b>Lung cancer</b>							
Screening (blood / sputum)	1-3 BIOMARKERS						
Diagnosis (BL* / brushings)	mSHOX2 + OTHERS			Q4 / 09		H1 / 10	Epigenomics
<b>Prostate cancer</b>							
Screening (urine)	1-3 BIOMARKERS						
Diagnosis (biopsies)	mGSTP1			Q1 / 08			Epigenomics, Quest Diagnostics
Prognosis (surgical tissue)	mPITX2			Q2 / 09			Epigenomics & Partner

\* Bronchial lavage  
 \*\* Early-Access-Program  
 \*\*\* Laboratory-developed Test

## Letter to Shareholders

### Dear Shareholders,

The year 2008 has been a very rewarding and exciting one for Epigenomics. After realigning our strategy in 2007 and signing a first nonexclusive partnering deal for our colorectal cancer program with Abbott Molecular, we spent 2008 focusing on executing our business plan. Following the successful capital raise in February 2008, two important licensing deals signed with Quest Diagnostics and OncoMethylome Sciences, a cross-license agreement with DxS and several service agreements with pharma partners, we signed an R&D and licensing agreement with Philips late in the year. The focus of this agreement is to determine the feasibility of DNA-methylation-based cancer tests on the future Philips molecular diagnostics platform. We will continue executing on our nonexclusive licensing strategy and have done so by signing an R&D collaboration with Japan-based Sysmex for our colorectal cancer blood test in early 2009. This agreement is another important step towards the commercialization of our <sup>m</sup>SEPT9 biomarker for colorectal cancer blood testing. It validates the clinical utility and the commercial attractiveness of our approach to colorectal cancer diagnostics as well as our nonexclusive partnering strategy.

On the operational level, our focus has been on driving the product development for our lead development programs. We have made significant progress in our colorectal cancer blood test development during 2008. Using the optimized and streamlined workflow, we successfully completed two case control studies in over 500 blood samples, validating the excellent performance of our <sup>m</sup>SEPT9 biomarker. Based on these results, Abbott Molecular as well as Quest Diagnostics moved forward with the development of an IVD test kit on the *m*2000 platform and a laboratory-developed test (LDT) for the U.S. market, respectively. We have also successfully completed beta testing of our <sup>m</sup>SEPT9 Research-Use-Only (RUO) kit in late 2008 and have transferred the workflow enabling first customer laboratories in Europe to offer <sup>m</sup>SEPT9 testing to aid the early diagnosis of colorectal cancer.

We have initiated PRESEPT, a large prospective clinical study, to demonstrate the performance of our <sup>m</sup>SEPT9 blood test in an U.S. screening-guideline-eligible population. The study aims at identifying around 50 colorectal cancer cases in about 7,500 subjects. To that end, we have built a network of about 22 clinical centers in the United States and in Germany. By the end of February 2009, we have successfully enrolled over 3,000 subjects into PRESEPT and have successfully identified many cancer cases. We expect to complete the PRESEPT Study in late 2009.

As part of the development of our tissue-based prognostic prostate cancer test, we successfully completed a clinical validation study demonstrating impressively the value added by our <sup>m</sup>PITX2 biomarker in discriminating patients with a high risk and low risk of biochemical recurrence following surgical removal of the prostate. We plan to make a testing service for <sup>m</sup>PITX2 available in collaboration with one or more European laboratories in the first half of 2009. Beyond this early access program, we are in ongoing partnering discussions with several interested parties that may help to optimally leverage the commercial value of this asset. During 2008, we also generated additional data on the diagnosis of prostate cancer in tissue as well as urine samples. As a first product in this area, in collaboration with our partner TIB Molbiol we have launched the LightMix® Kit GSTP1 for DNA methylation analysis of the GSTP1 gene as a research product in Europe. For commercialization in the United State we recently licensed the <sup>m</sup>GSTP1 biomarker to our partner Quest Diagnostics.

In our lung cancer program, we successfully completed another clinical study in over 250 patients and controls in 2008, successfully showing to demonstrate proof of concept for detecting lung cancer in blood

samples with our proprietary biomarkers. In addition, we have also shown significant progress in our second lung cancer project aiming at improving cancer diagnosis after a positive finding in a spiral CT scan. Here, we successfully completed a study with routinely obtained bronchial lavage samples of several hundred patients showing that our biomarkers can potentially be used to objectively confirm the CT result. With this success and a thorough assessment of the market opportunity, we decided to move forward in the development of products for this application.

As part of our transformation into a fully integrated molecular diagnostics company, we have systematically built Epigenomics' management team after the departure of former COO and former CSO. We have increased our product development capabilities by hiring a very experienced Senior VP Product Development, Dr. Uwe Staub, who joined us from Qiagen, and we have added to our molecular diagnostics marketing expertise with the hire of Dr. Friederike Gerdes as Head of Marketing & Sales who joined us from Agendia. She reports to Dr. Achim Plum, who since April 2008 also oversees our Business Development and our Corporate Communications as Senior VP Corporate Development. Most recently, Dr. Andrew Sledziewski has taken over as Global Head of Research at Epigenomics after heading our diagnostics research in Seattle for the past eight years.

Looking back on 2008, we have delivered on virtually all our promises. In all of our product programs, we have shown significant development progress and continued solid execution on the partnering front in managing our existing alliances and entering into new ones. Financing was secured to execute our business plan and we further implemented our "Initiative Epi 2010", both geared at evolving the organisation towards a more product-driven and commercially focused enterprise. We successfully implemented the necessary organisational changes and centralized the laboratory-based R&D in Berlin and focused the Seattle operation on managing large clinical trials such as the PRESEPT Study. We have achieved our primary financial goal of reducing cash burn to less than EUR 10 million while laying the foundation for top-line revenue growth at lower operating costs going forward.

The year 2009 will be another defining one for Epigenomics. We will continue the process of evolving Epigenomics into a fully integrated molecular diagnostics company. In 2009, we anticipate Quest as well as Abbott launching our colorectal cancer product in the market. At the same time, we expect to see the introduction of testing services for our biomarker <sup>m</sup>SEPT9 as well as tests for <sup>m</sup>PITX2 and <sup>m</sup>GSTP1 methylation in a selected number of European laboratories that make use of our RUO assays for these biomarkers. We will continue expanding our base of commercial partners and will continue to drive our development programs further.

Epigenomics is now even better positioned to deliver on its mission of bringing innovative diagnostic tests for cancer to the market, for the benefit of cancer patients throughout the world.

On behalf of the Executive Board, I would like to thank our employees, our partners, our customers, and in particular our shareholders for their commitment and trust in our organization. I am convinced that 2009 will turn out to be another very rewarding year for Epigenomics.

Yours sincerely,

Geert W. Nygaard



Geert Walther Nygaard  
CEO

# Report of the Supervisory Board

## Dear Shareholders,

As in the years before, the Supervisory Board during the fiscal year 2008 fulfilled all its duties assigned to it by law, the Articles of Association and the Rules of Procedure. The Supervisory Board advised and monitored the Executive Board in managing the Company. Based on detailed written and oral reports of the Executive Board and intensive discussion of all relevant issues concerning financial and operational business aspects as well as the Company's strategy during the Supervisory Board's meetings, our advice was given with a view to the best interests of Epigenomics' shareholders. Due to the changes in the composition of the Executive Board following the departures of Christian Piepenbrock, COO, and Dr. Kurt Berlin, CSO, the dialog between all members of the Supervisory Board and the Executive Board was further intensified and several conference calls as well as individual discussions were held. Thus, the Supervisory Board was kept continuously informed about the Company's financing efforts during the rights issue in difficult market conditions, the business strategy, and product development progress with key focus on the PRESEPT Study as major value driver. The Supervisory Board was also apprised of all corporate planning including financial, capital expenditure and human resources planning, as well as the general performance of the business. To the extent that German corporate law or existing Executive Board Rules of Procedure require approval for certain decisions or actions to be taken by the Executive Board, such approvals were given by the Supervisory Board after a detailed examination of the documentation provided and intensive discussions.

### *Work of the Supervisory Board*

During 2008, five ordinary plenary meetings of the Supervisory Board with the Company's Executive Board took place on February 6; March 25; June 3; September 16; November 18. These meetings were held in Berlin to cost-efficiency. Also, three conference calls between the Supervisory Board and the Executive Board were held at regular intervals throughout 2008 to discuss all important aspects of the ongoing financing transaction and organizational changes. In addition, the Chairman of the Supervisory Board and the members of the Executive Board were in regular contact between Supervisory Board meetings. Thus, the Supervisory Board was kept up to date on the Company's current business situation and key events, such as the capital increase by means of the rights issue in February 2008 as well as the closing of the nonexclusive strategic licensing deals with OncoMethylome Sciences and Quest Diagnostics.

At all of its meetings, the Supervisory Board specifically discussed the Company's corporate and financial situation, the progress of its product development programs, its business development priorities and activities as well as the Company's business strategy. Important topics of the Supervisory Board meetings in 2008 were the approval of the annual financial statements, the execution of the nonexclusive licensing strategy, the rights



issue from authorized capital, the Company's business development issues as far as approvals for terms and conditions of new collaboration contracts were required, the budget for 2009 and several strategic opportunities presented to the Company. At its meeting in November 2008, the Supervisory Board considered in detail the operational budgets, financial planning and resource allocations planned for the year 2009.

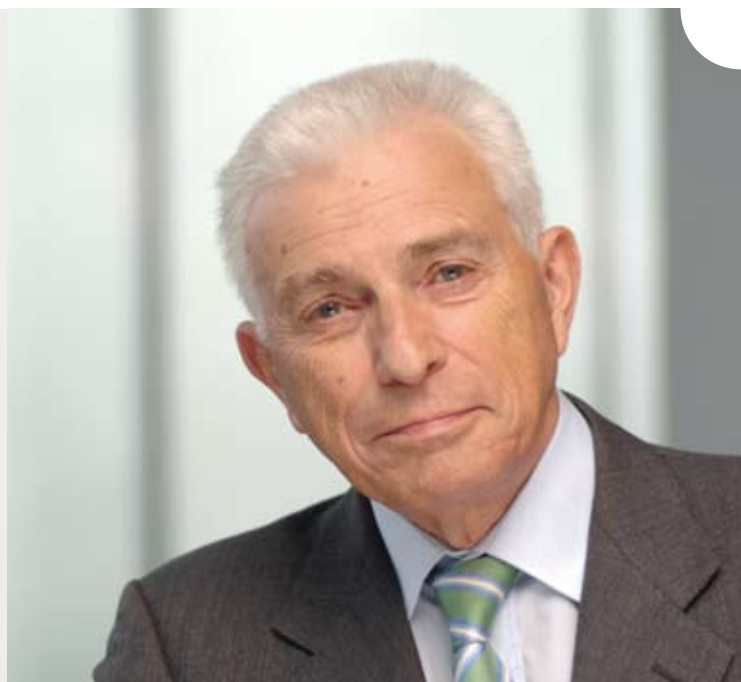
Due to the Company's difficult financial situation, key focus of the Supervisory Board's advisory and monitoring activity was the Company's capital needs and future financial stability. Whilst in early 2008, prime emphasis was put on monitoring the successful completion of the rights issue, later in 2008, the Supervisory Board interacted very closely with the Executive Board and the Company's advisors regarding future financing options. The Supervisory Board sought direct advice from outside legal counsel on the potential impact of individual shareholder lawsuits on the Company's future financing flexibility.

For each Supervisory Board meeting, all members of the Supervisory Board received extensive written reports well in advance of the individual meetings, prepared by the Executive Board with the input of the respective departments. These documents were sufficiently detailed and comprehensive to analyze and discuss all relevant topics of the respective agenda of the Supervisory Board meetings and to pass all required resolutions.



Professor Dr. Dr. h.c. Rolf Krebs  
Chairman of the Supervisory Board

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Between meetings, the Supervisory Board was informed in detail by means of written and oral reports about all ongoing projects and plans of particular importance to the Company. Whenever necessary, resolutions were passed by written vote in compliance with the Company's Articles of Association.

The Supervisory Board closely coordinated with the Executive Board and the Company's legal counsel during the lawsuits filed by two individual shareholders in July 2008 and supported the Executive Board during the preparation of an appropriate defense in these lawsuits. One of the shareholders abandoned his complaint in October 2008. In the second lawsuit, a court hearing is scheduled for July 2009.

#### *Committees*

The work of the Supervisory Board was supported by its two committees: the Audit and Corporate Governance Committee chaired by Prof. Dr. Reiter as well as the Personnel and Compensation Committee chaired by Prof. Dr. Dr. h.c. Krebs.

Both committees held several meetings in 2008. The Audit and Corporate Governance Committee convened four times in 2008 dealing mainly with accounting issues, the quarterly financial statements, the annual financial statements, and other topics within the scope of responsibility of the Committee. The auditors attended all of these meetings. The Audit and Corporate Governance Committee further advised and monitored the Executive Board in questions relating to the Company's risk management and ensured compliance with the German Corporate Governance Code with the purpose to continuously build trust of the shareholders in the management of the Company. The Personnel and Compensation Committee held two meetings in 2008 in order to discuss matters related to the compensation of the Executive Board as well as strategic personnel issues. Reports of the meetings of the committees were presented at the plenary sessions of the Supervisory Board.

#### *Corporate Governance*

The Supervisory Board, advised by the Audit and Corporate Governance Committee, also continuously reviewed all issues of legal compliance and adequate risk management given the extremely challenging global economic crisis, the ensuing difficult financial situation of the Company, particularly in early 2008 before closing the rights issue, as well as compliance to corporate governance principles by Epigenomics. Both the Executive Board and the Supervisory Board regard the commitment to good corporate governance an important measure for enhancing the confidence of current and future shareholders, corporate partners and employees. In December 2008, the Executive Board and the Supervisory Board issued a new declaration of conformity pursuant to Section 161 of the German Stock Corporation Act (AktG), which is included in the corporate governance report of this annual report and is also permanently made available to shareholders on Epigenomics' website. In its declaration, the Company has committed itself to the German Corporate Governance Code, and only in some cases adopted Company-specific principles deviating from these recommendations. For more detailed information regarding corporate governance issues, please refer to the corporate governance and remuneration reports of this annual report.

#### *Audit of the Annual Financial Statements*

The independent auditing company UHY Deutschland AG Wirtschaftsprüfungsgesellschaft, Berlin, has audited the annual financial statements and the related management report of Epigenomics AG for fiscal 2008 in compliance with the principles of the German Commercial Code (HGB) as well as the consolidated financial statements, the consolidated management report and the related notes for fiscal 2008 according

to International Financial Reporting Standards (IFRSs). UHY did not raise any objections for either of the financial statements and approved them with unqualified audit opinions. UHY refers however thereupon, that in consideration of the fresh liquid resources in the amount of EUR 5.2 million created by means of a capital increase before preparation of the consolidated financial statements in February 2009, the Group will be reliant on the allocation of fresh financial resources at the latest by the end of the business year 2010, as the resulting annual deficits in 2009 and 2010 will, according to plan, exceed the liquid resources on December 31, 2008. The consolidated financial statements and the consolidated management report were prepared in accordance with Section 315a of the HGB using international accounting standards IFRSs. UHY's audit was conducted in accordance with German generally accepted standards for the audit of financial statements promulgated by the Institut der Wirtschaftsprüfer in Deutschland e.V. (IDW, Institute of Public Auditors in Germany) and the International Standards of Auditing (ISA).

The above-mentioned documents were submitted to the Supervisory Board by the Executive Board in a timely manner. The Audit and Corporate Governance Committee discussed these documents in detail. The UHY audit reports were presented to all members of the Supervisory Board and were discussed in-depth at the plenary meeting on March 3, 2009, in the presence of the independent auditors, who reported on the main findings of their audit. At this meeting, the Executive Board explained the annual and consolidated financial statements as well as the Company's risk management system. UHY also provided a report on the scope, focal points, and costs of the audit.

As a result of the findings and examination by the Audit and Corporate Governance Committee and the entire Supervisory Board, the Supervisory Board raised no objections, but accepted and confirmed the results of the audit. Following its own review, the Supervisory Board formally approved the annual financial statements and the consolidated financial statements as of December 31, 2008, without exception and modification in its meeting of March 3, 2009, in the presence of the auditors. By the Supervisory Board's approval, the annual financial statements of Epigenomics AG are thus adopted as submitted in accordance with Section 172 of the German Stock Corporation Act (AktG).

Regarding the existing risk management system as the Company's early warning system, the auditors stated that in their opinion the system is suitable to meet all legal requirements. Both the Audit and Corporate Governance Committee and the entire Supervisory Board ensured that appropriate risk management and risk mitigation strategies were implemented during 2008 in light of a very challenging global capital market environment in combination with the limited financial resources of Epigenomics.

The Supervisory Board would like to thank the Executive Board, the senior management as well as all employees for their commitment, dedication and efforts during the difficult and challenging year 2008. The Supervisory Board would also like to thank Dr. Kurt Berlin and Christian Piepenbrock, both co-founders of Epigenomics, who resigned during 2008, for their substantial contributions to the development of the Company.

Berlin, March 2009  
For the Supervisory Board

Professor Dr. Dr. h.c. Rolf Krebs  
Chairman of the Supervisory Board

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## Epigenomics AG: Milestones 1998–2008



98

**Epigenomics** started by Alex Olek and a team of five in a typical Berlin backyard

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**First** round of VC financing with DVC and 3i Group/DNA methylation technologies established



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**Merger** with Seattle-based ORCA Biosciences, Inc., and second round of VC financing (MPM, Abingworth, DVC, 3i Group)



01

**Roche** pilot study in colorectal cancer / Seattle operations built

02

**EUR 100 million** worldwide exclusive deal signed with Roche Diagnostics for colon, prostate, breast, and lung cancer tests

When Epigenomics was founded in 1998 in a typical Berlin backyard on Kastanienallee, today one of the most trendy streets of Berlin and much better known for fashion than biotech, we had one vision: to improve cancer diagnostics to the benefit of patients by using DNA methylation. The Company since then has seen and survived the bloating and bursting of the German biotech bubble. It has been through ups and downs in its own history.

It has transformed itself from a technology-driven biotech start-up to a product-driven commercial organization. Many people left on the way, others took over. What never changed was our vision and our spirit. Today, together with our partners in the industry, we are just about to launch our first products – products that have the potential to revolutionize cancer diagnosis.



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**<sup>m</sup>SEPT9** as lead marker in CRC test established / third round of VC financing (The Wellcome Trust, MPM, Abingworth, DVC, 3i Group)

**Proof** of concept in CRC blood test for <sup>m</sup>SEPT9 and clinical data on <sup>m</sup>PITX2 in breast cancer

**Geert Nygaard** joins as new CEO / PIPE financing / Abbott Molecular deal signed

**IPO** on Frankfurt Stock Exchange – Prime Standard (ticker symbol: ECX)

**Successful** clinical studies in CRC blood test (<sup>m</sup>SEPT9) and prostate cancer prognosis (<sup>m</sup>PITX2) / Roche deal ended / founder Alex Olek resigns

**Quest** Diagnostics deal signed / successful rights issue financing / PRESEPT clinical study for CRC blood test using <sup>m</sup>SEPT9 started



## The Colorectal Cancer Screening Dilemma: Great Benefit, Little Acceptance \_\_

Since the early days of our Company, we have focused on developing a test for the early detection of colorectal cancer. Today, colorectal cancer screening is still our leading development program. For very good reasons: The improved early detection of this cancer can potentially save many lives and provides an unprecedented market opportunity in the diagnostic space. However, to address this market, screening tests are needed that solve the fundamental dilemma in colorectal cancer screening: the lack of patient acceptance of screening, despite the obvious medical benefit.

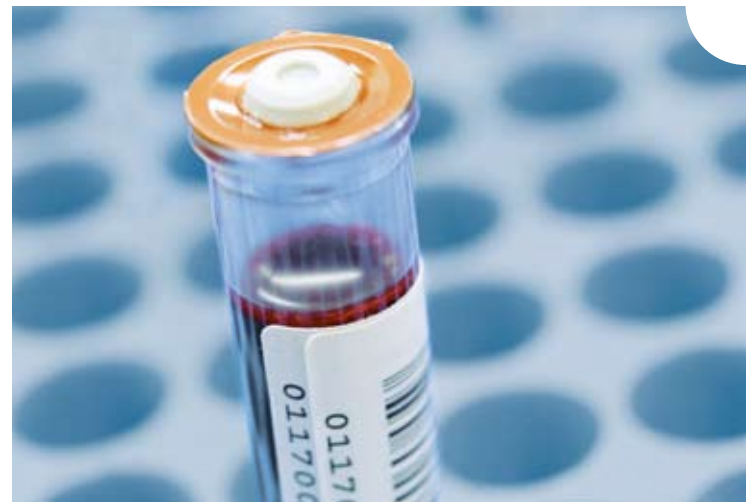
Colorectal cancer is very often curable. More than 90% of all patients survive if the cancer is diagnosed at an early stage while it is still localized. This may be a surprising fact since this dreaded disease is amongst the most frequent causes of cancer-related death in the industrialized world. In the U.S., approximately 150,000 people were diagnosed with the disease in 2008 and about 50,000 people died of this cancer in the same period.<sup>1</sup> In Europe, 413,000 people were diagnosed with colorectal cancer and 207,000 died of the disease in 2006.<sup>2</sup> This makes colorectal cancer one of the most frequent and the second-most deadly cancer after lung cancer. The dilemma: the majority of colorectal cancers are diagnosed in advanced stages when they already show symptoms lowering the chances of survival to less than 10% once the cancer has spread to distant organs. These figures clearly demonstrate that early diagnosis can potentially save many lives.

But catching colorectal cancer in its earliest stages requires systematic screening of the asymptomatic average risk population with suitable diagnostic procedures. Screening guidelines in many countries recommend regular fecal occult blood tests (FOBTs) – laboratory tests that are performed on stool samples – or invasive endoscopic procedures such as colonoscopy performed on average every ten years and which requires extensive bowel preparation.

Despite these recommendations and their life-saving effect, only a minority of the target population participates in regular colorectal cancer screening. Thus, annual FOBTs are only performed by 12% of the individuals aged 50 years and older, and less than half attend a colonoscopy within ten years.<sup>3</sup> The most widely reported reason for this low acceptance is the lack of convenience. The American Cancer Society identified screening compliance as the major issue in colorectal cancer and is committed to drive compliance up to 75% by 2015, a goal that is essentially shared by many patient advocacy groups and government initiatives throughout Europe.

Reaching this goal may be facilitated by novel screening tests that are competitive with the best available noninvasive test in differentiating between cancer patients and healthy individuals but convenient enough to ensure broad acceptance in the guideline-eligible population.

Such tests could address about 300 million people aged 50 years and older in the major markets that should be screened regularly for colorectal cancer, a unique opportunity in the *in vitro* diagnostics space that has a market potential in the billions of euros.



<sup>1</sup> American Cancer Society. Cancer Facts & Figures 2008. Atlanta: American Cancer Society; 2008.

<sup>2</sup> Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P. Estimates of the cancer incidence and mortality in Europe in 2006. *Ann Oncol*. 2007 Mar; 18 (3): 581-92.

<sup>3</sup> Shapiro JA, Seeff LC, Thompson TD, Nadel MR, Klabunde CN, Vernon SW. Colorectal cancer test use from the 2005 National Health Interview Survey. *Cancer Epidemiol Biomarkers Prev*. 2008 Jul; 17 (7): 1623-30.

## A Simple Innovative Blood Test to Revolutionize Colorectal Cancer Screening

At Epigenomics, we set ourselves the goal to develop innovative molecular diagnostic tests that address unmet needs in cancer screening and diagnostics. We believe the solution for the colorectal cancer dilemma is surprisingly simple: A blood test that reliably detects the cancer in its earliest stages and can easily be integrated into an annual physical check-up at the family doctor's office. With our unique DNA methylation technology, we have made this vision a reality. Our <sup>m</sup>SEPT9 colorectal cancer blood test will be available for the very first time to patients and doctors in the United States and in Europe this year.

Our cancer screening tests rely on a rather simple biological phenomenon: Even at the earliest stages, tumors shed DNA into body fluids they are exposed to. Thus, tumor DNA in blood or urine is a formidable indicator – or “biomarker” – for the presence of a tumor.

But how to detect this tumor DNA? With a great amount of DNA derived from healthy cells in the same body fluids, it is like looking for a needle in a haystack. At Epigenomics, we have solved this problem by analyzing differences in DNA methylation. DNA methylation is a fundamental biological mechanism that regulates genes. Cells chemically add methyl groups to the regulatory regions of genes that are not required, shutting them off permanently. As different cell types require different genes to be activated, the pattern of methyl groups on the DNA provides a unique “fingerprint” that differs between various healthy tissues but also changes specifically in diseases such as cancer. At Epigenomics, we

have developed the technologies to read this DNA methylation fingerprint and use it for the sensitive detection of tumor DNA in a blood or urine sample.

With this technology, we can reliably detect minute amounts of DNA in a routine blood sample. Most importantly, by looking at the DNA methylation of the right genes, the exact origin of the tumor DNA can be determined, an important prerequisite for the development of diagnostic tests that are specific for different cancer indications. Thus, we have shown in numerous clinical studies with more than 3,500 clinical samples from colorectal cancer patients of all stages and healthy controls, that the presence of methylated DNA of the gene SEPT9 in a blood sample reliably indicates the presence of colorectal cancer in all stages and all locations in the colon. The <sup>m</sup>SEPT9 test for colorectal cancer not only outperforms the currently most widely used laboratory test (Fecal Occult Blood Test or FOBT), but, more importantly, it has the potential to vastly drive



acceptance of colorectal cancer screening as it is noninvasive and does not require a stool sample.

When tests and test services based on <sup>m</sup>SEPT9 are available, any patient willing to have an additional tube of blood drawn in their primary care physician's office, can receive colorectal cancer screening. The blood sample will be picked up by established courier services and shipped to a regional diagnostic laboratory where it is analyzed for SEPT9 DNA methylation. The test result is then reported to the family doctor who can discuss it with the patient within a few days after the blood sample was taken. If the test comes back positive, a colonoscopy should be performed to confirm the test result and localize the tumor as a first step towards cancer therapy.

The year 2009 will be a decisive one in the development and commercialization of our colorectal cancer blood test: First laboratories in Europe and the United States are expected to start offering colorectal cancer blood tests as part of our early access initiative. Through this initiative we have licensed diagnostic laboratories in Europe and the United States to develop and commercialize laboratory-developed

tests for the <sup>m</sup>SEPT9 biomarker in compliance with applicable regulatory guidelines. While this initiative provides access to early adopters and key opinion leaders, we expect the broad market introduction of test kits that can be implemented in any molecular diagnostic laboratory to be available through our in vitro diagnostics industry partners in Europe in late 2009 and in the United States in late 2010.

With commercialization well on track, we also expect to complete our clinical PRESEPT Study in the second half of 2009. PRESEPT is one of the largest privately sponsored studies ever in colorectal cancer screening. Results from PRESEPT will be fundamental to the broad acceptance and commercial success of our colorectal cancer blood test.



Our colorectal cancer screening test is designed to be as convenient and patient-friendly as possible. All it will take for the patient is giving a blood sample in the doctor's office as part of the regular check-up. The sample will then be shipped to a local or regional diagnostic laboratory where it will be tested for the <sup>m</sup>SEPT9 biomarker. The test result is provided to the doctor who can discuss it with the patient within a few days after the blood sample was taken. If the test is positive, a colonoscopy would typically be performed to confirm the test result and localize the tumor as a first step towards cancer therapy.

## In the Sweet Spot of the Molecular Diagnostics Market

Molecular diagnostics is a segment of the global healthcare market that has received ever-increasing attention over the past few years. It is expected to be the driver of future growth in the diagnostics industry. This growth relies on new technologies that simplify molecular diagnostic tests and will allow to address unmet diagnostics needs, foremost in cancer screening, prognosis, monitoring and therapy selection. With our technology and biomarkers, we are in the sweet spot of this development and have successfully adopted a strategy that optimally leverages our assets in this dynamic environment.

With a compound annual growth rate (CAGR) expected to be around 5% over the next five years, the expectations for the total in vitro diagnostics market are moderate. However, within this market, molecular diagnostics, currently having an annual market size of about USD 3 billion, stands out with an estimated CAGR of 14% over the same period of time. This growth will rely on the number of obvious trends in the industry: Currently, molecular diagnostics heavily relies on infectious disease testing out of centralized laboratories capable of running these rather complex molecular diagnostic tests. Diagnostics companies, in particular new players in the

molecular diagnostics arena, significantly invest into innovative platforms that are fully integrated, flexible, smaller and easier to operate even outside a diagnostic laboratory environment to move molecular testing closer to the point of care. The other major force expected to drive growth in molecular diagnostics is innovative content that addresses unmet diagnostic needs. Here, cancer diagnostics for population-wide screening as well as companion diagnostics for personalized medicine take the lead.

With our DNA methylation technology and a pipeline of biomarkers with unique utility in cancer screening, diagnosis and prognosis, we believe we are ideally positioned to capture the enormous potential of this dynamic and innovation-driven molecular diagnostics market. Our strategy is based on a nonexclusive partnering model for technology and biomarkers short to mid term. At the same time we have begun building a commercial organization to progress our corporate development into a more fully integrated diagnostics company with direct access to the customer.

There is little doubt in the diagnostics industry that DNA methylation tests for cancer and other indications will play a major role in the future of molecular diagnostics. Almost all major diagnostics companies have embarked on projects to exploit this natural biological phenomenon for innovative diagnostics. By licensing our technologies for DNA methylation preanalytics and analytics broadly to diagnostics companies, we strive to set a unified technology standard for diagnostic products and services based on DNA methylation biomarkers. This strategy

was successfully executed resulting in technology licensing agreements with Qiagen, Abbott Molecular, Quest Diagnostics, OncoMethylome Sciences, DxS, TIB MOLBIOL, and, most recently, Philips, and Sysmex Corporation. With all of these agreements, we participate in our partners' current and future commercial success with products and services based on our technology – and in many cases also our biomarkers.

While some of our partners, like Abbott, adapt existing molecular diagnostics instrument platforms to DNA methylation analysis, we work with others to develop new platforms that are optimized for DNA methylation applications. To this end – and following one of the major trends in the industry – we are supporting Philips in developing an integrated and fully automated instrument platform. It will, in addition to standard molecular diagnostic tests, allow the fully automated processing of DNA methylation assays for the diagnosis of certain cancers.

With our biomarkers, we address diagnostic questions with high, unmet medical need in cancer serving the industry's need for innovative content. For our <sup>m</sup>SEPT9 colorectal cancer biomarker, we pursue a nonexclusive licensing strategy to maximize the penetration of the market for colorectal cancer screening through multiple partners. A colorectal cancer screening test addresses a target population of about 300 million men and women aged 50 years and older in the United States, in Europe, and Japan – the three largest diagnostics markets. This single new product opportunity has a market potential roughly the same size as today's entire molecular diagnostics market. To address this market efficiently, we are partnering our <sup>m</sup>SEPT9 biomarker with a balanced mix of strong global and regional players in the diagnostics industry. To date, we have partnerships in place with Abbott Molecular (global), Quest Diagnostics (U.S.), and Sysmex (initially Japan), addressing the most important markets for diagnostics, and we expect to sign more partnerships in the years to come. Our partners take the responsibility for IVD development, regulatory approval, manufacturing, marketing and sales. We bring in our expertise in DNA methylation technology and

biomarkers to support our partners in the development. We also provide them with samples for clinical trials regulatory approval i.e. by giving them access to samples already collected in the PRESEPT Study. With this support, we considerably shorten their time to market to our advantage as we participate in our partners' success through milestone payments upon product launches and significant royalties on product sales. In addition, we typically receive upfront licensing payments, R&D funding, and reimbursement of sample costs.

In the area of companion diagnostics for personalized medicine, we work with leading pharmaceutical and biotechnology companies to discover and validate biomarkers with utility in therapy decisions and patient stratification. While this approach provides a modest revenue stream short term and potential product opportunities long term, we will increasingly focus on exploring companion diagnostic applications of our biomarkers with already proven utility in stand-alone diagnostic and prognostic applications. This approach could provide the opportunity to further leverage the value of these biomarkers with relatively low incremental development costs and on a comparatively short timeline.

On our path to become a fully integrated diagnostics company, we have begun building a commercial organization with own marketing and sales. We are initially focusing on the commercialization of assays for our lead biomarkers as research products. Through these products, we enable diagnostic laboratories in Europe to establish laboratory-developed tests and give early adopters and opinion leaders timely access to our biomarkers, preparing the market for the launch of IVD products by our partners. Having built the necessary R&D capabilities in the past, we will increasingly focus on the development of IVD products for attractive niche markets and take increasing responsibility for their commercialization. First examples include our early access program for <sup>m</sup>PITX2, a biomarker that in our studies proved useful as a prostate cancer prognostic marker, as well as our lung cancer test.

## The PRESEPT Study —

Together with our clinical collaborators, we intend to demonstrate that <sup>125</sup>I-SEPT9 blood tests under development by us and our diagnostics industry partners meet the requirements of current U.S. screening guidelines for detection of the majority of cancers in the actual target population for colorectal cancer screening. Further, we plan to show that colorectal cancer screening with a <sup>125</sup>I-SEPT9 blood test is not only beneficial in early cancer detection but also may help reduce overall spending of healthcare systems for colorectal cancer management. Both aspects are fundamental to the broad acceptance of our approach to colorectal cancer screening and the objectives of the PRESEPT Study and initiative, one of the largest privately sponsored studies ever undertaken in colorectal cancer screening.

PRESEPT is a multi-center clinical study sponsored by Epigenomics to prospectively evaluate the clinical performance of Epigenomics' proprietary biomarker, <sup>125</sup>I-SEPT9, for colorectal cancer detection in guideline-eligible individuals as defined by the U.S. Multi-Society Task Force on Colorectal Cancer (CRC)<sup>1</sup>. It is one of the first studies ever to evaluate the performance of a noninvasive test to indicate the presence of colorectal cancer in a standard blood sample taken from a population of individuals in a screening setting. All key elements of the PRESEPT initiative are directed at building acceptance of the test for colorectal cancer screening by the medical community and patient advocacy groups. Accomplishment of widespread adoption will be evidenced by inclusion of the test into colorectal cancer screening guidelines of medical societies and coverage of the test costs by health care providers.

The primary objective of the PRESEPT Study is to evaluate the performance of the <sup>125</sup>I-SEPT9 biomarker to determine whether it meets the requirements of current U.S. guidelines for non-invasive screening tests for detecting the majority of colorectal cancer. Further, a companion study is being conducted to demonstrate the health economic benefit of colorectal cancer screening based on a standard blood draw to support future coverage by public and private health insurers worldwide. As a third objective, we intend to make available to industry partners developing <sup>125</sup>I-SEPT9 IVD tests access to the PRESEPT samples and clinical data to perform pivotal clinical trials necessary to obtain regulatory approvals. In October 2008, our first nonexclusive development partner, Abbott Molecular, obtained access to these samples and data by funding a significant

portion of the overall study costs. Abbott will use the samples to conduct a pivotal study supporting submission of an application to the FDA with an expectation of reaching the U.S. market in 2010. For the launch of a CE-marked Abbott product in Europe in late 2009, a much smaller case control study will be sufficient.

The PRESEPT Study is designed to enroll up to 7,500 screening guideline-eligible subjects aged 50 years or older at average to increased risk for colorectal cancer who have been scheduled for a screening colonoscopy at multiple clinical sites in the United State and in Germany. Statistically, this population is expected to harbor about 50 cases with undetected colorectal cancer.

These individuals are asked to provide an informed consent and are interviewed to determine whether they meet certain predefined inclusion (e.g. guideline-eligibility) and exclusion criteria (e.g. personal or family history of colorectal cancer). The decision to finally include enrolled individuals into the study will be dependant on all inclusion criteria and none of the exclusion criteria being met.

Following enrollment, up to 40 ml of blood will be drawn from each subject prior to bowel cleansing for the colonoscopy. Once collected, the blood plasma is separated and the plasma samples are frozen until they are processed for *m*SEPT9 testing by Epigenomics or one or more of our partners developing IVD tests for the *m*SEPT9 biomarker.

Once 50 colorectal cancer cases have been collected, we anticipate the samples to be processed at a certified independent laboratory. To establish the performance characteristics of *m*SEPT9 in the study population, the laboratory will analyze samples from all cases with cancer (stages I–IV) and larger polyps and a random selection of a subset of samples from individuals with smaller polyps and those without findings in the colonoscopy. In total, we expect to

test *m*SEPT9 in about 1,500 to 1,800 samples in order to obtain results with sufficient statistical power.

The primary study endpoint will compare the *m*SEPT9 test results to the presence or absence of colorectal cancer as determined by colonoscopy, the diagnostic gold standard. Colonoscopy findings will be confirmed by histopathological analysis of tissue removed during colonoscopy or surgical removal of tissue.

The PRESEPT Study subject enrollment started in June 2008 and is expected to continue through mid 2009. We expect results during the second half of 2009.

To insure the independence of the study and to meet FDA requirements for clinical trials, we established and empowered a Clinical Study Steering Committee that advises on PRESEPT Study design, oversees the study conduct, decides on the inclusion and exclusion of individuals and samples into the study, and will independently analyze and accurately report the final results of the study. The committee is chaired by David Ransohoff, M.D., Professor of Medicine, Cancer Epidemiology, Cancer Prevention and Control, University of North Carolina School of Medicine. Principal Investigator for PRESEPT is Timothy R. Church, Ph.D., Professor, School of Public Health, University of Minnesota. Epigenomics as sponsor is represented by Michael Wandell, Pharm.D., Epigenomics' Study Director, and Catherine Lofton-Day, Ph.D., Project Manager.

<sup>1</sup> Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the U.S. Multi Society Task Force on Colorectal Cancer, and the American College of Radiology CA Cancer J Clin 2008

## PRESEPT in Numbers I

<b>6 years</b>	of biomarker research
<b>12 months</b>	of study planning and preparation
<b>12-18 months</b>	of study duration
<b>22</b>	clinical sites
<b>235+</b>	gastroenterologists
<b>7,500</b>	study subjects
<hr/>	
<b>1 biomarker:</b>	<i>m</i> SEPT9



## Study Design and Preparation



Every study conducted under good clinical practice (GCP) requires thorough and detailed preparation. The study design, including study endpoints, study population, inclusion and exclusion criteria, and study size, needs to be developed, discussed with clinical experts and statisticians and fixed in a study protocol which is then approved by an Institutional Review Board. To meet FDA requirements, an independent Clinical Study Steering Committee and a Principal Investigator are selected and empowered. Informational materials and case report forms have to be designed and produced. Sample and data logistics are structured and implemented.

## Study Execution



Once the study protocol has been approved, clinical sites, i.e. large gastroenterology centers and practices, are qualified to participate in the study. If they meet the study requirements, the staff is trained thoroughly to follow the study protocol. Once the sites start enrolling subjects, the accrual rates, sample and data quality and adherence to the study protocol are continuously monitored by Epigenomics' experienced team of CRAs. Study progress, age and gender stratification and reported cancer cases are closely followed to ensure that the study is reflective of a guideline-eligible colorectal cancer screening population.



## Sample Processing and *m*SEPT9 Analysis



Altogether, we expect to collect blood plasma samples from about 7,500 study subjects, a population expected to harbor about 50 previously undetected colorectal cancer cases. The blood plasma samples are stored at  $-80^{\circ}\text{C}$  in up to 75,000 vials, sufficient material to run several *m*SEPT9 tests on each individual. Once all samples and all clinical data are collected, Epigenomics, ideally in collaboration with an external reference laboratory, will measure *m*SEPT9 in samples from all cancer patients and all individuals with larger polyps and a selection of individuals with small polyps and no suspicious findings in colonoscopy as determined by the Clinical Study Steering Committee. In addition, our partners co-funding the study can access the biobank and data collection to run their pivotal clinical trials for U.S. regulatory approval of diagnostic products based on *m*SEPT9.

## Data Analysis and Reporting of Results



The results of our *m*SEPT9 test will be compared to the results of the colonoscopy and histopathology, if applicable, following a predefined statistical analysis plan. Data analysis will be conducted by an independent statistician serving on the Clinical Study Steering Committee. The Committee is expected to report the study results in late 2009 and publish the data in a peer-reviewed scientific publication. Study data will be used to feed a validated health economic model to assess the health economic benefit of *m*SEPT9 blood testing for colorectal cancer screening.

## Interview:

## Lab-talk on PRESEPT \_\_

The PRESEPT Study is a huge and complex endeavor. What might seem simple on the surface – comparing <sup>m</sup>SEPT9 to colonoscopy in people scheduled for colonoscopy screening anyway – requires complex and subtle study design. Doctors Michael Wandell, Study Director, and Catherine Lofton-Day, Project Manager, representing Epigenomics on the Clinical Study Steering Committee, give some insight into the details of study design, the reasoning behind it and our expectations for PRESEPT.

- *Epigenomics did a number of case control studies with very consistent results in over 3,500 individuals. Why this additional study?*

**Michael Wandell:** Prior case control studies, necessary to characterize and verify <sup>m</sup>SEPT9 performance, were conducted using plasma samples from patients that were already diagnosed with colorectal cancer and normal controls matched according to age and gender. These studies were effective in demonstrating <sup>m</sup>SEPT9 performance in the various stages of cancer, however, the biases inherent in case control studies limit their applicability for establishing the performance criteria in the intended use (screening) population. Conversely, the PRESEPT Study was designed to enroll subjects that effectively reflect the intended use population, as such will generate valid estimates of marker performance for colorectal cancer screening. Therefore, the study was designed to enroll “average risk” individuals not diagnosed with colorectal cancer, in spite of the fact some unknowingly have the disease. This model simulates the circumstances under which the test will be

ultimately used, and due to the relatively low prevalence (approximately 7 in 1000), larger numbers of participants are required to detect enough colorectal cancer cases (50) to demonstrate <sup>m</sup>SEPT9’s effectiveness in detecting the disease.

- *In your case control studies, you repeatedly reported that you could find about 70% of the tumors. Can we expect the same sensitivity from PRESEPT?*

**Catherine Lofton-Day:** The sensitivity with which our assay can detect colorectal cancer in a blood specimen is dependent on the stage of disease. Smaller, early stage tumors shed less DNA into the blood stream and as a consequence are harder to detect than larger tumors that shed much more DNA. In our case control studies, we typically saw that we can detect about half of the stage I tumors, about three quarters of the stage II and III tumors, and practically all stage IV tumors. We expect to see roughly the same sensitivity by stage in the PRESEPT Study. However, the stage distribution in a screening population like the PRESEPT cohort is expected to yield more

early stage tumors and thus we expect the overall sensitivity may be slightly lower than in our case control studies.

- *So what sensitivity threshold do you want to meet on the lower end?*

**Michael Wandell:** Our primary goal in the PRESEPT Study is to demonstrate that the <sup>m</sup>SEPT9 biomarker meets or exceeds the performance requirements of the medical community. The Joint Guideline from the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology, published May 2008<sup>1</sup>, stated that “a screening test must be able to detect the majority of prevalent or incident cancers at the time of testing.” Therefore, we consider PRESEPT a clear success if we detect more than 50% of the tumor cases in the study population.

- *What are your expectations on the specificity in the PRESEPT Study, i.e. the number of false positives?*

**Michael Wandell:** In our case control studies, we typically observed about 10% false positives (90% specificity) when the assay was optimized for sensitivity, and approximately 5% (95% specificity) when we used an interpretive algorithm optimizing specificity. We expect the specificity to be in the same range in the PRESEPT Study, and perhaps a bit better. It is important to remember that the “gold standard” for determining the accuracy of the <sup>m</sup>SEPT9 marker in the PRESEPT Study is colonoscopy. A recent publication observed the sensitivity of colonoscopy performed by less experienced gastroenterologists may well be as low as 60% to 70%. This bodes well for the clinical effectiveness and medical community acceptance of <sup>m</sup>SEPT9 relative to established procedures, but raises the possibility that the case control studies underestimated sensitivity and overestimated the specificity of the marker. In order to mitigate the relative inaccuracy of colonoscopy and its impact on the observed performance of <sup>m</sup>SEPT9, the PRESEPT

Study protocol has been designed to assure the quality of colonoscopies performed on study subjects.

- *What is acceptable as a false positive rate for a screening test? What do the guidelines say?*

**Michael Wandell:** The most recent guidelines do not state an acceptable level of specificity inasmuch as they focus on strategies to detect as many cancers as early as possible. A low false positive rate, i.e. a high specificity, is crucial to make a health economic case and secure reimbursement for the test. A simple calculation shows this: If you test 10,000 individuals in a screening population with a test that has 70% sensitivity and 90% specificity, about 1,000 individuals will be sent to colonoscopy and among these five out of the seven cancers cases likely to be harbored in this population will be detected. Therefore, the false positive rate (specificity) influences the screening costs. Lower specificity results in more colonoscopies which increase the costs, not the cancer cases. Based on our health economic models and advice from our medical advisory board, we believe that a specificity of 85% to 90% in the average risk population is sufficient to demonstrate the cost-effectiveness of our <sup>m</sup>SEPT9 assay. As an element of the PRESEPT initiative we are concurrently demonstrating the health economic benefit of blood-based colorectal cancer screening using the <sup>m</sup>SEPT9 marker to support adoption of the assay by health providers and insurers.

- *As you mention numbers, is the study large enough to provide sufficient statistical power?*

**Catherine Lofton-Day:** It is the number of cancer cases that is critical to reliably determine the sensitivity of the assay in this population. We settled for 50 cancer cases as this gives us a reasonable statistical power. Obviously this is not an issue for the non-cancerous individuals of the study, which are the vast majority in this population. In fact we will not measure all of them, as this would not give us any further information.

<sup>1</sup> American Cancer Society, U.S. Multi-Society Task Force on Colorectal Cancer and American College of Radiology





Instead we will measure <sup>m</sup>SEPT9 in the blood samples of all the patients with cancer and larger polyps and a random selection of about 500 individuals with smaller polyps and about 500 to 1,000 individuals with no suspicious findings in the colonoscopy. Still, we have to collect samples of all of the about 7,500 study subjects since at the time of sampling we do not know who has cancer or not.

- *Detecting and removing polyps, that are widely regarded as precursor lesions to malignant tumors, is advocated by some opinion leaders. What is your view on this and can your <sup>m</sup>SEPT9 assay find polyps?*

**Michael Wandell:** Although preventing colorectal cancer is a laudable goal, the reality of identifying the 1% to 2% of polyps destined to become cancer is much more complex. Removing all polyps in order to avoid the progression of a few comes at a price, as it is associated with a considerable risk for complications such as bleeding, infections, etc. With about 35% of screening individuals identified with polyps during colonoscopy, this adds up to a significant morbidity and even mortality associated with colonoscopy and polypectomy. So most experts agree that improved noninvasive tests to detect colorectal cancer will be of great value while methods to noninvasively detect polyps and identify those at high risk of progressing are being developed.

**Catherine Lofton-Day:** The evaluation of <sup>m</sup>SEPT9 performance in polyp detection is a secondary endpoint of the PRESEPT Study. The marker was identified and developed as a colorectal cancer marker present in tumors of all stages and all locations in the colon and

rectum. Results from our previous studies demonstrate that methylated <sup>m</sup>SEPT9 is present in the blood of a portion of those individuals harboring polyps. We now want to find out whether the larger polyps with high-grade dysplasia that are thought to have the highest risk of progressing are the ones that are <sup>m</sup>SEPT9 positive. While we do not believe that detection of every polyp adds to the clinical utility of a colorectal cancer test, a significant detection of these high risk polyps could be seen as an additional benefit.

- *You plan to have the PRESEPT Study samples measured by an independent laboratory as well as share them with your partners like Abbott. Why measure them at all if your partners will be assaying them as part of pivotal clinical trials for regulatory submission of their <sup>m</sup>SEPT9 assays not long thereafter?*

**Michael Wandell:** We believe it is very important to establish the clinical utility of our biomarker for colorectal cancer as early and independently as possible. We are confident, the performance of <sup>m</sup>SEPT9 biomarker will live up to our expectations in an average risk screening population. That's why we empowered an independent steering committee to advise us on PRESEPT Study design, oversee the quality of the study conduct according to worldwide clinical research practice standards, and independently analyze and accurately report the results. The independence of this committee, as well as the prestige of its members, guarantees the credibility and acceptance of the study results.

It also gives us a headstart in creating awareness for this new screening test based on a standard blood draw. Even before we see peer-reviewed presentations and publications of the PRESEPT results, it will already be offered as a laboratory-developed test by large diagnostic labs in the United States and in Europe. In addition, the PRESEPT Study results, combined with the concurrent health economic analysis, allow us to submit for public and private insurer coverage and reimbursement before an approved test hits the U.S. market. As with comparable tests, reimbursement is probably the most critical step to commercial success of the test. Of course, we are collecting sufficient samples and data in strict compliance to the “Good Clinical Practices” standard to enable Abbott and at least one future IVD partner to validate their <sup>m</sup>SEPT9 assay in a pivotal study and submit the results for FDA approval in the U.S. In fact, we have already successfully presented this clinical plan to FDA and these efforts are estimated to

save our partners one to two years of time to market in the U.S. In summary, we envisioned PRESEPT not just as one of the largest commercially sponsored colorectal cancer screening study ever conducted, but as a whole initiative with the goal of establishing the <sup>m</sup>SEPT9 blood test as a widely accepted new modality for colorectal cancer screening that has the potential to save thousands of lives every year once it is on the market.



Catherine Lofton-Day, Ph.D.  
Project Manager PRESEPT Study



Dr. Michael Wandell,  
Study Director PRESEPT Study

## PRESEPT in Numbers II

**6+ miles** of colonoscopy

**40,000+** pages of case report forms

**50** colorectal cancer cases

**8,000+** sample collection kits

**75,000** blood plasma vials

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**1 biomarker:** *m*SEPT9



## Interview:

# Prime Time for Launch ... here is the “How”! \_\_

Epigenomics' vision for future colorectal cancer screening is simple: a blood test that is performed as part of your regular annual physical exam by the family doctor. But how can we market such a test to the ten thousands of family practices and tens of millions of screening-eligible patients? The opportunity is unique in the molecular diagnostic space but so are the challenges in making this innovative product a commercial success. Dr. Friederike Gerdes, who recently joined Epigenomics as our new Head of Marketing & Sales, shares her views on how to tap this market efficiently and effectively.

- *How does Epigenomics want to address the huge market for colorectal cancer screening? Considering the size of the Company, this seems quite difficult...*
- *Why do you need a marketing function at Epigenomics if you partner your product?*

*Dr. Gerdes:* Yes, this is true indeed. By ourselves we could only reach a very small regional segment of this market. For this reason, we have partnered our <sup>m</sup>SEPT9 blood test for colorectal cancer with established companies in the diagnostics industry that have the marketing muscle and the sales force to address this market effectively and efficiently. This initiative started in 2007 by bringing Abbott Molecular on board as a first global partner and was successfully continued with further partners like Quest Diagnostics in the United States and Sysmex in Japan. Through these and future partners and the installed base of their molecular diagnostics instruments in the market, we will get a much broader access to a larger variety of customers and faster penetration of the market. Increased awareness and acceptance of the test will also help to lobby for reimbursement in the various regions.

*Dr. Gerdes:* Although it will be much easier to access the colorectal cancer screening market through multiple partners, we have to make sure that all partners go out and deliver the same key messages regarding our <sup>m</sup>SEPT9 biomarker and its clinical utility. Also, we are in the unique position to take the lead in a number of activities from which all of our partners will benefit. This includes establishing a network of key opinion leaders, running academic studies with these people to prepare the market, giving access to our market research and providing input for creating the required marketing material and training of the sales teams. For these reasons, we decided to build a small core team of central marketing at Epigenomics to support our partners.



- *Isn't there fierce competition between the partners? How do you deal with this?*

*Dr. Gerdes:* There is certainly some degree of competition between the partners. However, in the diagnostics industry, companies will typically position themselves against their competition by focusing on a specific type of laboratory or geographic region rather than by the IVD tests they offer. While one player might address high-throughput centralized laboratories another may have an instrument that is better suited for smaller diagnostic laboratories. Some companies may be strong in Europe while others focus on the Asian market. By making use of the complementarities when choosing our partners, we want to cover a much broader segment of the overall market very efficiently.

- *What are your activities in the important year 2009? What can we expect for 2009 with regard to the <sup>m</sup>SEPT9 market introduction?*

*Dr. Gerdes:* 2009 will be a very important year for our colorectal cancer blood test. In Europe, we have already started preparing the market by enabling individual diagnostic laboratories with our <sup>m</sup>SEPT9 research assay product. Under this Early Access Program, they can gather first experience and data with the biomarker and the assay and do studies with opinion leaders. This will facilitate the launch of an IVD product by our partner Abbott Molecular towards the end of 2009. We expect some of the laboratories of our Early Access Program that have the required instrumentation to switch to the IVD products offered by our partners and more customers to come on board. Similarly, in the U.S., we will see the launch of a testing service based on a laboratory-developed test by our partner Quest, which will prime the market there. Due to the regulatory requirements in the U.S., we expect an IVD launch by Abbott Molecular no earlier than at the end of 2010.

- *How do you want to position your test in the market? Who do you want to target predominantly?*

*Dr. Gerdes:* We eventually want to position our test as an alternative to current noninvasive screening tests for colorectal cancer, which are stool-based. Our test squarely puts the family doctor in a position to offer a test that requires no patient involvement, is reliable, convenient and affordable. If tested positive, the family doctor would typically recommend to the patient to undergo colonoscopy to confirm the diagnosis and to localize the tumor. This positioning requires, that our partners and we make the assay available in those laboratories that family practices would send their patient samples to. Most importantly, we need to make the family doctors aware of the test and its advantages for their patients and themselves.

Here, we are working through opinion leaders in gastroenterology and public health who have a keen interest in getting more individuals screened to catch the cancer early when it is still curable. There are already a number of very good initiatives by gastroenterologists and patient advocacy groups to educate family doctors and patients, respectively, on the importance of colorectal cancer screening, and we intend to work closely with these groups.

- *What role does the PRESEPT Study play in your efforts to establish your blood test for colorectal cancer screening?*

*Dr. Gerdes:* The PRESEPT Study is an important cornerstone of our overall efforts to introduce <sup>m</sup>SEPT9 testing as a new colorectal cancer screening modality. While the study is needed for regulatory approval of an IVD product with a screening claim in the United States, this is not required in Europe.





Dr. Friederike Gerdes,  
Head of Marketing & Sales



Nevertheless, in Europe as well as in the United States, acceptance of such a new test by the medical community and the future recommendation of the test in colorectal cancer screening guidelines will strongly depend on demonstrating its performance in the true target population.

This is the objective of the PRESEPT Study. If successful, the study will also provide the necessary data points to run health economic models that show how this test can help save costs in public health spending, an important factor when petitioning for coverage and reimbursement.

- *Reimbursement of the test will be important for the commercial success of the <sup>m</sup>SEPT9 test. How can reimbursement be secured and how long does it take?*

*Dr. Gerdes:* As with any other new test, the patient will initially have to pay for the test. With the PRESEPT data available and the first tests being on the market in the respective countries, we can start petitioning for reimbursement. Initially, this effort will be focused on private health insurers and wherever possible will make use of existing reimbursement codes. Eventually, we want to be included into the reimbursement catalogs of the major national public health insurance systems in each respective region. We expect the whole process to take several years. Here, our partnering strategy will pay off, as our partners will be driving the process with all their experience in the different countries.

- *Do you eventually want to market products yourself?*

*Dr. Gerdes:* Absolutely. Epigenomics' ultimate goal is to become a fully integrated molecular diagnostics company with its own marketing and sales. We are already selling and launching research products for our lead biomarkers such as <sup>m</sup>SEPT9, <sup>m</sup>PITX2, and <sup>m</sup>GSTP1. In Europe, these research products are used to establish laboratory-developed and validated tests that enable diagnostic laboratories to offer testing services for these biomarkers. But we also expect to take increasing responsibility in marketing and selling of diagnostic products. We have some very interesting products in our pipeline for specialty markets e.g. in lung cancer diagnosis that are characterized by very high unmet diagnostic need that can be addressed by our own marketing and sales team in the foreseeable future.



## A Strong and Balanced Pipeline with Short-, Mid-, and Long-term Opportunities —

Although our colorectal cancer blood test is our main focus, we are far from being a one-product company. Having consolidated our pipeline in 2007 and 2008, we now realigned and balanced our R&D portfolio with respect to time to market, market size and commercialization strategy. While we focus all our projects on diagnostic questions of highest unmet medical need, the current mix includes short-, mid- and long-term product opportunities addressing mass markets as well as high-value niches, some of which lend themselves to partnering while others can be commercialized effectively by ourselves.

Outside colorectal cancer, we focused on lung and prostate cancer as cancer indications with high unmet medical needs. Lung cancer diagnosis – despite highest medical need – suffers from the lack of any in vitro diagnostic tools that, in combination with imaging technologies, would make population-wide screening for this most deadly cancer feasible.

The current dilemma in lung cancer screening is, that, although screening by spiral CT can identify more cancers early, it has not been proven to provide a mortality benefit and its lack of specificity funnels too many people into a diagnostic follow-up consisting of e.g. bronchoscopy, biopsy or surgery. These procedures may be associated with morbidity and even mortality partly eliminating the potential benefit of spiral CT screening.

In our lung cancer program, we address this challenge with two approaches that could complement existing diagnostics procedures. With both, we have made exceptional progress throughout 2008 partly owing to the overwhelming support by clinical opinion leaders and experts in the field. In both approaches we make use of a number of proprietary lung cancer biomarkers we discovered in 2007. As a short-term opportunity, we have now decided to develop a follow-up test to consisting diagnostics procedures. In a first version, this test will aid in the diagnosis of bronchial carcinoma in bronchial lavage samples obtained routinely during bronchoscopy of patients with suspected lung cancer.

During the procedure, fluid is aspirated from the suspicious area of the lung after injection of saline solution first. This lavage fluid is then analyzed by the pathologist for tumor cells often resulting in inconclusive results, leaving the final diagnosis to the chest physician. This includes to decide between



The Pipeline can be found in the cover

sending the patient off to biopsy, risky surgery or repeating imaging some weeks later to see whether the suspicious nodule has grown and thereby can be confirmed as a malignant tumor losing valuable time for treatment. In two consecutive studies we have successfully shown that our biomarkers can detect cancer from a significant portion of bronchial lavage samples, even if the cytological findings are negative or inconclusive. As the biomarkers are very specific, i.e. we only see a very small number of false positive results, a test based on our biomarkers should have a very high positive predictive value, i.e. a positive test result may provide a high degree of certainty that the patient has cancer and requires immediate follow-up. This additional information will thus support the pathologist and the clinician in establishing a diagnosis in particular incases with inconclusive histology and cytology.

Based on the clinical data we generated and a thorough assessment of the clinical utility as well as the significant market potential, in spring 2009 we took the decision to develop such a bronchial lavage test, as a CE-marked IVD product that we plan to commercialize ourselves in the german domestic market and via distributors in further regions.

As a second, rather long-term opportunity for partnering we pursue the development of a blood- or sputum-based screening test for lung cancer, that would enrich true cancer cases – either alone or as part of a risk model – in the target population for screening by low-dose CT-scanning. Such a screening test has the potential to complement diagnostic imaging resulting in a better balance between medical benefits and risk associated with population-wide screening for lung cancer.

In a first sizeable study on clinical blood samples in 2008, we could demonstrate the feasibility of detecting lung cancer in these samples with our proprietary biomarkers. In 2009, we will continue

to optimize the biomarkers for this application and explore sputum as an additional diagnostic sample. At the same time, we are expanding our network of clinical collaborators in the lung cancer field and are in active discussion with imaging companies on the integration of in vitro diagnostic and imaging information.

In prostate cancer, screening currently relies on PSA (Prostate Specific Antigen) which is not cancer-specific leading to many unnecessary prostate biopsies. Further, prostate cancer is often a slowly progressing form of cancer, there is a lot of uncertainty in how to manage men with diagnosed cancer. There is a high medical need for better tools in early detection, diagnosis and risk assessment of clinically relevant prostate cancer that warrants immediate therapy. To this end, we have progressed our prognostic prostate cancer test for biochemical recurrence risk assessment after prostatectomy that is based on our proprietary biomarker <sup>18</sup>F-PITX2 through clinical validation. We are in the process of making this test available first within an early access program with selected clinical centers in Europe and eventually as an IVD test through commercialization partners.

Together with our partner TIB Molbiol, we introduced a research product to analyze methylation of the GSTP1 gene in biopsy tissue in Europe in early 2008. First clinical centers currently make use of this product to establish and independently validate laboratory-developed tests to improve the diagnosis of prostate cancer on biopsies. After having demonstrated our biomarkers performance in urine-based screening for prostate cancer, similar to PSA blood testing. We may in the midterm invest further research into the question of how to combine diagnostic and prognostic information into a screening test to provide benefits beyond the standard currently set by PSA.

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## Our Stock

The year 2008 has been a very challenging one for the global financial markets, global economies and the entire life sciences industry. Whilst financing transactions were at the lowest level in a long time, life sciences stocks actually held and out-performed their own major market indices.

### Key data on Epigenomics' stock

ISIN	DE000A0BVT96
Security code number	A0BVT9
Stock exchange abbreviation	ECX
Reuters	ECXG.DE
Stock exchange	Frankfurter Wertpapierbörse, Amtlicher Markt (Prime Standard)
1st day of trading	July 19, 2004
Designated sponsor	Close Brothers Seydler AG Wertpapierhandelsbank
Number of shares (Dec 30, 2008)	26,723,636
Free float (Dec 30, 2008)	86.67%
Market capitalization (Dec 30, 2008)	EUR 53.4 million
Year-end closing price	EUR 2.00
Highest price	EUR 2.73
Lowest price	EUR 1.50

In spite of the solid fundamental progress, the announcement of new cooperation partners and the successful progress in the development of our colorectal cancer screening product, there has only been a very modest positive impact on our share price. However, since our successful financing transaction in February 2008, where we issued more than 8.5 million new shares at a price of EUR 1.60 each and raised about EUR 13.5 million in gross proceeds, the Epigenomics stock has performed better than all major indices. Our stock closed at EUR 2.00 (XETRA) at year-end, up 20% since the capital increase and showing an increase 2.5% against the previous year's close of EUR 1.95.

Trading volumes in Epigenomics stock (Ticker symbol: ECX) have slightly decreased during 2008 and volatility has been remarkably low compared to the overall development of the financial markets. As of December 31, 2008, a total number of 26,723,636 shares was issued. After adding Federated Kaufmann as the major shareholder in our rights issue in February 2008 and BB Medtech's announcement of having acquired more than 5% of our shares outstanding in summer, the following major shareholder groups controlled more than 3% each of Epigenomics' total shares outstanding:

Voting rights treshold	Shareholder
> 15%	Federated Kaufmann
> 10%	Abingworth Management Holdings Ltd.*
	Deutsche Bank*
> 5%	Omega Funds
	BB Medtech AG
> 3%	BB Biotech AG

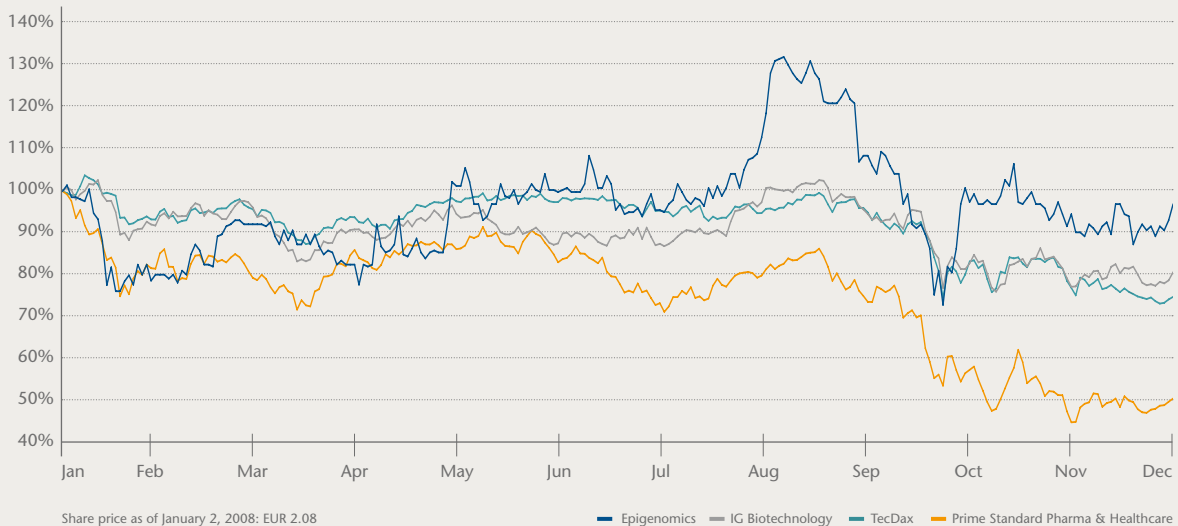
\* Managed or advised by

Three analysts maintained coverage of Epigenomics' stock to date providing updates on their views and recommendations. Fairesearch's Dr. Martin Schnee (via Close Brothers Seydler Research AG), First Berlin's Christian Orquera and independent analyst Thomas Schiessle (via Midas Group) all gave "buy" recommendations and price targets significantly above year-end trading prices.

### Corporate Communications

In 2008 as in the previous years, we continuously provided all our shareholders with timely, accurate and comprehensive information giving them the best possible basis for making informed investment decisions in Epigenomics' stock. We invited to an annual press conference and an analyst meeting at the end of Q1 2008 in Frankfurt am Main, hosted our Annual General Shareholders' Meeting in Berlin on June 3, 2008, with a participation of approximately 70% of the share capital and offered conference calls on important Company updates. We also presented at several investor meetings, as well as presenting updates on our clinical data at major scientific conferences throughout the year. Furthermore, we continued to provide opportunities for a close dialog with shareholders as well as interested investors at numerous road show meetings in Germany, Switzerland, the United Kingdom, Benelux and the United States.

Epigenomics' stock price development from January 2 to December 30, 2008



# Consolidated Management Report 2008

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## Economic Environment

### Global economic situation

The year 2008 was characterized by the worst worldwide economic crisis for decades. It had started with the first signals coming from the U.S. real estate markets already in 2007. But the ensuing collapse of this segment developed so dramatically and hit the global capital markets so rapidly and profoundly that nobody could have adequately forecast the second half of 2008 even in a worst-case scenario. The world has seen the end of the investment banks as known before, severe repercussions in nearly all financial institutions (banks, hedge funds, mutual funds and insurance companies), a near-collapse of the U.S. automotive industry and it saw that even whole national economies can be pushed to the brink of ruin.

These turbulences were accompanied by roller-coaster rides of the world market prices for oil, precious metals and most major currency relations. Especially the exchange rate between the euro and the U.S. dollar displayed extreme volatility and started at the beginning of 2008 with a rate of EUR/USD 1.47, peaked at a new record high of 1.60 in the summer, fell back to 1.25 in the late fall and closed finally at 1.39. Daily variances reached up to 4.6% from one day to the next. The forecasts of analysts showed broader spreads than ever before from each other – some of them even stopped forecasting at all with reference to the situation. International stock indices plunged to levels last seen at the beginning of the century, i.e. at the end of the “new economy” era and the 9-11 impact.

By the second half of 2008 the crisis had reached the worldwide labor markets with full force. Even as Germany's unemployment statistics still looked rather positive at the year-end 2008, all other major economies reported rapidly rising unemployment numbers. Big global players across many different industries – from real estate to banking, from automotive to healthcare, from electronics to consumer retail – have announced major restructuring plans including mass layoffs.

These escalating events have compelled governments into acting forcefully. Big rescue operations and bail-out packages were started to keep the staggering banks and insurance companies from total collapse. The role model of many national economies was reversed to Keynesian economic policies and even nationalizing individual banking institutions in the U.S.A. and in Europe. Based on these dramatic changes in the so-called “economic environment”, it is not surprising that outlooks of leading experts for 2009 diverge widely and it is hardly possible to decide which of the scenarios is most likely to become true.

### Impact of the global crisis on the life sciences industry and on Epigenomics in particular

The healthcare and life sciences industry, however, had so far been seen as a “defensive sector”, with less dependency on strong ups and downs of the economic development and a demand for its goods and services independent of crises. Basically, this assumption should be valid for the future as well. However, some big players in the pharmaceutical industry have already announced cost saving programs and layoffs as well and demonstrated that probably nobody will be completely left untouched by this crisis.

As Epigenomics is not immediately dependent on general consumer demand and our customers to date are exclusively laboratories and diagnostic as well as pharma corporations, we expect the danger of our own business getting hit hardly by the crisis as rather low when it comes to the revenue side. Nevertheless, there is an increased risk on the financing side. In times when share prices plunge and institutional investors are facing increasing problems with their own liquidity and their own investments it is becoming at this time harder and harder to raise money and especially to raise money at an acceptable valuation.

We are fully aware of this situation and we are preparing ourselves as far as possible for a future that was never as uncertain. In the chapters "Opportunities and Risk Report" and "Prognosis Report" of this management report reference is made to the individual implications that the worldwide crisis could have on our business and our Company if applicable. Nonetheless, despite all the difficult times and crises, in February 2009, we have been able to find investors that are willing to further invest in our Company and its future development.

## Business Activities, Strategy and Organization

### Group structure and business activities

Epigenomics' mission is to build a world-leading cancer molecular diagnostics company based on DNA methylation. All our R&D activities as well as commercialization efforts are geared towards fulfilling that mission. Epigenomics AG is headquartered in Berlin, Germany, and operates a wholly owned subsidiary, Epigenomics, Inc. in Seattle, Washington, U.S.A.

Epigenomics is developing and plans to commercialize either via direct marketing and sales efforts or through partnerships cancer diagnostic tests in colorectal cancer, lung cancer and prostate cancer indications. All our cancer molecular diagnostic tests target substantial market opportunities and address significant unmet medical needs with a view to providing patients with benefits from more convenient and superior diagnostic tests.

### Corporate goals, strategy and management

For 2008, the most important corporate goal was to progress development as well as commercialization of our key value driver and lead product, a blood-based test for colorectal cancer detection. We follow a dual strategy of nonexclusive partnering and licensing rights to our high-volume cancer screening tests as well as developing and commercializing Research-Use-Only (RUO) kit versions of these products and addressing certain market segments through internal product development as well as direct marketing and sales efforts.

In addition to diagnostics partnering and licensing activities, we also provide access to our extensive portfolio of DNA methylation technologies by way of nonexclusive licenses that enable others to develop and commercialize products based on our IP. Finally, wherever commercially attractive, we also provide high-value-added biomarker research services and solutions to customers in the pharmaceutical and life sciences industry. We take a very focused and goal-oriented approach to managing and monitoring progress of strategy execution. Every year, the Supervisory Board and the Executive Board set a specific set of milestones and deliverables in terms of revenue, operating results, partnering and deal-making targets, as well as product development and clinical data goals.

We continually strive to evolve our organization into a product-development-driven and commercially focused enterprise. During 2008, we centralized all laboratory R&D operations and personnel in Berlin and transformed the Seattle operation into an organization focused on running large, prospective clinical trials in the U.S.A. Whilst Christian Piepenbrock (former COO) and Dr. Kurt Berlin (former CSO), two of the Company's co-founders and members of its Executive Board, decided to resign from the Executive Board of Epigenomics AG in 2008, we have attracted additional very experienced managers to head our research, product development, marketing and sales. Kurt Berlin became chairman of our Scientific Advisory Board and continues to consult on scientific matters and IP-related issues.

As part of our "Epi 2010" initiative, we pursued a strategy of focusing on key value drivers, streamlining operations, de-emphasizing noncore programs and research activities unrelated to our lead products. Given the extremely challenging global financial market environment and continued need for capital infusion into Epigenomics, we manage our resources such that cash reach well into 2010 can be ensured. Due to the successful capital increase and PIPE placement of new shares in February 2009 our liquidity position has been augmented further and based on today's assessment should cover all of 2010.

### Overview of our business – a review

During 2008, we have made significant progress in our commercialization efforts for Septin 9, the proprietary biomarker in our blood-based colorectal cancer test. Having signed a worldwide, nonexclusive R&D collaboration and licensing agreement with Abbott Molecular in late 2007, fiscal year 2008 saw the implementation and successful expansion of that partnership. Following the transfer of the Septin 9 assay onto the Abbott *m2000* platform, both parties agreed to codevelop the product with the goal of getting a CE-marked test kit into the European market by late 2009. It is our common goal for Abbott to file with the U.S. Food and Drug Administration ("FDA") in 2010 in order to obtain regulatory approval of the Septin-9-based colorectal cancer test in the U.S.A. Therefore, we agreed with Abbott to expand the agreement such that in return for certain license fees, R&D funding and reimbursements and milestone payments we would provide Abbott with access to aliquots of our blood samples collected as part of our PRESEPT Study for their FDA approval trial of an IVD kit version of the Septin 9 CRC test.

Early in 2008, we also signed a nonexclusive licensing agreement with Quest Diagnostics. Under this agreement, Quest is expected to commercialize a laboratory-developed test (LDT) – or homebrew test – for Septin 9 methylation.

During 2008, we also developed a Research-Use-Only kit version of the Septin 9 assay. Beta testing was successfully completed in fall of 2008 and the first clinical testing laboratories have been trained in the use of the Septin 9 RUO kit to establish and validate LDT for aid in colorectal cancer detection. Based on the successful beta testing and prelaunch phase, we expect testing services to be available in selected European laboratories in the first half of 2009. During 2008, we also launched several other RUO kits into the European market together with our manufacturing and distribution partner TIB Molbiol.

In January 2008, we signed a strategic cross-licensing agreement with DxS Ltd. and obtained worldwide nonexclusive rights to DxS' proprietary Scorpions<sup>®</sup> technology for R&D use and research kits as well as an option to expand the license to the in vitro diagnostics (IVD) field. DxS in return received an option for a worldwide nonexclusive license and further options to certain Epigenomics IP covering the use of the Scorpions<sup>®</sup> technology for DNA methylation applications.

In addition to revenue recognised under the Abbott and Quest deals, we also generated significant revenue from our technology licensing efforts. In the first quarter of 2008, we signed a worldwide nonexclusive licensing agreement with OncoMethylome Sciences (OMS). In return for a significant upfront payment and downstream royalties on any product sales including our IP, we provided OMS with access to several of our leading DNA methylation technologies such as the Heavy Methyl (HM) sensitive amplification, MethyLight real-time PCR detection, Scorpions<sup>®</sup> methylation detection and certain array technologies. This business deal complements our licensing agreements with Qiagen (bisulfite-based DNA methylation preanalytics for research market and IVD products) and Affymetrix (certain microarray licenses). These technology-licensing agreements underscore the continued leadership position enjoyed by Epigenomics in the field of DNA methylation.

Other revenue generating activities in the area of "biomarker solutions" in 2008 included successful collaborations with Johnson & Johnson (J & J), Centocor, Pfizer, Merck and several academic collaborators such as the Karolinska Institute, Stockholm, Sweden, the Universitätsklinikum Magdeburg, Germany, and the University of Minnesota, U.S.A. In addition, we signed a follow-up agreement with one of our large pharma partners. Furthermore, a significant portion of our internal research activities were supported and partially funded by grants from the European Union as well as the German Federal Ministry of Education and Research.

On December 19, 2008, we entered into a collaboration and licensing agreement with Royal Philips Electronics focusing on novel technologies and methods targeted at the diagnosis of various cancers. Under the agreement, both parties will jointly perform feasibility studies aimed at developing an integrated and fully automated instrument platform for the diagnosis of certain cancers based on DNA methylation biomarkers. As an example, the collaboration initially focuses on biomarkers from Epigenomics' lung cancer program. In addition, Philips obtained the option to license the required technologies and biomarkers separately or in combination for diagnostic applications. The option may be exercised against certain payments upon the successful completion of the feasibility studies.

## Research and development

### *Colorectal Cancer Test (Septin 9)*

During 2008, our R&D focus remained firmly on the most advanced product development program: our Septin-9-based colorectal cancer blood test. The following achievements in that program formed the cornerstones of our 2008 R&D efforts:

February	Quest takes licence to develop LDT for Septin 9
April	Successfully completed two case control studies validating Septin 9 in this additional study of over 500 blood samples showing excellent test performance
June	Enrolled first subjects into the PRESEPT clinical study
July	Received notice of allowance for very broad Septin 9 patent in Europe
October	Reported substantial progress in PRESEPT study
Fall	Transfer of the Septin 9 assay onto the Abbott <i>m2000</i> platform
Fall	Started CLIA validation process for Septin 9 LDT via Quest Diagnostics

During 2008, we presented results from our clinical studies and clinical data on Septin 9 at a number of scientific conferences and meetings such as the AACR Annual Meeting in San Diego, during Digestive Disease Week in San Diego, at the Biomarker World Congress in Philadelphia, at AACR Cancer Epigenetics in Boston, (all U.S.A.) and others.

### *PRESEPT (Septin 9)*

The design, roll-out, implementation and execution of our PRESEPT Study was the primary R&D activity throughout 2008.

PRESEPT is a multinational, multicenter clinical study sponsored by Epigenomics to prospectively evaluate the clinical performance of our proprietary biomarker, Septin 9, for colorectal cancer population screening in guideline-eligible individuals. It is one of the first studies ever to evaluate the performance of a noninvasive test to indicate the presence of colorectal cancer in asymptomatic individuals in a standard blood sample. The study is designed to enroll up to 7,500 asymptomatic subjects aged 50 or older at average to increased risk for colorectal cancer who have been scheduled for a regular screening colonoscopy at up to 21 clinical sites in the U.S.A. and in Germany. This population is expected to harbor about 50 cases with undetected colorectal cancer.

Since starting the PRESEPT Study in Q2 of 2008, we have successfully qualified 21 clinical sites, 17 of which were actively enrolling more than 1,800 subjects by year-end 2008. The increased number of clinical sites is now expected to ramp up accrual of subjects over the next several months.

When the total of 22 clinical sites – including four in Germany – are initiated, PRESEPT will be one of the largest commercially sponsored colorectal cancer screening clinical studies ever conducted.

The study is intended to characterize the performance characteristics and evaluate the health economic benefit of the Septin 9 marker with the goal to demonstrate it will meet the requirements of current U.S. screening guidelines for noninvasive screening tests. The clinical performance and health economic analysis results are expected to support future coverage by public and private health insurers worldwide. Further, Epigenomics will provide industry partners developing Septin 9 IVD tests access to the PRESEPT samples and data to perform pivotal clinical trials necessary to obtain regulatory approvals. Epigenomics is providing clinical collaborators, medical professionals, and the interested public with study details and regular updates on the progress of the PRESEPT Study on the website [www.presept.net](http://www.presept.net).

We assembled and empowered a Clinical Study Steering Committee (CSSC) to advise Epigenomics as the sponsor on the PRESEPT Study design, oversee the quality of the study conduct according to worldwide clinical research practice standards, and independently analyze and accurately report the results. The members of the CSSC include:

- *David Ransohoff, M.D.*, Professor of Medicine, Cancer Epidemiology, Cancer Prevention and Control, University of North Carolina School of Medicine (Chair);
- *Neal Osborn, M.D.*, Co-Director of Clinical Research, Atlanta Gastroenterology;
- *Timothy R. Church, Ph.D.*, Professor, School of Public Health, University of Minnesota;
- *Brent Blumenstein, Ph.D.*, Principal, Trial Architecture Consulting;
- *Dale Snover, M.D.*, Adjunct Professor, Department of Laboratory Medicine and Pathology, University of Minnesota Medical School;
- *Robert Day, M.D., Ph.D.*, President Emeritus of The Fred Hutchinson Cancer Research Center (ex officio) and
- *Prof. Dr. Thomas Rösch*, Director of the Clinic for Interdisciplinary Endoscopy, University Hospital Hamburg-Eppendorf.

In addition to the external participants, two sponsor representatives, Michael Wandell, Pharm.D, Study Director, and Catherine Lofton-Day, Ph.D., Project Manager, are CSSC members.

The design of the PRESEPT Study was developed in close collaboration with Epigenomics' Medical Advisory Board for Colorectal Cancer Screening (MAB) that represents a cross section of primary care physicians and gastroenterologists with particular expertise in colonoscopy, colorectal cancer screening, evidence-based medicine, outcomes research, and health economic analysis. The Medical Advisory Board supports us in development and commercialization of our colorectal cancer screening test in the U.S.

It will support us through design of our clinical studies, speaking on behalf of the application of DNA methylation technology to colorectal cancer screening in the U.S., advising on product positioning in the U.S. and support inclusion of blood screening assays into screening guidelines promulgated by U.S. professional societies. The members of the MAB now include:

*Richard Wender, M.D.*, Alumni Professor and Chair of the Department of Family and Community Medicine at Thomas Jefferson University in Philadelphia, PA;

*Douglas Rex, M.D.*, Chancellor's Professor and Professor of Medicine at Indiana University School of Medicine and Director of Indiana University Hospital in Indianapolis, IN;

*Philip S. Schoenfeld, M.D. M.ED., M.Sc.*, Associate Professor, Department of Internal Medicine, University of Michigan in Ann Arbor, MI;

*Deborah Fisher, M.D., MHS*, Assistant Professor of Medicine, Duke University in Durham, NC;

*Scott Ramsey, M.D., Ph.D.*, Associate Professor of Medicine and Health Services, Associate Member, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center in Seattle, WA.

### *Prostate Cancer*

In October 2008, we reported the successful completion and positive results from our clinical study in prostate cancer prognosis. After testing all patient samples for methylation in the PITX2 gene, we successfully conducted our final analysis. This analysis showed that PITX2 gene methylation is indeed a strong, independent prognostic marker that can help guide physicians to determine a prostate cancer patient's risk for relapse. The analysis demonstrated statistical significance for all study endpoints.

The clinical study successfully analyzed paraffin-embedded tissue samples from 476 prostate cancer patients collected at four major clinical centers in Europe and the U.S.A. who had undergone radical prostatectomy, with the objective of validating the prognostic utility of Epigenomics' proprietary biomarker, PITX2. The primary endpoint of the study was to evaluate the methylation status of the PITX2 gene as an independent prognostic biomarker indicative of the risk of prostate cancer biochemical recurrence in patients following removal of the entire prostate, known as radical prostatectomy. This primary endpoint of the study was met by the statistically significant demonstration that patients with elevated PITX2 gene methylation level had a threefold higher risk of relapse following prostatectomy compared to patients with low PITX2 methylation (hazard ratio 3.0;  $p < 0.00005$ ).

The study confirmed the clinical utility of the PITX2 biomarker for prostate cancer prognosis, first established in a 2006 clinical study on 605 prostatectomy tissue samples using real-time PCR. In the current study the PITX2 gene methylation was measured reliably using an Affymetrix GeneChip™ platform, confirming the robustness of the marker across various assay technologies suitable for routine laboratory use.



We designed and analyzed the study together with our clinical collaborators at Baylor College of Medicine, Houston, Texas, U.S.A., at Erasmus Medical Center, Rotterdam, The Netherlands, at Duke University Medical Center and the VA Medical Center at Durham, North Carolina, U.S.A., and University Hospital Erlangen, Erlangen, Germany.

A publication of the clinical study data is planned in a peer-reviewed journal in due course. Results from this clinical study were also presented at the American Molecular Pathology (AMP) Conference in Grapevine, Texas, U.S.A.

During 2008, we also generated additional data in our prostate cancer early detection program using both tissue as well as urine samples. As a first product, Epigenomics and TIB Molbiol have launched the LightMix<sup>®</sup> Kit GSTP1 for DNA methylation analysis of the GSTP1 gene at the Analytica conference in Munich, Germany, in April 2008. GSTP1 is among the best-described DNA methylation biomarkers in cancer. Our own research as well as other prominent research have shown that methylated DNA in particular regions of the GSTP1 gene in tissue as well as in urine is a potential biomarker for prostate cancer indications. The LightMix<sup>®</sup> kits are based on Epigenomics' proprietary HeavyMethyl<sup>®</sup> (HM) technology for sensitive and quantitative DNA methylation detection and optimized for use with Roche LightCycler<sup>®</sup> instruments and Roche FastStart<sup>®</sup> PCR kits.

### *Lung Cancer*

During 2008, we successfully completed a clinical study in our lung cancer program. The study was run in close collaboration with Prof. Dr. Christian Witt and Dr. Bernd Schmidt at the Charité University Hospital, Berlin, Germany ("Charité"). The clinical study of 84 patient samples demonstrated that a panel of two proprietary biomarkers detected 79% of lung cancers in bronchial lavage specimens at a specificity of 95%, i.e. only two false-positive results were obtained in 45 patients with benign lung diseases.

Bronchial lavage specimens are routinely taken during bronchoscopy that is performed to diagnose lung cancer. In current clinical routine, the bronchial lavage fluid is analyzed by a pathologist to identify tumor cells. However, this microscopic analysis often cannot either confirm or exclude lung cancer. A molecular diagnostic test that sensitively and objectively detects the presence of tumor cells in this specimen could potentially improve clinical decision-making for patients with suspected lung cancer. "Molecular markers with the performance demonstrated in our study could be of substantial benefit in this situation", says Prof. Dr. Christian Witt, Head of the Department of Pneumology at the Charité.

During the latter parts of 2008, we conducted a larger clinical study using bronchial lavage specimens to validate earlier results in a larger cohort. Data analysis and optimization of the biomarker panel used to best address the medical question is still ongoing.

We also successfully completed another larger clinical study in our lung cancer program. The study was also run in close collaboration with Prof. Dr. Christian Witt and Dr. Bernd Schmidt at the Charité.

The study on 256 patient samples confirmed that a two-biomarker panel correctly identified two thirds of all lung cancers in blood plasma (66% sensitivity) at a false-positive rate of 12% (88% specificity). Notably, about two thirds of the blood samples used in the study were obtained from patients with early-stage I and II cancer. Sensitivity in stage II lung cancer patients reached 73%. Patients with early-stage cancer are significantly underdiagnosed in the current diagnostic practice for lung cancer but could benefit most from early therapeutic intervention.

These latest results independently confirm previous data from a much smaller proof-of-concept study performed by Epigenomics in 2007 that was weighted towards later-stage disease reflecting the unfavorable stage distribution found in the current diagnostic practice.

We have presented data from our lung cancer program to very positive response at the International Lung Cancer Conference in Liverpool, UK, at the European Respiratory Society Annual Congress in Berlin, Germany, and at the International Thoracic Oncology Congress in Dresden, Germany.

## Marketing and business development

During 2008, we substantially strengthened our team and started building a small commercial organization to drive adoption of our RUO kits in European laboratories. We hired a Head of Marketing & Sales experienced in the cancer molecular diagnostics industry. We also hired our first sales representative and a technical sales support person.

Our business development efforts were primarily geared towards managing ongoing collaborations such as the Abbott Molecular and Qiagen deals, as well as identifying potential new partners in our nonexclusive partnering model for Septin-9-based colorectal cancer test development and commercialization as well as our other programs.

In January 2008, we closed the OncoMethylome licensing deal and the strategic cross-licensing agreement with DxS Ltd., in February 2008, we signed a nonexclusive licensing deal with Quest Diagnostics and in April 2008, we launched the first RUO kits with TIB Molbiol. In Q3, we signed another biomarker research collaboration with J & J and CellTrend, in November, we expanded our Abbott collaboration to include the PRESEPT clinical study and in December, we signed a collaboration and licensing agreement with Royal Philips Electronics.

As of the end of 2008, we were engaged in several negotiations with regard to signing up licensees and partners for the development and commercialization of diagnostic products and test services based on our proprietary biomarkers Septin 9 (colorectal cancer), PITX2 (prostate/breast cancer prognosis) and GSTP1 (prostate cancer diagnosis) as well as some of our proprietary lung cancer markers. It is our goal to enter into a total of three to no more than four nonexclusive partnering arrangements for Septin 9 in the medium term to maximize market penetration and platform flexibility whilst maintaining highest levels of commitment to the product from each licensee and partner.

### Controlling system

The Company's controlling system is primarily based on miscellaneous planning, monitoring and reporting tools. Qualitative information derives from a self-developed project documentation database and quantitative information is processed by Navision™, a widely used enterprise resource planning software. Our accounting and controlling department provides all relevant controlling information to the Executive Board on a monthly basis. An ongoing education of the team members is ensured.

For internal control purposes we set up an annual budget developed from the actual mid- to long-term business planning of the Company. The budget is developed bottom-up from all cost centers and our R&D projects. A final approval of the annual budget by our Supervisory Board is mandatory.

Prime focus of our regular internal management reporting lies in comparing actual versus budgeted values for a comprehensive set of metrics. From these we compile the external quarterly reports. The reporting is supplemented as needed with additional data requested by the Supervisory Board or the Executive Board as well as the controlling team. Each quarterly report is accompanied by an internal forecast, which provides us with an updated estimate of expected full-year results and performance vis-à-vis target numbers.

### Quality management

We have established a comprehensive quality management system. This system includes numerous standard operating procedures and policies for the design and development of products. The quality function is headed by a designated quality manager reporting directly to the CEO. A project to prepare for ISO certification in 2009 has been initiated in the reporting year.

## Five-year Overview

- according to the consolidated financial statements -

EUR thousand (unless stated otherwise)	2004	2005	2006	2007	2008
<b>Income Statement</b>					
Revenue	7,931	9,594	3,504	2,567	2,586
Gross profit	1,509	1,904	-1,516	1,693	888
R & D costs	-7,336	-8,121	-8,702	-10,471	-10,028
EBIT <sup>1</sup>	-10,351	-10,234	-15,761	-13,504	-12,750
EBITDA <sup>2</sup>	-8,907	-8,560	-14,193	-12,259	-10,242
Net loss for the year	-10,975	-8,788	-15,402	-13,151	-12,271
Earnings per share basic and diluted (in EUR) <sup>3</sup>	-0.80	-0.54	-0.92	-0.74	-0.47
<b>Balance sheet</b>					
Non-current assets	9,677	9,471	10,559	9,070	5,857
Current assets	43,607	35,526	19,575	13,844	14,426
Total assets	53,284	44,997	30,134	22,914	20,283
Equity	47,739	39,375	26,198	17,821	16,568
Equity ratio (in %)	89.6	87.5	86.9	77.8	81.7
Non-current liabilities	41	4	0	0	38
Current liabilities	5,504	5,618	3,935	5,093	3,677
<b>Cash flow statement</b>					
Cash flow from operating activities	-8,885	-7,501	-14,378	-11,516	-9,800
Cash flow from investing activities	-10,214	-1,689	2,610	1,049	1,468
Cash flow from financing activities	32,757	228	807	4,547	11,500
Net cash flow (currency-adjusted)	13,747	-8,647	-10,953	-5,920	3,168
Cash and cash equivalents at year-end	32,166	23,519	12,566	6,646	9,814
<b>Other information</b>					
Investments in tangible and intangible assets	964	1,007	2,920	65	258
Number of employees at year-end	146	141	145	112	90
Share price at year-end (in EUR)	8.67	6.45	3.50	1.95	2.00

<sup>1</sup> EBIT = earnings before interest and taxes

<sup>2</sup> EBITDA = earnings before interest, taxes, depreciation and amortization

<sup>3</sup> The outstanding stock options granted by the Company are antidilutive according to IAS 33.41 and 33.43 *Earnings per Share*. Therefore, the earnings per share (diluted) equal the earnings per share (basic).

## Financials

### Results of operations

Compared to 2007, our revenue position could be improved slightly in absolute terms. Revenue in the amount of EUR 2.6 million (2007: EUR 2.6 million) was generated from new business collaborations and several ongoing R & D partnerships and licensing agreements. Our diagnostics business generated EUR 1.7 million, resulting from licensing contracts and reimbursements, whereas our Biomarker Solutions business contributed EUR 0.9 million for its services.

Cost of sales increased from EUR 0.9 million in 2007 to EUR 1.7 million, due to new collaborations, which required more resource allocations in advance. Gross margin read 34% in 2008 (2007: 66%).

Other income decreased from EUR 1.4 million in 2007 to EUR 1.1 million in 2008. While income funded by research grants declined significantly as our major granted projects were completed before or during 2008, this effect was partially offset by a strong increase in currency exchange rate gains which account for nearly half of the reported other income.

Compared to 2007, R & D costs dropped by EUR 0.4 million to EUR 10.0 million at the end of 2008. This is a result of the concentration on our key value drivers, the screening products. The R & D costs for 2008 also include a one-time write-off of impaired development licenses and laboratory equipment totalling EUR 1.6 million and hence from an operational standpoint – excluding these extraordinary effects – the R & D costs were reduced by more than EUR 2.0 million or 20% compared to 2007. The write-off of the licenses and the equipment followed a decision not to use the underlying technology anymore for the development of an IVD platform.

Marketing and business development costs significantly decreased by 33% to EUR 0.9 million (2007: EUR 1.3 million), primarily due to our more focused strategy in product development and the reorganization of our marketing and business development team.

General and administrative costs could be reduced by 20% to EUR 3.4 million (2007: EUR 4.3 million) due to the ongoing progress made in our “Epi 2010” initiative.

Other expenses remained virtually constant at EUR 0.4 million in 2008, mainly caused by currency exchange rate losses and expenses related to previous years.

In 2008, operating result (EBIT) improved by EUR 0.7 million to EUR -12.8 million (2007: EUR -13.5 million). In sum, overall activities are now focused on the execution with more streamlined operations, which are a reason for lower costs.

As described before, due to the ongoing financial discipline, our operating cost basis decreased significantly in 2008. Furthermore, this development was partly attributable to the progress of our “Epi 2010” initiative, under which we decided to centralize our R&D operations in Berlin and to focus Seattle-based Epigenomics, Inc. on managing and running clinical trials such as the PRESEPT Study. This optimization led to cost savings, in most of the significant cost categories.

Costs for consumables and supplies were reduced by 31%, staff costs saw a reduction of 13%, travel costs decreased by 20%, legal and consulting costs were reduced by 28% and costs for rent and maintenance went down by 12%. All of the above-mentioned cost reductions were partially compensated by the increase of depreciation and amortization arising from the afore-mentioned one-off impairment effect in licenses and equipment.

In the reporting period, our net loss amounted to EUR 12.3 million at the end of 2008. Hence, the result could be improved by 7% (2007: EUR 13.2 million).

### Financial position and cash flow

At the end of the reporting year, Epigenomics had cash, cash equivalents and marketable securities of in total EUR 12.1 million. In 2008, Epigenomics’ cash flow and financial position were strengthened through the successful capital increase completed in February 2008, but the financial position was mainly affected by the continued cash consumption for operating activities.

Total net cash flow in 2008 amounted to EUR 3.2 million and was positive compared to a negative net cash flow of EUR 5.9 million in 2007.

Cash outflow from operating activities amounted to EUR 9.8 million and was lower than the cash outflow of 2007 (EUR 11.5 million). A streamlined organization and the focus on the execution of our screening products reduced our operating expenditures by EUR 1.7 million.

Our net cash flow from investing activities was positive at EUR 1.5 million in 2008. Proceeds from the redemption of securities and non-current financial assets of EUR 1.6 million overcompensated our cash outflow for investments in tangible and intangible assets.

Net cash inflow from financing activities amounted to EUR 11.5 million attributable to the capital increase in February 2008 and its gross proceeds of about EUR 13.5 million. In February 2009, an additional EUR 5.2 million in net proceeds augmented our cash inflow.

## Net asset position

At the end of 2008, Epigenomics' balance sheet total decreased from EUR 22.9 million to EUR 20.3 million. Although the capital increase realized in February 2008 improved our balance sheet during the period, the ongoing net consumption of liquidity by our operations lowered the balance sheet total.

Total non-current assets dropped by EUR 3.2 million to EUR 5.9 million at the end of the year. As in previous periods, goodwill of EUR 2.6 million, which is part of the total non-current assets position was tested for impairment and no impairment was determined. Besides keeping capital expenditures at a very low level, the decrease of total non-current assets was also driven by closing the laboratory R&D operations in Seattle, which led to some impairment at the end of 2008.

In addition, an extraordinary depreciation and amortization was realized in Berlin for assets, which had a lower residual value for the Company.

As of December 31, 2008, tangible assets decreased by EUR 0.5 million to EUR 0.7 million, because some minor investments were highly overcompensated by depreciation and amortization.

Current assets rose from EUR 13.8 million to EUR 14.4 million. Cash and cash equivalent could be improved by EUR 3.2 million, as a result of the rights issue in February 2008 and its gross proceeds of about EUR 13.5 million.

At the end of December 31, 2008, our subscribed capital increased by 8,470,812 shares at a notional par value of EUR 1.00 each compared to the previous balance sheet date. This increase was due to the aforementioned capital increase, with a remainder (12,750 shares) resulting from the exercise of stock options. After the offset of the retained losses against the capital reserve, the latter decreased as of the balance sheet date to EUR 3.6 million. The net loss for the reporting year of EUR 12.3 million thus exceeds the remaining capital reserve even though our equity ratio improved from 77.8% at the end of 2007 to 81.7% as of December 31, 2008.

Current liabilities decreased by EUR 1.4 million. Trade payables were EUR 0.5 million lower, whereas deferred income increased by EUR 0.6 million, due to an upfront payment received in 2008. Other liabilities were reduced by EUR 1.5 million due the realization of the financing transaction in 2008. Accrued expenses were charged against the proceeds from the financing.

## Employees

	Berlin	Seattle	Total
<b>Number of employees as of Dec 31, 2008</b>	<b>70</b>	<b>20</b>	<b>90</b>
Number of employees as of Dec 31, 2007	78	34	112
<b>Employees on average 2008</b>	<b>72</b>	<b>25</b>	<b>97</b>
Employees on average 2007	85	36	121

The Epigenomics Group employed a total staff of 90 as of December 31, 2008, a sharp decrease compared to the number of 112 a year ago. Year-end numbers include a number of important new hires during 2008 such as our new head of product development, a head of marketing, a marketing & sales manager, as well as technical sales support staff.

During 2008, the average number of employees on a monthly basis amounted to 97 (2007: 121). The significant decrease against 2007 was attributable to our restructuring process as part of our “Epi 2010” initiative announced in spring of 2008. Whilst our Berlin operations were somewhat streamlined in terms of administrative functions, IT support and research, all laboratory operations in Seattle were discontinued and concentrated in Berlin.

The number of employees in Berlin also includes three apprentices.

Overall personnel costs totalled EUR 7.1 million in 2008, compared to the previous year’s cost of EUR 8.2 million. This decrease by 13.1% is attributable to our aforementioned reorganization.

## Compensation Report

The Executive Board of Epigenomics AG consists of the two members Geert Walther Nygaard (CEO) and Oliver Schacht, Ph.D., (CFO). During 2008, Dr. Kurt Berlin (CSO) and Christian Piepenbrock (COO) resigned from their respective Executive Board positions.

The Executive Board is responsible for independently managing and running operations, developing and implementing corporate strategy and budgetary planning, appointing and guiding senior management and overseeing general management of the Company. There is a continuous and intensive dialog between the Executive Board and the Supervisory Board and their respective members. In its charter, the Executive Board has been given a clear set of rules and procedures for certain actions and decisions that would require Supervisory Board approval.



## Compensation of the Executive Board

The compensation of the members of the Company's Executive Board is composed of a fixed and a variable component. The variable amount is determined on the basis of a variety of criteria, including the achievement of individual performance goals and performance goals for the Company. Total compensation – which is reviewed by the Supervisory Board annually – is compared to national and international benchmarks. Compensation takes into account the economic and financial situation as well as size and complexity of international operations and responsibilities. Apart from the fixed and the variable component, there is a third compensation component; a long-term performance-based compensation in the form of stock option grants.

In 2008, the aggregate compensation of the members of the Executive Board amounted to EUR 1.3 million. It consisted of EUR 0.8 million in fixed salary and the remainder of EUR 0.5 million in variable and other salary components.

The service agreements of all members of the Executive Board contain post-contractual noncompete provisions, each for a period of two years after the service agreement has ended. During such period, Mr. Nygaard is entitled to 100% of his last basic salary as a compensation payment (Karenzentschädigung), whilst Mr. Schacht is entitled to 50% of his last base salary during this period.

For Chief Finance Officer Oliver Schacht, Ph.D., Epigenomics paid rent – due to his activity as CEO for Epigenomics, Inc. (Seattle, U.S.A.) – in monthly installments for his apartment in Berlin, Germany, and reimbursed other apartment expenses.

For its former Chief Scientific Officer, Dr. Kurt Berlin, Epigenomics paid a life insurance, a casualty insurance and made capital forming payments until his retirement.

Effective April 30, 2008, Christian Piepenbrock, co-founder and Chief Operating Officer of Epigenomics, resigned from his Executive Board position and left Epigenomics to pursue other career opportunities. Mr. Piepenbrock received a one-time payment in the amount of EUR 290 thousand due to contractual claims. There are no other future obligations between Epigenomics AG and Mr. Piepenbrock.

On August 5, 2008, the Supervisory Board and Dr. Kurt Berlin, Chief Scientific Officer (CSO) of Epigenomics AG, agreed that Dr. Berlin would step down as CSO and Executive Board member effective August 31, 2008. Dr. Kurt Berlin, one of the co-founders of the Company, now serves as chairman of Epigenomics' Scientific Advisory Board and is continuing to advise Epigenomics on scientific, technological, licensing and IP-related matters as a consultant throughout 2008 and 2009.

The individual compensation is shown below, whereby "other compensation" consists of payments for vacation days not taken and other reimbursed components as mentioned before.

in EUR	Fixed compensation 2008 (2007)	Variable compensation 2008 (2007)	Other compensation 2008 (2007)	Total compensation 2008 (2007)
<b>Members of the Executive Board in 2008</b>				
<b>Geert Walther Nygaard</b> Chief Executive Officer, Berlin (D)	<b>380,000</b> (348,333)	<b>56,625</b> (68,500)	<b>0</b> (76,513)	<b>436,625</b> (493,346)
<b>Oliver Schacht, Ph.D.</b> Chief Financial Officer, Seattle, WA (U.S.A.)	<b>187,010</b> (169,922)	<b>117,000</b> (123,750)	<b>10,326</b> (11,116)	<b>314,336</b> (304,788)
<b>Dr. Kurt Berlin (until August 31, 2008)</b> Chief Scientific Officer, Stahnsdorf (D)	<b>119,733</b> (170,319)	<b>62,500</b> (97,500)	<b>630</b> (11,746)	<b>182,863</b> (279,565)
<b>Christian Piepenbrock (until April 30, 2008)</b> Chief Operating Officer, Berlin (D)	<b>59,867</b> (170,000)	<b>0</b> (93,750)	<b>290,000</b> (2,500)	<b>349,867</b> (266,250)
<b>Total compensation</b>	<b>746,610</b> (858,574)	<b>236,125</b> (383,500)	<b>300,956</b> (101,875)	<b>1,283,691</b> (1,343,949)

In accordance with Section 6.6 Paragraph 2 of the German Corporate Governance Code, the ownership of shares in the Company or related financial instruments by the Executive Board and the Supervisory Board will be reported if these directly or indirectly exceed 1% of the shares issued by the Company.

As of December 31, 2008, CEO Geert Walther Nygaard owned 20,000 shares of the Company (Dec 31, 2007: 0) and CFO Oliver Schacht, Ph.D., owned 117,050 shares of the Company (Dec 31, 2007: 104,550).

At the balance sheet date, the members of the Executive Board held 326,613 stock options of the Company:

	Stock options held as of Dec 31, 2008 (Dec 31, 2007)	Weighted average exercise price in EUR as of Dec 31, 2008 (Dec 31, 2007)	Vested options as of Dec 31, 2008 (Dec 31, 2007)	Weighted average exercise price in EUR as of Dec 31, 2008 (Dec 31, 2007)	Exercised options in 2008 (2007)
<b>Members of the Executive Board</b>					
<b>Geert Walther Nygaard</b>	<b>180,000</b> (180,000)	<b>4.50</b> (4.50)	<b>60,000</b> (0)	<b>4.50</b> -	<b>0</b> (0)
<b>Oliver Schacht, Ph.D.</b>	<b>146,613</b> (159,363)	<b>4.51</b> (4.29)	<b>86,613</b> (0)	<b>4.52</b> -	<b>12,750<sup>1</sup></b> (0)

In 2008 no stock options were granted to members of the Executive Board.

<sup>1</sup> The share price at exercise of the options amounted to EUR 1.88.

## Compensation of the Supervisory Board

Epigenomics AG's Supervisory Board consists of six members. All members have broad experience in the pharmaceutical, diagnostics and financial industries.

Members of the Supervisory Board in 2008<sup>1</sup> were:

*Prof. Dr. Dr. h.c. Rolf Krebs*, Mainz (D), Chairman

Retired speaker of the Executive Board of Boehringer Ingelheim Pharma GmbH & Co. KG

- Other supervisory board mandates as of Dec 31, 2008: Air Liquide S.A., Ganymed Pharmaceuticals AG, Merck KGaA, Merz GmbH & Co. KGaA, Merz Pharma GmbH & Co. KGaA
- Mandates terminated in 2008: none

*Prof. Dr. Dr. Uwe Bicker*, Bensheim-Auerbach (D), Deputy Chairman

Associated professor at the University of Heidelberg

- Other supervisory board mandates as of Dec 31, 2008: Siemens Healthcare Diagnostics Holding GmbH (formerly: Dade Behring Marburg GmbH) (Chairman), Definies AG, Future Capital AG, Sanofi Aventis S.A.
- Mandates terminated in 2008: none

*Günter Frankenne*, Berg/Neumarkt (D)

Managing partner of STRATCON Strategy Consulting

- Other supervisory board mandates as of Dec 31, 2008: 4SC AG, Concentro AG (Chairman), KeyNeurotek AG (Chairman), November AG (Chairman), Verbena AG
- Mandates terminated in 2008: LCG LifeSciences Consulting Group International AG

*Ann Clare Kessler, Ph.D.*, Rancho Santa Fe, CA (U.S.A.)

Independent consultant

- Other supervisory board mandates as of Dec 31, 2008: MedGenesis Therapeutix, Inc., The Vaccines Company Ltd.
- Mandates terminated in 2008: none

*Heino von Prondzynski*, Einsiedeln (CH)

Independent consultant

- Other supervisory board mandates as of Dec 31, 2008: BB Medtech AG (Chairman), Koninklijke Philips Electronics N.V., Qiagen N.V.
- Mandates terminated in 2008: none

*Prof. Dr. Günther Reiter*, Pfullingen (D)

Professor at the European School of Business, Reutlingen

- Other supervisory board mandates as of Dec 31, 2008: Deltoton AG
- Mandates terminated in 2008: none

<sup>1</sup> The "other supervisory board mandates" indicate memberships in other supervisory boards or domestic and international control boards according to Section 125 Paragraph 1 Sentence 3 of the German Stock Corporation Act.

The Supervisory Board of Epigenomics AG has established two committees: First, an Audit and Corporate Governance Committee, assisting the Supervisory Board in approving all financial statements, commissioning the auditors, choosing appropriate topics for the main focus of the audit, determining the audit fees, and ensuring the independent status of the auditors as well as all aspects of compliance and corporate governance. Second, a Personnel and Compensation Committee, dealing with all aspects of the nomination of Executive Board members, their compensation as well as preparing other compensation-related decisions that require Supervisory Board approval.

The Supervisory Board, upon discussion with the Executive Board, also sets the strategic, financial and business goals for each fiscal year that form the basis for measuring performance of each member of the Executive Board as pertains to the respective variable compensation component.

*Compensation of the members of the Supervisory Board in 2008:*

in EUR	Annual retainer compensation	Meeting fees	Compensation as committee chairman	Total compensation
Prof. Dr. Dr. h.c. Rolf Krebs	30,000	5,000	5,000	40,000
Prof. Dr. Dr. Uwe Bicker	20,000	10,000	0	30,000
Günter Frankenne	10,000	10,000	0	20,000
Ann Clare Kessler, Ph.D.	10,000	10,000	0	20,000
Heino von Prondzynski	10,000	10,000	0	20,000
Prof. Dr. Günther Reiter	10,000	10,000	5,000	25,000
<b>Total compensation 2008</b>	<b>90,000</b>	<b>55,000</b>	<b>10,000</b>	<b>155,000</b>
Total compensation 2007	88,333	60,000	10,000	158,333

In addition, the members of the Supervisory Board were reimbursed for expenses totaling EUR 29 thousand in 2008 (2007: EUR 25 thousand).

The compensation structure approved by the Annual General Shareholders' Meeting in 2007 has been unchanged in 2008 and is based on an annual cash retainer, meeting-related fees plus additional payments for committee chairing work. The compensation did not comprise any performance-related elements or long-term incentive components.

During the reporting year, the members of the Supervisory Board held no stock options nor any other convertible instrument nor any other equity-linked compensation entitlement of the Company. Ann Kessler, Ph.D, purchased 14,000 shares as part of the February rights issue and held these shares as of December 31, 2008.

## Supplementary Report

### Information on material events after the balance sheet date

#### *Epigenomics AG signs strategic R&D collaboration agreement in colorectal cancer with Sysmex Corporation*

On January 22, 2009, Epigenomics AG announced a strategic research and development collaboration agreement in molecular diagnostics with Sysmex Corporation, headquartered in Kobe, Japan.

Under the terms of the agreement, Sysmex and Epigenomics will assess the suitability of Sysmex's molecular diagnostics instrumentation for the detection of DNA methylation cancer biomarkers in blood. As a benchmark for the development of its assay system, Sysmex will use Epigenomics' <sup>m</sup>SEPT9 methylation detection assay commercially available as a research-use-only product. If successful, Sysmex intends to develop and commercialize initially in Japan a blood test for the early detection of colorectal cancer based on Epigenomics' proprietary SEPT9 DNA methylation biomarker (<sup>m</sup>SEPT9). At entering into this collaboration, both parties have started negotiations for a nonexclusive <sup>m</sup>SEPT9 licensing agreement.

Under the terms of the collaboration agreement, Sysmex gets access to Epigenomics' technologies through R&D licenses and technology transfer and will be supported by Epigenomics in its R&D work. In return, Epigenomics will receive certain license fees, R&D funding and reimbursements and will sell its <sup>m</sup>SEPT9 research-use-only product to Sysmex.

The collaboration agreement with Sysmex will lead to some modest upfront payments from Sysmex to Epigenomics and further payments to fund Epigenomics' R&D support within the collaboration.

#### *Epigenomics AG increases share capital*

On February 11, 2009, Epigenomics AG announced that the Executive Board and the Supervisory Board have resolved to increase the share capital of the Company against contribution in cash and without subscription rights. Epigenomics has placed 2,671,088 new shares by way of a direct private placement with institutional investors in Europe. All new shares were placed to a 100% subsidiary of BB Medtech AG (Schaffhausen, Switzerland) and two funds managed by Abingworth LLP (London, UK).

The issue price has been set at EUR 1.94 per share. This constitutes a 5% premium over and above the volume-weighted average XETRA trading prices over the five trading days preceding the announcement of the capital increase. The capital raise yielded gross proceeds of approximately EUR 5.18 million. After registration of the capital increase, the signed capital of Epigenomics AG increased from EUR 26,723,636 to a total of EUR 29,394,724.

Epigenomics intends to apply the proceeds from this transaction towards the final stages of product development and commercialization of its most advanced product, a blood-based molecular diagnostic test for the early detection of colorectal cancer. Proceeds will also be used for clinical R&D in its lung cancer and prostate cancer programs.

The registration of the implementation of the capital increase with the commercial register (Handelsregister) was on February 23, 2009.

#### *Epigenomics AG licenses biomarker for development of prostate cancer test to Quest Diagnostics*

On February 25, 2009, Epigenomics AG announced that it has entered into a nonexclusive licensing agreement for its proprietary biomarker <sup>m</sup>GSTP1 with U.S.-based Quest Diagnostics Incorporated, the world's leading provider of diagnostic testing, information and services.

Under the agreement, Quest Diagnostics has obtained rights to use the GSTP1 DNA methylation biomarker (<sup>m</sup>GSTP1) to establish and commercialize a molecular-based laboratory-developed test that can help pathologists better diagnose prostate cancer based on testing of a patient's tissue specimen. Financial terms were not disclosed.

## Opportunities and Risk Report

### Opportunities and risk management system

Epigenomics is a globally operating cancer molecular diagnostics company and as such subject to many industry- and company-specific opportunities and risks. In line with the German "Corporation Sector Supervision and Transparency Act" ("Gesetz zur Kontrolle und Transparenz im Unternehmensbereich" - KonTraG), Epigenomics has an established, comprehensive and effective system to identify early, assess, communicate and manage opportunities and risks across all of its functions and operations. The underlying principles and guidelines have been documented in a groupwide "Risk Management Policy". The goal of this policy and all related systems is to identify risks systematically at the earliest possible stage, estimate their likelihood of occurrence as well as potential qualitative and quantitative impact, and design and implement effective countermeasures. The risk management has been regularly discussed and is being developed further at the Executive Board and the Supervisory Board levels.

Core principle is a transparency of risks and opportunities across functions and businesses, interactive evaluation of these and a culture of seizing opportunities and accepting risks as integral part of doing business in cancer molecular diagnostics, but doing so responsibly and seeking an optimal balance of opportunities and risks.

Every risk has a clearly identified "Risk Owner" whose responsibility it is to continuously monitor and control it as well as manage implementation of any countermeasures. At quarterly intervals, these risk owners report to the corporate "Risk Manager" who in turn communicates the risks to the Executive Board and the Supervisory Board. In case of any material risk, this risk is immediately brought to the attention of the corporate "Risk Manager" and discussed at the appropriate board levels. Important risks and the risk management system itself have also been discussed in broader management groups throughout the year.

Hence, our management structure, our organizational forums for identifying and assessing opportunities and risks, the monthly internal and external reporting as well as our controlling systems all form an integral part of the overall risk management system in a standardized fashion across all functions and locations. All of these tools are regularly monitored for effectiveness and optimized as well as reviewed by our auditors and the Audit and Corporate Governance Committee of our Supervisory Board.

For a comprehensive overview of the types of Company risks, please refer to the prospectus that was published as part of our rights offering in early 2008.

There are a number of important risks Epigenomics is faced with which individually or in combination could severely impact our revenue, earnings and financial situation as well as our stock price. These are described below:

### Business-related opportunities and risks

We are dependent on partners to partially fund our research and development costs and to manufacture, market, sell and distribute our products. Partnering and licensing is one way we already generate revenue prior to product sales and royalty income. With the end of our Roche collaboration in 2007, we were facing a challenge to find suitable development and commercialization partners for our main IVD products in early cancer detection. During 2008, we have worked closely together with Abbott as part of our worldwide nonexclusive partnership to develop and commercialize a Septin 9 blood-based in vitro diagnostic test for colorectal cancer. In 2008, we have also added Quest Diagnostics as a nonexclusive licensee to U.S. rights for an LDT for Septin 9 and in January 2009 Sysmex for the Japanese market.

However, we continue to be subject to certain partnering-related risks. Our partnerships are still in a co-development or R&D phase and need to deliver their full commercial potential in the future. Also, we still need to close additional nonexclusive licensing and partnering deals for Septin 9 in order to fully leverage multiple platforms in all key markets around the world and address the broadest possible market potential.

Given the substantial changes in the FDA's stance towards LDTs and several warning letters sent to some of our competitors, we have taken every precaution and very carefully designed and limited the interactions with Quest Diagnostics to the extent permitted under these rules and regulations. We therefore have very limited insight into the specifics of their LDT development progress, exact timelines and steps taken in the CLIA validation process.

The DNA methylation field has seen significantly intensified competition over the past years. Several competitors have made progress to enter the DNA methylation market or have indicated to be working on DNA-methylation-based research products. The competition for a convenient blood-based colorectal cancer test is also intensifying. It is important that our partners and we defend the lead we have in terms of clinical validation and are expanding by our ongoing PRESEPT Study compared to others who are targeting the same market such as Canadian GeneNews, Belgian OncoMethylome, Swiss Diagnoplex and others. So far, there is no convenient blood-based colorectal cancer test in the market in Europe or the U.S.A. nor in Asia.

Epigenomics' Septin 9 RUO kit is the first commercially available assay to measure a biomarker that has been shown in over 3,500 samples to be indicative of colorectal cancer.

Building the extensive clinical network for our PRESEPT Study as well as a network of clinical sites for additional case-control studies has somewhat mitigated the risk of having timely and sufficient access to large numbers of high-quality patient samples. This clinical network in the U.S.A. and in Europe allows us to tap into vast resources and leverage the opportunities we have in our partnered programs with Abbott, Quest and future partners. Yet, access to samples remains simultaneously one of the critical risks and biggest opportunities we monitor and address on a continuous basis.

Failure to obtain regulatory approval, lack of market acceptance and penetration, payor resistance to reimburse our tests would all have material impact on our revenue, earnings, financial position and our ability to raise further capital and can lead to a total loss. Similar risks exist in all our partnered programs and might also make the entering into additional alliances harder.

### IP-related opportunities and risks

Our business relies heavily on commercializing our intellectual property in the form of know-how as well as licenses to patents and patent applications. Therefore, any negative impact on scope, duration, depth and breadth of claims granted, regional coverage, competing IP that we could depend on, difficulties in enforcing the protection, inadvertently infringing other IP, preventing others from infringing our IP, our ability to inlicense key IP etc. would negatively impact our cost base, our ability to compete as well as to commercialize our products and to close alliances, our revenue and ultimately our earnings and overall commercial success.

At the same time, the progress made in expanding our IP portfolio and getting several key patents for cancer testing (such as our Septin 9 marker) granted puts Epigenomics in a unique position to provide attractive licensing opportunities for the growing number of commercial players active in DNA methylation. This opportunity has been underscored by the strategic licensing agreements with Qiagen GmbH (2005 and 2007), OncoMethylome Sciences S.A. and DxS Ltd. (both Q1 2008).



## Opportunities and risks related to the regulatory environment

The regulatory environment in cancer molecular diagnostics has become more challenging especially with regards to LDTs/homebrew assays. This could impact the timing, cost and our ability to meet such regulatory standards. In parts, the regulatory frameworks are not fully established or clarified as evidenced by a number of warning letters sent by the FDA to a number of diagnostics companies and large reference laboratories. This in turn could negatively impact on revenue generation and put a burden on our cost base and earnings, financial position and ability to compete effectively. To mitigate this risk, we have established a corporate function dealing with quality systems as well as regulatory affairs. We seek advice from experienced advisors to prepare the organization for any potential issues. Strict management of our interactions with reference laboratories as well as seeking an early dialog with the U.S. FDA and other relevant authorities is an integral part of our risk management policies.

## Financial opportunities and risks

As of December 31, 2008, our available liquidity amounted to EUR 12.1 million. To ensure availability of sufficient liquidity for our medium- and longer-term operations, the necessity to further strengthen our financial position over the next years is understood. With the successful completion of the capital increase on February 7, 2008, yielding gross proceeds of about EUR 13.5 million, as well as the successful completion of the capital increase on February 12, 2009, yielding gross proceeds of about EUR 5.2 million, the immediate short-term financing risk has been substantially reduced. The implementation of our "Epi 2010" initiative, which in 2008 has reduced cash burn to EUR 9.8 million is also contributing to risk mitigation.

Operating in Germany as well as in the United States means we are subject to a foreign exchange rate risk even though it is predominantly limited to the Euro/U.S. dollar relation. We monitor this risk on a regular basis and evaluate as the case arise whether hedging transactions could minimize the exposure. Wherever possible within our investment policy, we also take advantage of opportunities that lie in higher interest rates in the euro compared to the U.S. dollar following the lowering of U.S. interest rates to historically low levels.

Our portfolio of securities faces price risks in the form of interest rate, issuer and impairment risks. Our investment policy stipulates to open only positions with an "investment grade" rating, however, we have not made any investments in securities available for sale for more than three years. In close cooperation with our banks, advisors, the Audit and Corporate Governance Committee of the Supervisory Board, we aim continuously at finding an appropriate balance between exposure to these opportunities and risks. This has been a key area of focus in 2008 due to the global financial crisis that has led to further loss of value in some securities available for sale. Due to a fundamental loss of confidence in the markets, the financial crisis made it very hard to liquidate any security at short notice no matter how good the rating of the issuer was.

All investments in marketable securities have been made under the Company's investment policy, which is approved by the Supervisory Board. The securities must be nominated in euro currency to limit currency risks and an investment grade rating for the issuer or the security itself is mandatory to limit credit risks. In 2009 and going forward, we are looking to maintain as much of our liquid assets in the most secure money market instruments as possible.

## Other opportunities and risks

We continuously monitor all applicable environmental, health and safety, operational as well as other applicable statutory or industrial guidelines and have implemented functions to comply with all of these effectively at each of our business locations.

To minimize the potential impact from manifold tax, corporate, employment, competition, IP and other legal frameworks, we base our decision-making and design of our policies and processes on the advice of external as well as internal experts in each of these areas. Wherever appropriate and indicated, we set aside provisions to cover any potential liability.

There are risks particularly associated with our stock: The large holdings of a small number of institutional shareholders in Epigenomics shares, comparatively low levels of liquidity in the stock, very high volatility based on all of the above-described factors, as well as external influences and negative perceptions by others of any share sale. However, at the same time, the existing shareholdings in Epigenomics' stock provide the opportunity to have a very interactive dialog with key shareholders on a regular basis. This has been further strengthened in 2008 by the addition of Federated Kaufmann as the Company's single-largest institutional shareholder after the rights issue and the position built by BB Medtech in summer of 2008 and in the 2009 capital increase to become the second-largest shareholder.

There could potentially be other risks as well as significant opportunities beyond the ones described here that we currently either deem insignificant or are not aware of at the time of this report.

## Overall risk situation of Epigenomics Group

Whilst the good progress in our product development, the so far excellent clinical data in our colorectal, prostate and lung cancer programs and the ramp-up of subject enrolment in our PRESEPT Study have reduced many of the technical, clinical and operational risks, there are still many very significant risks facing Epigenomics overall. The outcome of the PRESEPT Study is uncertain and for the study to be successful we need to show that Septin 9 detects the "majority of colorectal cancer cases" in a single testing. This would ensure that the test is within the requirements of current U.S. CRC screening guidelines. The outcomes of any product development and further clinical studies in lung and prostate cancer indications are even more risky and uncertain as the stage of development is earlier and there has been less clinical validation work to date.

Any delay in our key development programs or the PRESEPT Study would require additional funding to complete the work. Delays in meeting milestones could make it harder to raise additional capital in the financial markets that despite our PIPE at the beginning of 2009 were all but shut for equity offerings of biotech companies in the U.S.A. and in Europe.

Addressing the need to raise additional cash either through partnering deals, leveraging individual assets, but also by potentially issuing additional shares to investors will remain a critical aspect of our risk management and risk mitigation strategy. There is clearly a risk of not being able to fully execute on all development and commercialization plans due to a lack of sufficient cash resources in the medium term. This bears the risk of losing key staff, their experience and know-how, and has the potential to destroy long-term value as a result of short-term liquidity constraints.

We do not consider the pending lawsuit of an individual shareholder against the Conditional Capital VI as approved by the ordinary Shareholder Meeting in 2008 to be a material risk.

## Prognosis Report

### Planned strategic direction of Epigenomics in the next two years

Over the next two years, we will continue to evolve Epigenomics into a product-development-driven and commercially focused cancer molecular diagnostics company. The key strategic focus will be on driving our colorectal cancer blood test based on Septin 9 assays through the final stages of clinical validation. To that end, our operational execution in 2009 will focus heavily on executing the PRESEPT Study and delivering positive clinical results from that trial. Also we will be working with Abbott Molecular to complete the final phases of product development with the strategic goal of having Abbott launch an IVD test kit for CRC screening based on Septin 9 in Europe as a CE-marked kit by the end of 2009 and to file with the FDA for approval of an IVD kit for the U.S. market in 2010. We will strive to broaden the number of laboratories in Europe and the U.S.A. that offer Septin 9 testing either using our RUO kits (Europe) or develop LDTs (U.S.A.).

Key to the successful implementation of our corporate strategy for broad and rapid market penetration will be to close additional nonexclusive licensing deals for CRC screening and Septin 9 in 2009 – as already happened with Sysmex – and 2010. This will be a key strategic focus of our marketing and business development efforts going forward.

During the next 24 months, we will also gradually move our other programs in lung cancer and possibly future tests in colorectal and prostate cancer indications towards and into product development. The goal is to establish Epigenomics as a cancer molecular diagnostics player with its own products in the market either through distributors or by direct sales and marketing activities. We follow a model of early market access via RUO kits in Europe, establishing relationships with reference labs in the U.S.A. for LDT development and launch, and then following with CE-marked IVD kits in Europe and eventually taking products through the FDA approval process where appropriate.

According to our current plans, our research and development shall focus on our current product pipeline in colorectal, lung and prostate cancer to develop successive generations of better products with higher performance and line extensions. We will also strive to maintain or expand our clear leadership in DNA methylation technologies and provide access to our know-how, expertise and IP in the field via licenses and services. To that end, we will fully integrate our biomarker solutions activities into the overall research organization.

## Expected economic conditions in the next two years

We expect overall economic conditions and the capital market environment to continue to be very challenging in 2009 and probably to significantly improve from 2010 onwards. This will continue to put pressure on stock prices globally and will make fund-raising in the life sciences arena very difficult. As the banking industry and the global financial system struggle to rebuild trust and make loans available, we foresee a lot of pressure even on larger corporations' budgets and expense lines.

With unemployment rates rapidly rising in the U.S.A. and labor markets expected to come under pressure in key European economies in 2009, we believe that hiring for open positions and filling positions with top candidates will be comparatively easy. However, as companies contract and cut budgets and R&D spending, it may become harder to close business deals that are front-loaded and provide Epigenomics with much-needed cash inflow.

As the financial crisis is expected to continue through much of 2009, liquidating the few remaining securities available for sale if that were to become necessary in a timely and efficient manner may be a challenge.

With currency movements extremely volatile between the U.S. dollar and the euro in the past twelve months and prognoses over the next twelve months anywhere from EUR/USD 1.10 to EUR/USD 1.55, we have decided to take a middle ground and lock in our budget rate for 2009 of EUR/USD 1.30. There is an upside to a weaker U.S. dollar for Epigenomics in terms of a potentially lower cost base in the PRESEPT Study which is predominantly U.S.-based and our U.S. operations.

## Outlook on earnings situation

We are expecting some moderate increases in revenue from our partnering activities in diagnostics as milestones are reached (e.g. CE-marked Septin 9 kit launch by Abbott), as RUO kit sales for our Septin 9, PITX2 and GSTP1 kits start getting some traction, and as new partnerships such as the Philips and Sysmex collaborations come into play. As the bulk of the PRESEPT expenses will hit 2009 operating expenses, we expect EBIT and net loss for 2009 to be at similar levels to 2008 actuals despite the increased revenue. Cash burn for fiscal 2009 should be at a very similar level compared to 2008, i.e. below EUR 10 million, possibly slightly below 2008 actuals.

For 2010, we expect first royalties from Abbott's Septin 9 kit sales in Europe, some growth in revenue from the RUO and LDT business opportunities built in 2008 and 2009, as well as continued additions to the R&D collaborations that contribute to revenue. As 2010 should clearly not have any significant PRESEPT expenses, depending on next products in the pipeline this could be an opportunity for adding some revenue in the meantime by potentially offering study management and clinical trial services to third parties and overall improvements in our earnings situation.

## Outlook on financial situation

With EUR 12.1 million in liquid resources at year-end 2008 and a projected cash burn of below EUR 10 million in 2009, current financial resources, combined with the cash inflow from our PIPE in February 2009 of EUR 5.2 million, should last until approximately the end of 2010. We expect to aggressively pursue all avenues of nondilutive financing in our business development and deal making efforts. We would anticipate to possibly leverage noncore assets and programs to maximize cash inflow over the next 24 months. However, in addition to keeping tight fiscal discipline on the expense side and trying to grow cash inflows, we will also consider our options for raising additional capital in the financial markets.

Lastly, it is the Annual General Shareholders' Meeting's prerogative to approve additional alternate financing mechanisms. We will explore the best possible options as part of the preparation for the 2009 Annual General Shareholders' Meeting to be held on May 11, 2009, in Berlin.

## Opportunities over the next two years

The next 24 months hold the opportunity to provide a solid commercial proof of concept for DNA-methylation-based cancer diagnostics. The technologies at Epigenomics for DNA methylation testing have come of age and matured to a stage where they are ready for prime time.

There is a huge opportunity to demonstrate that a Septin-9-based colorectal cancer blood test can be sold as RUO kit in Europe, and can be commercialized as LDT in the U.S.A. by leading reference labs. We also expect it can be successfully introduced to the European market by Abbott and other diagnostics partners as CE-marked kits, and shown to fulfil U.S. CRC screening guideline criteria in the PRESEPT trial and Abbott can file for FDA approval in 2010.

There are clear opportunities in prostate cancer testing with PITX2, which has potential in a prognostic setting in prostatectomy specimen as well as biopsy samples – by far the larger market opportunity – but long-term potentially also in other cancers. These are partnering and licensing opportunities, RUO kit opportunities and opportunities for IVD development.

Lung cancer raises many clinical questions that show huge medical needs for better diagnostics based on molecular tests. We have several proprietary biomarkers that present an opportunity to address such market needs and provide clear benefits to patients and physicians in this dreadful disease.

For our shareholders there is the clear opportunity to see the increased enterprise value from catalytic events reflected in the share price and have attractive capital market opportunities through an investment and trading in Epigenomics shares, but also potentially strategic options for the Company's future as commercial proof of concept is firmly established.

## Overall prognosis for the Epigenomics Group

On balance, there are many pivotal milestones to be reached over the next 24 months. These two years should see the final stages of a transformation of Epigenomics from a research- and technology-driven company to a commercially sound and sustainable molecular diagnostics company for the medium and long term.

Taken together all of the measures noted above should put Epigenomics in a financial position that allows the Company to reach breakeven on a medium term, based on a growing molecular diagnostic products business, increasing royalty streams and deal-making revenues, a lean organization and cost structure, and some added financing measures.

## Corporate Governance

To the Executive Board and the Supervisory Board, corporate governance lies at the heart of responsible and ethical management at Epigenomics. The very interactive dialog and regular communication with the Supervisory Board and its committees aimed at generating long-term value to our shareholders are central to good corporate governance. Openness and transparency in our corporate communications with all shareholder groups, employees, the general public, and other stakeholders are the overarching principle.

As in previous years, corporate governance was important for all of us at Epigenomics. We fully welcome the German Corporate Governance Code and its most recent amendments. We systematically and regularly monitor compliance with the German corporate governance principles making amendments wherever possible to ensure fair and responsible corporate management according to the new and amended version of the German Corporate Governance Code.

Epigenomics' corporate governance principles in certain aspects go well beyond legal requirements and recommendations of the German Corporate Governance Code. For example, we have established binding internal guidelines on insider trading and made these part of all employment agreements. We have appointed a Corporate Governance Compliance Officer to ensure adherence to the corporate governance principles. The Compliance Officer is required to submit regular compliance reports to the Executive Board, which are then passed on to the Supervisory Board. All 2008 reports of the Compliance Officer confirmed Epigenomics to be in line with corporate governance principles.

There are punctual notable exceptions based on certain Company specifics and peculiarities we chose to deviate from the German Corporate Governance Code. These exceptions are detailed below. There is a clear commitment to adhere to the Code going forward to the greatest extent possible.

## Directors' dealings and directors' share ownership

According to Section 15a of the German Securities Trading Act (Wertpapierhandelsgesetz) and Section 6.6 Paragraph 1 of the German Corporate Governance Code, persons discharging managerial responsibilities within an issuer of financial instruments are required to disclose their personal transactions in shares of the issuer and financial instruments based on them, especially derivatives, to the issuer and to the German Federal Financial Supervisory Authority (BaFin). The duty to disclose applies to the members of the Executive Board and the Supervisory Board. Moreover, the duty of disclosure also applies to persons who have regular access to insider information about the Company and are empowered to make significant managerial decisions. The duty to disclose also applies to persons and certain legal entities closely associated with a person discharging managerial duties at the Company. The duty to disclose does not apply if the purchase and sale transactions do not exceed EUR 5 thousand in a calendar year.

### Declared securities transactions during 2008:

	Transaction date	Type	Total number of shares traded	Transaction value in EUR
<b>Members of the Executive Board</b>				
Oliver Schacht, Ph.D., CFO	Jan 28, 2008	buy	12,500	20,000
Oliver Schacht, Ph.D., CFO	Nov 28, 2008	exersale	12,750	23,970
Geert Walther Nygaard, CEO	Jan 29, 2008	buy	20,000	33,841
<b>Members of the Supervisory Board</b>				
Ann Clare Kessler, Ph.D.	Jan 25, 2008	buy	14,000	23,800

## Declaration of Compliance 2008 with the German Corporate Governance Code

The governmental committee "Regierungskommission Deutscher Corporate Governance Kodex" appointed by the Ministry of Justice in September 2001 has approved the German Corporate Governance Code (the "Code") on February 26, 2002, as well as the latest amendments thereto on June 6, 2008. The Code contains recommendations and suggestions for the management and supervision of German listed companies and is based on international and national recognized standards of good and responsible management. The Code also includes recommendations (so-called Soll-Vorschriften) and suggestions (so-called Sollte- or Kann-Vorschriften) on corporate governance with respect to shareholders, general meetings, executive board and supervisory board, as well as transparency, accounting and auditing.

Compliance with the Code is not mandatory. Pursuant to Section 161 of the German Stock Corporation Act (Aktengesetz), it is required that the executive board and the supervisory board of a listed company explain each year, which recommendations were or were not complied with. This statement must be provided to shareholders in writing. With respect to the suggestions of the Code, noncompliance must not be disclosed.

In its declaration of compliance with the Code pursuant to Section 161 of the German Stock Corporation Act (Aktiengesetz) as of December 2008, the Executive Board and the Supervisory Board declared that since the last statement of compliance in December 2007, the Company has complied with the recommendations of the Government Commission on the German Corporate Governance Code in the version of June 14, 2007, and June 6, 2008, respectively, and will comply with the recommendations of the Government Commission on the Code in the version of June 6, 2008, with the following exceptions, partly due to specific corporate particularities:

#### Section 2.3.2

The Company cannot comply with the recommendation to communicate electronically to all domestic and foreign financial service provider, shareholders and associations of shareholders the convening of the general shareholders' meeting including all convocation documents, if the prerequisites for agreement are fulfilled, as with the regard to the existing freefloat no sufficiently secure identification and addressing of the shareholders can be assured. However, irrespective of the requirement pursuant to § 125 AktG, the Company will send these documents electronically for information purposes to those shareholders who wish to receive and request them electronically.

#### Section 3.8 Paragraph 2

The D & O (directors' & officers') liability insurance taken out by Epigenomics AG for its Executive Board and Supervisory Board members includes a deductible. However, we think a deductible is not a precondition for responsible management; responsible management rather is a self-evident duty of all board members. Therefore, the "adequacy" of the amount of a deductible is not of particular importance. Accordingly, we did not and will not comply with the recommendation in Section 3.8. paragraph 2 regarding the adequacy of the deductible.

#### Section 4.2.3 Paragraph 3, Sentence 4

The stock options granted to Executive Board members in the past were not related to relevant comparison parameters. With regard to existing stock option programs a retroactive change of performance targets is not excluded, and for extraordinary, unforeseen developments a possibility of limitation (cap) has not been agreed upon. We think that the responsibility and motivation of Executive Board members are not improved by referring to comparison parameters and that a possibility of limitation (cap) is not necessary due to the structure of the existing stock option programs. Therefore, the aforementioned recommendations pursuant to Section 4.2.3 paragraph 3 of the Code were not adhered to with regard to stock options granted in the past and with regard to existing stock option programs and will not be complied with.

#### Section 5.1.2 Paragraph 2, Sentence 3

An age limit for members of the Executive Board has not been specified. Such a general limit could restrict the members of the Supervisory Board in their selection of particularly qualified and experienced candidates. From our point of view, age is not necessarily an adequate criterion for the disqualification of candidates. Furthermore, the age structure of the Executive Board does not suggest the adoption of an age limit within the foreseeable future. Accordingly, we did not and will not comply with the recommendation in Section 5.1.2 paragraph 2 regarding an age limit for members of the Executive Board.



### Section 5.3.3

The Supervisory Board takes the view that the requirement to form a nomination committee composed exclusively of shareholder representatives which proposes suitable candidates to the Supervisory Board for recommendation to the General Shareholders' Meeting is with regard to the Company's size not necessary. Furthermore, this task is already been addressed by the Company's Personnel and Compensation Committee.

### Section 5.4.1, Sentence 2

Due to the aforementioned reasons, an age limit for members of the Supervisory Board has neither been specified. An age limit would inappropriately narrow the shareholders' right to elect the members of the Supervisory Board. Accordingly, we did not and will not comply with the recommendation in Section 5.4.1 sentence 2 regarding an age limit for members of the Supervisory Board.

### Section 5.4.3

The recommendation to communicate the nominee proposals for the Supervisory Board Chairmanship to the shareholders cannot be followed, as pursuant to section 10 subsection 4 of the Company's Articles of Association the Supervisory Board itself elects among its members a Chairperson. According to section 2 subsection 1 sentence 2 of the Rules of Procedure of the Supervisory Board the election of the Chairperson shall occur subsequent to the general shareholders' meeting in which at least one new member of the Supervisory Board has been elected, in a meeting to be held without specific convocation. As a consequence, a previous announcement of the nominee proposal cannot be realised.

### Section 5.4.7 Paragraph 1, Sentence 3

The Company adheres to the recommendation in Section 5.4.7 paragraph 1 concerning compensation for committee work with the exception that there will be no separate compensation for the mere membership in committees apart from presidency. Since the committee work is evenly distributed among the members of the Supervisory Board, a differentiated compensation appears not necessary regarding the bare membership in committees.

### Section 5.4.7 Paragraph 2

The compensation of the Supervisory Board members contains no performance-related component. A performance-related compensation would not lead to an additional increase in incentive or motivation. The adoption of performance related compensation components in the future shall be subject of a future decision of the Annual General Shareholders' Meeting, as the case may be.

Berlin, December 2008

#### On behalf of the Supervisory Board:

Prof. Dr. Dr. Rolf Krebs  
(Chairman of the Supervisory Board)

#### On behalf of the Executive Board:

Geert Walther Nygaard (CEO)      Dr. Oliver Schacht (CFO)

### Financial market reporting

In line with fair and open disclosure and the requirements of the Prime Standard segment of the Frankfurt Stock Exchange, quarterly financial reports are made available within 60 days of a quarter's end and annual financial statements within 90 days of year-end. All information is made available simultaneously on our website [www.epigenomics.com](http://www.epigenomics.com). All material news are announced following the latest guidelines and legal requirements on ad hoc notification.

### Additional Mandatory Disclosures for Listed Companies Pursuant to Section 315 Paragraph 4 of the German Commercial Code (HGB)

According to Section 315 Paragraph 4 of the German Commercial Code the Company is required to report on certain structures governed by company law and other legal relationships, in order to provide a better overview of the Company and disclose any impediments to a takeover.

### Shareholders with direct or indirect shareholdings of more than 10% of the voting rights

shareholder	notification date	shareholdings in %
Federated Equity Management Company of Pennsylvania	September 10, 2008	20.21

### Composition of share capital

The share capital of Epigenomics AG comprises exclusively common shares with equal rights and a par value of EUR 1.00 each as of December 31, 2008. During the reporting year, the number of shares increased from 18,252,824 to 26,723,636 shares. The Company has no treasury shares as of the balance sheet date. Under certain conditions, shareholders may not be entitled to vote – according to Section 136 of the German Stock Corporation Act. We are not aware of any contractual restrictions related to voting rights or the transfer of shares.

### Legislation and provisions of the Articles of Association applicable to the appointment and withdrawal of members of the Executive Board and governing amendments to the Articles of Association

The appointment and withdrawal of members of the Executive Board is subject to the provisions of Sections 84 and 85 of the German Stock Corporation Act (Aktiengesetz).

The Supervisory Board shall appoint members of the Executive Board for a maximum period of five years. It is permissible to appoint members to the Executive Board on more than one occasion or to extend their period of office, on each occasion for a maximum of five years.

The Executive Board may consist of one or more persons. The number of members of the Executive Board shall be determined by the Supervisory Board in accordance with the statutory provisions. The Supervisory Board may appoint a member of the Executive Board as chairperson of the Executive Board and one or more members of the Board as his deputy(ies). Deputy members of the Executive Board may be appointed. The statutory provisions regarding the amendment of the Articles of Association are governed in Sections 179-181 of the German Stock Corporation Act.

Pursuant to Section 14 of the Articles of Association, the Supervisory Board is entitled to adopt amendments and completions to the statutes which only involve the version thereof.

### Authority of the Executive Board to issue shares

The share capital is conditionally increased by up to EUR 13,508.00 divided into 13,508 bearer shares of common stock with a calculatory par value of EUR 1.00 each (Conditional Capital I). This conditional capital increase is only implemented to the extent that the option rights from the share option plan of the Company set up according to the resolution of the Annual General Shareholders' Meeting dated August 3, 2000, amended according to the resolutions of the Annual General Shareholders' Meeting dated April 27, 2001, August 1, 2003, and June 22, 2004, is exercised. The new shares will participate in the profit from the beginning of the financial year in which the respective option rights were exercised.

The share capital is conditionally increased by up to EUR 139,625.00 divided into 139,625 of bearer shares of common stock with a calculatory par value of EUR 1.00 each (Conditional Capital III). The conditional capital increase can only be carried out to the extent that option rights were issued on the basis of the share option program 01-05 of the Company, amended according to the resolution of the Annual General Shareholders' Meeting dated August 1, 2003, resolved at the Annual General Shareholders' Meeting on April 27, 2001, and the holders of these share options exercise their right to subscribe to shares of the Company and the Company does not transfer its own shares in fulfillment of these option rights. The new shares will participate in the profit from the beginning of the financial year in which they are issued. The Supervisory Board is authorized to lay down the further details regarding the implementation of the conditional capital increase as far as the granting of options to members of the Executive Board is concerned. In other cases, the Executive Board is authorized to lay down the further details.

The Supervisory Board is authorized to amend the wording of Section 5 Paragraphs 1, 2 and 5 of the Articles of Association in accordance with the volume of the capital increase from conditional capital.

The share capital is conditionally increased by up to EUR 617,426.00 divided into 617,426 of bearer shares of common stock with a calculatory par value of EUR 1.00 each (Conditional Capital IV). The conditional capital increase can only be carried out to the extent that option rights were issued on the basis of the share option program 03-07 of the Company, amended according to the resolution of the Annual General Shareholders' Meeting dated August 1, 2003, and the holders of these share options exercise their right to subscribe to shares of the Company and the Company does not transfer its own shares in fulfillment of these option rights. The new shares will participate in the profit from the beginning of the financial year in which they are issued.

The Supervisory Board is authorized to lay down the further details regarding the implementation of the conditional capital increase as far as the granting of options to members of the Executive Board is concerned. In other cases, the Executive Board is authorized to lay down the further details. The Supervisory Board is authorized to amend the wording of Section 5 Paragraphs 1, 2 and 6 of the Articles of Association in accordance with the volume of the capital increase from Conditional Capital.

The share capital is conditionally increased by up to EUR 647,679.00, divided into up to 647,679 no par-value bearer shares with a par value of EUR 1.00 each (Conditional Capital V). The conditional capital increase can only be carried out to the extent that option rights are issued to the shareholders on the basis of the Company's share option program 06-10, which was resolved by the Annual General Shareholders' Meeting on July 10, 2006, and the holders of these share options avail themselves of their right to acquire shares in the Company and the Company does not grant any shares of its own to fulfill these option rights. The new shares will participate in the profit as of the beginning of the fiscal year in which they were issued. The Supervisory Board is empowered to establish the further details of the execution of the conditional capital increase as far as the granting of subscription rights to Executive Board members is concerned. In all other respects, the Executive Board is empowered to establish such details. The Supervisory Board is empowered to amend the version of Section 5 Paragraphs 1 and 8 of the Articles of Association to reflect the conditional capital increase.

The share capital is conditionally increased by up to EUR 2,671,088.00 by issuing up to 2,671,088 new bearer shares of common share representing a notional portion of the share capital of EUR 1.00 per share (Conditional Capital VI). The conditional capital increase serves the purpose of granting shares to holders of convertible bonds issued on the basis of the above-mentioned authorization. The new shares are issued at the conversion price determined in accordance with the above-mentioned authorization. The conditional capital increase is to be effected only insofar as the conversion rights are exercised or any conversion obligations under such convertible bonds are fulfilled and insofar as no cash settlement is granted and no shares from authorized capital or own shares are used for servicing. The new shares issued upon the exercise of conversion rights or to fulfill a conversion obligation will participate in the profit from the beginning of the fiscal year in which they come into existence by the exercise of conversion rights or the fulfillment of a conversion obligation. The Executive Board is authorized to determine with the consent of the Supervisory Board further details of the implementation of the conditional capital increase.

The Executive Board is authorized until June 2, 2013, to increase with the consent of the Supervisory Board the share capital of the Company once or several times by up to EUR 2,671,088.00 against contribution in cash and/or in kind by issuing new no-par value bearer shares (Authorized Capital 2008/I). The shareholders are to be granted subscription rights. The new shares can be subscribed by a financial institution or a syndicate of financial institutions under the obligation to offer the shares to the shareholders for subscription (indirect subscription right). The Executive Board is, however, authorized to exclude with the consent of the Supervisory Board the shareholders' subscription rights in the following events:

- for fractional amounts;
- in the event, the new shares are issued against contribution in cash to an issuing price which is not materially lower than the market price of, in essence, similar listed shares during the last five stock exchange trading days prior to the day of the determination of the issuing price by the Executive Board pursuant to Section 203 Paragraph 1 Sent. 1 and 2, Section 186 Paragraph 3 Sent. 4 AktG; this authorization to exclude subscription rights, however, applies only insofar as the new shares and such shares issued by the Company during the term of this authorization, as the case may be, with the exclusion of subscription rights pursuant or in accordance with Section 186 Paragraph 3 Sent. 4 AktG under an ordinary capital increase, an authorized capital or after a repurchase or for which, during the term of this authorization, a conversion or option right under convertible or warrant bonds has been granted with the exclusion of subscription rights in accordance with Section 186 Paragraph 3 Sent. 4 AktG do not exceed 10% of the share capital at the time of the registration of this authorization in the commercial register or – if lower – at each time this authorization is executed;
- for capital increases against contribution in kind in order to offer the new shares to third parties with regard to mergers or upon the purchase of enterprises, parts of enterprises, shares in enterprises or other assets;
- as far as it is necessary to grant as many subscription rights on new shares to holders of option rights or creditors of convertible bonds issued by the Company or its subordinated Group companies as such holders and creditors could claim for upon the exercise of the option or conversion rights respectively upon fulfillment of conversion obligations.

The Executive Board is authorized to establish further details of the implementation of the capital increase under the Authorized Capital 2008/I. The Supervisory Board is authorized to amend the wording of the Articles of Association after implementation of the capital increase under the Authorized Capital 2008/I or after expiry of the term of the authorization in accordance with the capital increase under the Authorized Capital 2008/I.

### Compensation agreements with the Executive Board members in the event of a takeover bid

In case of a change of control, Mr. Nygaard is entitled to terminate his service agreement and would in such case be entitled to receive payment of the fixed compensation amount for the time remaining until his service agreement would have anyhow be terminated.



epigenomics AG

# Consolidated Financial Statements for Fiscal 2008

according to International Financial Reporting Standards (IFRS)

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# Group Income Statement

for the period from January 1 to December 31, 2008

EUR thousand	Notes	2007	2008
<b>Revenue</b>	1	<b>2,567</b>	<b>2,586</b>
Cost of sales	2	-874	-1,698
<b>Gross profit</b>		<b>1,693</b>	<b>888</b>
Other income	3	1,355	1,129
Research and development costs	4, 7	-10,471	-10,028
Marketing and business development costs	5, 7	-1,286	-857
General and administrative costs	6, 7	-4,315	-3,442
Other expenses	9	-480	-440
<b>Operating result (EBIT)</b>	10	<b>-13,504</b>	<b>-12,750</b>
Interest income	11	629	682
Interest expenses	11	-30	-30
Other financial result	11	2	40
<b>Net loss for the year before taxes on income</b>		<b>-12,903</b>	<b>-12,058</b>
Taxes on income	12	-248	-213
<b>Net loss for the year</b>		<b>-13,151</b>	<b>-12,271</b>
<b>Earnings per share (basic and diluted) in EUR</b>	13	<b>-0.74</b>	<b>-0.47</b>



# Group Balance Sheet

as of December 31, 2008

<b>ASSETS</b> EUR thousand	Notes	Dec 31, 2007	Dec 31, 2008
<b>Non-current assets</b>			
Intangible assets	15, 18	6,084	4,536
<i>thereof: goodwill</i>	15, 18	2,625	2,625
Tangible assets	16, 18	1,208	692
Financial assets	17, 18	1,000	0
Deferred taxes	19	778	629
<b>Total non-current assets</b>		<b>9,070</b>	<b>5,857</b>
<b>Current assets</b>			
Inventories	20	237	125
Trade receivables	21	439	727
Marketable securities	22	3,370	2,286
Cash and cash equivalents	23	6,646	9,814
Other current assets	24	3,152	1,474
<b>Total current assets</b>		<b>13,844</b>	<b>14,426</b>
<b>Total assets</b>		<b>22,914</b>	<b>20,283</b>
<b>EQUITY AND LIABILITIES</b> EUR thousand			
<b>Equity</b>			
Subscribed capital	25	18,253	26,724
Capital reserve	26	13,712	3,567
Net loss for the year		-13,151	-12,271
Other comprehensive income	27	-993	-1,452
<b>Total equity</b>		<b>17,821</b>	<b>16,568</b>
<b>Non-current liabilities</b>			
Liabilities from leasing contracts	29	0	38
<b>Total non-current liabilities</b>		<b>0</b>	<b>38</b>
<b>Current liabilities</b>			
Trade payables		1,562	1,027
Liabilities from leasing contracts		0	28
Deferred income	30	637	1,254
Other liabilities	31	2,354	887
Provisions	32	540	481
<b>Total current liabilities</b>		<b>5,093</b>	<b>3,677</b>
<b>Total equity and liabilities</b>		<b>22,914</b>	<b>20,283</b>

# Group Cash Flow Statement

for the period from January 1 to December 31, 2008

EUR thousand	Notes	2007	2008
<b>Cash and cash equivalents at the beginning of the year</b>		<b>12,566</b>	<b>6,646</b>
<b>Operating activities</b>	34		
Net loss for the year before taxes on income		-12,903	-12,058
Corrections for:			
Depreciation on tangible assets		787	667
Amortization of intangible assets		458	1,839
Losses from the disposal of assets		16	6
Stock option expenses	8	457	120
Foreign currency exchange losses		68	12
Price gains of securities		0	-21
Interest income		-629	-682
Interest expenses		31	30
Taxes		-259	-296
<b>Operating result before changes in net current assets</b>		<b>-11,974</b>	<b>-10,383</b>
Increase in trade receivables and other current assets		-1,670	-2,800
Decrease (2007: increase) in inventories		-38	112
Increase in current liabilities		1,580	2,609
<b>Liquidity earned from operating activities</b>		<b>-12,102</b>	<b>-10,462</b>
Interest received		586	662
<b>Cash flow from operating activities</b>		<b>-11,516</b>	<b>-9,800</b>
<b>Investing activities</b>	35		
Payments for investments in tangible assets		-36	-74
Proceeds from the sale of non-current assets		1	1
Proceeds from investment grants	14	93	100
Payments for investments in intangible assets		-29	-184
Proceeds from the sale of marketable securities		1,021	625
Proceeds from divestments in financial assets	17	0	1,000
<b>Cash flow from investing activities</b>		<b>1,049</b>	<b>1,468</b>
<b>Financing activities</b>	36		
Payments for the creation of new shares		-316	-2,037
Proceeds from the issue of new shares	25	4,861	13,533
Payments for lease financing		0	-19
Proceeds from the exercise of stock options		2	22
<b>Cash flow from financing activities</b>		<b>4,547</b>	<b>11,500</b>
<b>Cash flow</b>		<b>-5,920</b>	<b>3,168</b>
<b>Cash and cash equivalents at the end of the year</b>		<b>6,646</b>	<b>9,814</b>

# Statement of Changes in Group Equity

as of December 31, 2008

EUR thousand	Notes	Subscribed capital	Capital reserve	Retained earnings	Net loss for the year	Other compreh. income	Group equity
<b>Dec 31, 2006</b>		<b>16,916</b>	<b>25,294</b>	<b>-15,402</b>	<b>0</b>	<b>-610</b>	<b>26,198</b>
Net loss for the year 2007		0	0	0	-13,151	0	-13,151
Fair value adjustments of securities		0	0	0	0	-383	-383
<b>Total comprehensive income</b>		<b>0</b>	<b>0</b>	<b>0</b>	<b>-13,151</b>	<b>-383</b>	<b>-13,534</b>
Capital increase from the issue of shares		1,336	0	0	0	0	1,336
Premium from the issue of shares		0	3,526	0	0	0	3,526
Financing costs		0	-164	0	0	0	-164
Exercise of stock options		1	1	0	0	0	2
Stock-based compensation		0	457	0	0	0	457
Deduction of net loss for the year 2006		0	-15,402	15,402	0	0	0
Transfer of net loss for the year 2007 to retained earnings		0	0	-13,151	13,151	0	0
<b>Dec 31, 2007</b>		<b>18,253</b>	<b>13,712</b>	<b>-13,151</b>	<b>0</b>	<b>-993</b>	<b>17,821</b>
<b>Dec 31, 2007</b>		<b>18,253</b>	<b>13,712</b>	<b>-13,151</b>	<b>0</b>	<b>-993</b>	<b>17,821</b>
Net loss for the year 2008		0	0	0	-12,271	0	-12,271
Fair value adjustments of securities	27	0	0	0	0	-459	-459
<b>Total comprehensive income</b>		<b>0</b>	<b>0</b>	<b>0</b>	<b>-12,271</b>	<b>-459</b>	<b>-12,730</b>
Capital increase from the issue of shares	25	8,458	0	0	0	0	8,458
Premium from the issue of shares	25	0	5,075	0	0	0	5,075
Financing costs		0	-2,198	0	0	0	-2,198
Exercise of stock options		13	9	0	0	0	22
Stock-based compensation	8	0	120	0	0	0	120
Deduction of net loss for the year 2007		0	-13,151	13,151	0	0	0
Transfer of net loss for the year 2008 to retained earnings		0	0	-12,271	12,271	0	0
<b>Dec 31, 2008</b>		<b>26,724</b>	<b>3,567</b>	<b>-12,271</b>	<b>0</b>	<b>-1,452</b>	<b>16,568</b>

# Notes to the Consolidated Financial Statements

## Basic Information, Principles and Methods

### *Description of business activity*

Epigenomics (“Epigenomics” or the “Company”) was founded as a limited liability company (GmbH) in 1998 and has its headquarters in Berlin, Germany. In 2000, the Company was converted into a stock corporation (AG) and entered into the commercial register (“Handelsregister”) Charlottenburg under HRB 75861. Since July 19, 2004, it is listed in the Prime Standard segment of the Frankfurt Stock Exchange (ticker symbol: ECX).

In accordance with its Articles of Incorporation, the object of the Company is the development and marketing of procedures and devices for the production in quantity of particular epigenetic parameters such as DNA methylation patterns as well as the information technology bases necessary for their procurement and evaluation. The focus of the Company lies on the development of novel molecular diagnostic products for cancer.

### *General principles*

The consolidated financial statements of Epigenomics AG have been prepared according to Article 315a of the German Commercial Code (“HGB”) and the International Financial Reporting Standards (IFRSs) of the International Accounting Standards Board (IASB), London, in effect at the closing date December 31, 2008, as mandatory and applicable in the European Union. Further, these statements are in accordance with the German Accounting Standards (GASs).

The “going concern” principle according to IAS 1.23 *Presentation of Financial Statements* has been considered.

The reporting period as defined in these consolidated financial statements is the period from January 1, 2008, to December 31, 2008. The reporting currency is the euro.

The income statement has been prepared using the cost of sales method.

### *New and revised standards and interpretations effective in the reporting period*

Although several new standards were issued by the IASB during 2008, none are mandatory effective for December 2008 year-end financial statements. In October 2008, the IASB announced some amendments to IAS 39 *Financial Instruments: Recognition and Measurement* and IFRS 7 *Financial Instruments: Disclosures* regarding possible reclassifications of financial assets. The Group has not adopted those amendments.

In 2008, four new interpretations issued by the International Financial Reporting Interpretations Committee (IFRIC) became effective for the reporting period (IFRIC 12, IFRIC 13, IFRIC 14 and IFRIC 16). None of those interpretations has led to any changes in the Group’s accounting policies.

### *Management's judgment and expectations*

The management of the Company has made several judgments in the process of applying the entity's accounting policies that have a significant effect on the amounts recognized in the financial statements. Those judgments concern the valuation of goodwill, the capitalization of development costs and the recognition of deferred taxes. The judgments are described for each relevant position in the enumeration of accounting and valuation principles.

Management's expectations on the future are usually based on the current economic outlook according to the consensus prognoses by leading economic and financial research institutions and independent analysts. Among those it is expected that the financial turbulences – which started to upset the worldwide markets in 2008 significantly – will have a deep impact on the future development of the major economies. Therefore, a scenario of economic growth cannot be assumed for 2009 but rather in the best case a stabilization at or near the 2008 levels. History shows that the life sciences sector is rather a defensive field and does not react too much to economic up- and downturns. However, management has learned that being skeptical about all kind of outlooks and conclusions derived from historical data has become more and more appropriate. Therefore, it has based the strategic plans for the Group as much as possible detached from any critical developments of the financial markets<sup>1</sup>.

The Group's operating activities are not very dependent on the availability or the price development for commodities or industrial supplies but rather on the relevant labor markets. Management does not expect significant changes in those markets for the coming months, which could affect the Group's operating activities. The Group is still cash flow negative but debt free and has limited liquid resources as of year-end 2008. Therefore, any volatility in the financial markets and in the interest rates is not expected to significantly affect the operating result. In fact, the financing activities are likely to be more sensitive to the economic development of the Group as it faces the need for additional capital inflows over the course of the next 12 to 24 months.

In the mid term, the euro currency is expected to remain stable vis-à-vis the U.S. dollar. Management plans are based on an average exchange rate of EUR/USD 1.30 throughout 2009. It also took note of the predictions of financial experts and banks, which are diverging more than ever with regard to this relation.

Major changes in the legislation of the major countries that could significantly affect the biotechnological industry are not assumed. Changes in the tax laws of Germany and the U.S.A. that would in any material way affect our financial situation in the foreseeable future are also not anticipated. All future scenarios further assume an essentially unchanged access to relevant clinical and biological samples, corresponding data and resources for the execution of the Company's commercial projects.

<sup>1</sup> For more detailed considerations reference is made to the Outlook section of the consolidated management report of this annual report.

### *Consolidation group*

The consolidated Group comprises Epigenomics AG as the parent company (principal office: Kleine Präsidentenstrasse 1, 10178 Berlin, Germany) and Epigenomics, Inc. (principal office: Suite 300, 1000 Seneca Street, Seattle, WA 98101, U.S.A.), its wholly owned subsidiary.

For the reporting year, the two companies have submitted individual, audited financial statements independent of their consolidation.

### *Principles of consolidation*

In the consolidation of capital, the acquisition values of the investment are balanced with the share of equity capital of the subsidiary applicable to them on the date of acquisition. A resulting difference is added to the assets and liabilities in the amount in which their current market value deviates at the time of the initial consolidation from their carrying value. An amount in excess is capitalized as goodwill.

All intercompany transaction results, revenue, expenses, profits, receivables and payables are eliminated in full on consolidation.

### *Accounting and valuation principles*

#### *Goodwill*

Goodwill arising on acquisition is initially recognized as an asset at cost and subsequently measured at cost less any accumulated impairment losses. Therefore, the goodwill has to undergo an impairment test at least once a year according to IFRS 3 *Business Combinations* in connection with IAS 36 *Impairment of Assets*. The regular application of this impairment test is scheduled for the end of each calendar year, subsequent to the annual budgeting process of the Company. The recorded goodwill has been allocated to the Group's screening business as cash-generating unit (CGU). The impairment test compared the net carrying value of the assets of the screening business to their value in use. The value in use has been defined as the discounted future cash flows of this business.

Management's expectations regarding the future cash flows of the screening business were based on the most recent business plans and are, however, subject to risks and uncertainty. The underlying expectations are based on the Company's collaboration with its development partner Abbott Molecular Inc., which has licensed the Company's key value driver – the colorectal cancer IVD test – for further development and worldwide commercialization. Based on this collaboration, the product development plans of the Company's screening business have been extrapolated accordingly and present the basis of the capitalized goodwill (for the generally underlying assumptions to the aforementioned business plan see also "Management's judgments and expectations"). All of those assumptions are key sources of estimation uncertainty and bear a significant risk of causing a material adjustment to the carrying amounts of the capitalized goodwill. However, no impairment of the capitalized goodwill has been determined in 2008.

### *Intangible assets*

Other intangible assets than goodwill are valued at acquisition cost less scheduled amortization on a straight-line basis. Depending on the investment, useful life will be defined between three years (software) and twenty years (patents). For patents, the useful life in individual cases depends on the term of the patent protection. Amortization of intangible assets is allocated to the functional area in which they are used. IAS 38 *Intangible Assets* is applied. In accordance with this standard, an intangible asset is reported if it is likely that a future financial advantage is associated with the use of such asset and that its cost can be reliably determined. An impairment test will be done annually for assets or groups of assets for which an unplanned decrease in value is assumed. If there is no longer any reason for unplanned depreciation, an appreciation will take place up to the amortized acquisition costs as a maximum.

### *Capitalized development costs*

Expenditure on research activities is recognized as an expense in the period in which it is incurred. An internally generated intangible asset arising from internal development is recognized if, and only if, all of the following requirements according to IAS 38.57 *Intangible Assets* have been fulfilled:

- prove of the technical feasibility of completing the intangible asset so that it will be available for use or sale;
- prove of the intention to complete the intangible asset to use or sell it;
- prove of the ability to use or sell the intangible asset;
- show how the intangible asset will generate probable future economic benefits;
- prove of the availability of adequate technical, financial and other resources to complete the development and to use or sell the intangible asset;
- demonstrate the ability to measure reliably the expenditure attributable to the intangible asset during its development.

The amount initially recognized for the capitalization of development costs is the sum of expenditure incurred from the date when the intangible assets first met the aforementioned recognition criteria. Where no internally generated intangible asset can be recognized, development expenditure is charged to profit or loss in the period in which it is incurred. Subsequent to initial recognition, capitalized development costs are reported at cost less accumulated amortization and impairment losses, on the same basis as intangible assets acquired separately.

### *Tangible assets*

Tangible assets are measured at acquisition or production cost, less scheduled depreciation caused by usage. Apart from directly attributable costs, pro rata overhead cost and depreciation are also included in the production costs of internally produced equipment. Public and governmental investment grants lower acquisition or production cost. Interest on third-party capital is not included in production cost. Repair costs are immediately calculated as an expense. Depreciation for leasehold improvements is applied on a straight-line basis over the remaining term of the underlying leases. Mobile fixed assets are depreciated in principle on a straight-line basis. The useful life is three to eight years for technical and electronic equipment and five to ten years for operational and office equipment.

In the “Assets schedule” (item 18), fully depreciated tangible assets are shown under acquisition/production cost and accumulated depreciation until the assets in question are decommissioned. In the case of disposal, assets and related depreciation are eliminated from the accounts. Income or expense resulting from the disposal of assets (proceeds less residual carrying value) is shown in the income statement under other income/other expenses.

Investment grants and subsidies are offset directly against the acquisition costs of the subsidized assets, i.e. the asset value is reduced. The grant is thus liquidated by depreciation of the reduced investment over the remaining term.

If the value of the tangible capital assets calculated according to the above principles exceeds the fair value of these assets on the closing date, it will be taken into account by means of an unplanned depreciation. The amount to be adjusted is determined by sale proceeds or – if higher – the net present value of future cash flows estimated from value in use of the asset. An impairment test will be done annually for assets or groups of assets for which an unplanned decrease in value is assumed. If there is no longer any reason for unplanned depreciation, an appreciation will take place up to the amortized acquisition costs as a maximum.

#### *Leasing contracts*

Leasing contracts qualify as finance lease, if the contractual conditions transfer all risks and opportunities in connection with the ownership to the lessee. All other leasing contracts are recognized as operating leasing.

#### *Deferred taxes*

Deferred taxes are calculated according to the rules of IAS 12 *Income Taxes* and are recognized for temporary differences between the carrying amount of assets and liabilities in the financial statements and the corresponding tax balance sheets of the companies involved. Further, deferred tax assets are recognized from tax loss carryforwards to the extent that it is probable that there will be sufficient taxable profits against which to utilize the benefits of the temporary differences and that they are expected to reverse in the foreseeable future. If such a realization is not probable, a valuation allowance is recognized against the tax loss carryforwards.

Deferred tax assets and liabilities are measured at the local tax rates enacted or the rates, which are expected to apply at the time of realization. Deferred tax assets and liabilities are offset only if they are subject to compensation with regard to the same tax authority and if the Group intends to settle its current tax assets and liabilities on a net basis.

#### *Inventories*

Inventories comprise raw materials, low-value consumables and other production supplies as well as finished goods. They are valued at the lower of acquisition or manufacturing cost and net realizable value. The manufacturing costs of the finished goods include directly attributable unit costs, depreciation and overheads attributable to the production process. For the balance sheet date, a physical inventory of all consumables, materials and finished goods was taken.



#### *Primary financial instruments*

The reported primary financial instruments comprise cash and cash equivalents, marketable securities, trade receivables, trade payables and other liabilities. Those instruments are initially recognized at acquisition costs or at fair value and then at amortized acquisition costs or at their fair value.

#### *Financial assets held to maturity*

Financial assets held to maturity are shown under long-term financial assets, recognized at their amortized cost, using the effective interest method less any impairment losses. If such financial assets are disposed of or are determined to be impaired, the realized differentials are recognized through profit or loss. Impairment is determined when the fair value of a financial asset falls significantly below its amortized acquisition costs and the resulting differential is expected to be permanent.

#### *Marketable securities*

According to the definitions of IAS 39.9 *Financial Instruments: Recognition and Measurement*, the Company's marketable securities are classified either as "financial assets at fair value through profit or loss" (FVTPL) or as "available-for-sale financial assets" (AFS). The Group does not hold financial assets for trading purposes. Irrespective of this classification, financial assets are recognized at fair value and accounted for at trade date. Changes in fair value are recognized through profit or loss or – if the securities classify for AFS – in other comprehensive income until the securities are disposed of or are determined to be permanently impaired. Impairment losses recognized in profit or loss are subsequently reversed if an increase in the fair value of the instrument can be objectively determined.

#### *Derivative financial instruments*

Derivative financial instruments are carried at fair value and accounted for at trade date. As a matter of principle, the fair values of derivative financial instruments correspond to the market values. For unlisted derivatives the fair values are determined by individual settlement quotes from the Company's house banks. Changes in the fair value of derivative financial instruments are recognized through profit or loss.

#### *Impairment of financial assets*

At the balance sheet date, a financial asset, other than those measured at fair value, is measured whenever there is an indication that the asset might be impaired. Financial assets are impaired when there is objective evidence that, as a result of one or more events that occurred after the initial recognition of the financial asset, the estimated future cash flows of the investment have been impacted.

The carrying amount of a financial asset is reduced by the impairment amount directly for all financial assets with the exception of trade receivables, where the carrying amount is reduced through the use of an allowance account. When a trade receivable is considered to be no longer collectible, it is written off against the allowance account. Subsequent recoveries of amounts previously written off are credited against the allowance account. Changes in the carrying amount of the allowance account are recognized in profit or loss.

#### *Cash equivalents*

A cash equivalent is defined as a financial instrument being readily convertible on a short-term basis to a known amount of cash and carrying an insignificant risk of changes in value (IAS 7.6 *Cash Flow Statements*). Financial instruments generally qualify as cash equivalents when they are more closely related to the money markets than to the bond markets and are issued by a debtor rated “investment grade”. All such cash equivalents must be convertible into primary cash at any time.

#### *Prepaid expenses*

Payments before the balance sheet date, which will be expenses for a specific period after that date, are deferred and reported as prepaid expenses in other current assets.

#### *Current liabilities*

Liabilities are classified as current when certain criteria in accordance with IAS 1.60 *Presentation of Financial Statements* are met. Basically, the Company’s normal operating cycle according to this definition is twelve months. In the licensing business the operating cycle is even more than twelve months. Liabilities are measured at amortized costs, which are basically equivalent to their fair values.

#### *Trade payables*

Trade payables are derecognized if the obligation on which this liability is based is fulfilled or cancelled. Foreign currency liabilities are recognized at market exchange rates at the reporting date.

#### *Deferred income*

Deferred income is recognized for grants and research and development payments (“R&D payments”) received in advance. Grants received in advance that were provided by governmental or comparable central, regional or local authorities, are recognized through profit or loss over the subsidized terms of each project according to its progress of fulfillment. Payments received in advance from customers for R&D services to render or for licenses are deducted and recognized through profit or loss over the term of the contract according to the progress of fulfillment.

#### *Provisions*

In accordance with IAS 37 *Provisions, Contingent Liabilities and Contingent Assets*, a provision is recognized if a present obligation as a result of a past event exists, if it is probable that an outflow of resources embodying benefits will be required to settle this obligation and if a reliable estimate of the amount of the obligation can be made. The amount recognized as a provision is the best estimate of the expenditure required to settle the present obligation at the balance sheet date, taking into account the risks and uncertainties surrounding the obligation. Where a provision is measured using the cash flows expected to be required to settle the present obligation, its carrying amount is the present value of these cash flows.

#### *Revenue recognition*

Revenue from research and development collaboration agreements is recorded and recognized in accordance with the applicable performance requirements and terms of the respective contracts as contract research costs are incurred, using the percentage of completion method.

Milestone payments are recognized as revenue according to the milestone payment method. Revenue under the milestone payment method is recorded and recognized when acknowledgement of having achieved applicable performance requirements is received from the partner.

Nonrefundable upfront payments are deferred and recognized on a straight-line basis over the contractual collaboration term. Optional prolongation terms are considered individually according to the underlying exercise conditions and anticipated likelihood of their exercise.

Royalty revenue is recognized on an accrual basis in accordance with the substance of the relevant contract. Royalties determined on a time basis are recognized on a straight-line basis over the contracted period. Royalty arrangements that are based on sales and other measures are recognized by reference to the underlying contract.

Revenue from the sale of products and the rendering of other services is recognized when delivery has taken place, transfer of risk has been completed, the amount of future returns can be reasonably estimated and collection of the receivable is probable.

#### *Stock option expenses*

The fair value of granted stock options is calculated using the Black-Scholes option pricing model and is expensed over the expected option term of up to four years against the capital reserve. According to IFRS 2.11 *Share-based Payment*, the valuation date is the grant date.

#### *Management judgments in the application of accounting policies/assumptions and estimates*

The preparation of the consolidated financial statements in compliance with International Financial Reporting Standards requires, in the case of several items, that assumptions or estimates be made that affect the valuation in the Group's balance sheet and/or income statement. This also applies to the listing of contingent assets and liabilities. The actual amounts may vary from these assumptions and estimates.

In particular, assumptions and estimates are required for:

- determining, if the criteria for the capitalization of development costs and the recoverability of internally generated intangible assets are met;
- testing a potential impairment of assets (especially regarding intangible assets like goodwill and licenses);
- determining the terms of inlicensed intellectual property rights;
- determining the useful lives of tangible and intangible long-term assets;
- determining, if deferred taxes are realizable;
- determining, if securities classify as "held to maturity", "available for sale" or "at fair value through profit or loss";
- determining the fair value of financial instruments;
- setting the parameters regarding the valuation of stock option grants; and
- accounting for provisions (especially the determination of the likelihood of occurrence).

### *Currency translation*

In the individual financial statements, receivables and liabilities in foreign currencies are valued using the corresponding euro reference rate issued by the European Central Bank on the last business day prior to the closing date. Items that are hedged by forward transactions are valued at the forward price.

For consolidation purposes, the reporting currency of the U.S.-based Epigenomics, Inc. is the euro as well. Therefore, the translation risk from Epigenomics, Inc.'s functional currency (U.S. dollar) to the Group's presentation currency (euro) lies completely in the individual financial statements of this subsidiary and not in its consolidation.

Transactions in foreign currencies are translated with the exchange rates at the transaction date. Exchange rate differences resulting from such transactions and from the translation with the reporting date rates are recognized through profit or loss.

The exchange rate of the U.S. dollar and the British pound, the two major foreign currencies in the consolidated financial statements, changed during the reporting year as follows:

#### *Reporting Date Rates*

	Dec 31, 2007	Dec 31, 2008
EUR/USD	1.4721	1.3917
EUR/GBP	0.73335	0.95250

#### *Average rates*

	2007	2008
EUR/USD	1.3797	1.4726
EUR/GBP	0.68728	0.80255

## Notes to the Group Income Statement

### 1. Revenue

Total revenue was comprised of the following revenue types:

	2007		2008	
	in EUR thousand	in % of total	in EUR thousand	in % of total
Licensing & royalty income	693	27	1,167	45
R & D payments	1,386	54	954	37
Reimbursements	363	14	463	18
Milestone revenue	125	5	0	0
Other	0	0	2	0
<b>Total</b>	<b>2,567</b>	<b>100</b>	<b>2,586</b>	<b>100</b>

Of total revenue, 64% (2007: 79%) was generated from European customers and 36% (2007: 21%) from customers in North America.

### 2. Cost of sales/gross profit

Cost of sales include material and personnel expenses, IP costs and depreciation that can be directly allocated to the sales revenue, as well as pro rata overheads.

The gross profit of EUR 888 thousand (2007: EUR 1,693 thousand) equals a gross margin of 34% (2007: 66%).

### 3. Other income

EUR thousand	2007	2008
Exchange rate gains from currency conversion	138	539
Income from the reversal of provisions	230	279
Third-party research grants	744	86
Income from subleasing	46	59
Corrections of invoices of the previous year	0	54
Various refunds	77	51
Income from the sale of assets	37	34
Insurance recoveries	25	1
VAT refund for previous years	27	0
Other	31	26
<b>Total</b>	<b>1,355</b>	<b>1,129</b>

#### *4. Research and development costs (R&D costs)*

The following are recorded as research and development costs:

- the direct personnel and material expenses of the R & D divisions;
- the depreciation and amortization of the R & D divisions;
- the other direct expenses of the R & D divisions;
- the pro rata overheads of the R & D divisions.

#### *5. Marketing and business development costs (M&BD costs)*

The following are recorded as marketing and business development costs:

- the direct personnel and material expenses of the M & BD divisions;
- the depreciation and amortization of the M & BD divisions;
- the other direct expenses of the M & BD divisions;
- the pro rata overheads of the M & BD divisions.

#### *6. General and administrative costs (G&A costs)*

The following are recorded as general and administrative costs:

- the direct personnel and material expenses of the administrative divisions;
- the depreciation and amortization of the administrative divisions;
- the other direct expenses of the administrative divisions;
- the pro rata overheads of the administrative divisions;
- the Company's statutory costs,

if the costs listed are not carried forward as internal services. The administrative divisions comprise the business departments and systems administration.

## 7. Cost analysis

2007						
EUR thousand	Materials/ consumables	Depreciation and amortization	Personnel costs	Other costs	Capitalized development costs	Total
Cost of sales	197	42	184	451	0	874
R & D costs	1,433	1,093	5,156	2,794	-5	10,471
M & BD costs	0	2	753	531	0	1,286
G & A costs	0	109	2,058	2,148	0	4,315
<b>Total costs</b>	<b>1,630</b>	<b>1,246</b>	<b>8,151</b>	<b>5,924</b>	<b>-5</b>	<b>16,946</b>

2008						
EUR thousand	Materials/ consumables	Depreciation and amortization	Personnel costs	Other costs	Capitalized development costs	Total
Cost of sales	259	265	733	441	0	1,698
R & D costs	1,223	2,180	4,028	2,680	-83	10,028
M & BD costs	0	10	498	349	0	857
G & A costs	0	51	1,822	1,569	0	3,442
<b>Total costs</b>	<b>1,482</b>	<b>2,506</b>	<b>7,081</b>	<b>5,039</b>	<b>-83</b>	<b>16,025</b>

## 8. Personnel costs

EUR thousand	2007	2008
Personnel remuneration	6,742	6,089
Stock option expenses	457	120
Social security expenses	952	872
<b>Total personnel costs</b>	<b>8,151</b>	<b>7,081</b>
Employees (average)	121	97
Personnel costs / employee	67.4	73.0

Social security expenses include the employer's contribution to the national German pension fund of EUR 280 thousand (2007: EUR 318 thousand) and contributions to a 401(k) savings plan in the U.S.A. of EUR 66 thousand (2007: EUR 88 thousand).

### 9. Other expenses

EUR thousand	2007	2008
Exchange rate losses from currency conversion	363	348
Expenses related to former periods	58	41
Additional claims from social security audit	0	36
Losses from the disposal of assets	0	15
Write-downs of doubtful receivables	52	0
Other	7	0
<b>Total</b>	<b>480</b>	<b>440</b>

### 10. Operating result (EBIT)

In the reporting year, the recorded operating result before interest and taxes (EBIT) and the operating result before interest, taxes, depreciation and amortization (EBITDA) improved as follows:

EUR thousand	2007	2008	variance in %
<b>EBIT</b>	<b>-13,504</b>	<b>-12,750</b>	<b>5.6</b>
Depreciation	788	669	15.1
Amortization	458	1,839	-301.5
<b>EBITDA</b>	<b>-12,259</b>	<b>-10,242</b>	<b>16.4</b>



## 11. Financial result

EUR thousand	2007	2008
<b>Interest and related income</b>	<b>629</b>	<b>682</b>
interest from held-to-maturity investments	4	1
interest from available-for-sale financial assets	205	151
interest from cash and cash equivalents	390	521
interest from receivables	30	9
<b>Other financial income</b>	<b>30</b>	<b>43</b>
fair value adjustment for derivative instruments	26	43
adjustment from disposal of available-for-sale financial assets	4	0
<b>Total financial income</b>	<b>659</b>	<b>725</b>
<b>Interest expenses</b>	<b>-30</b>	<b>-30</b>
interest expenses for derivative instruments	-30	-30
<b>Other financial expenses</b>	<b>-28</b>	<b>-3</b>
other finance costs	-3	-3
premium paid on cash equivalents	-25	0
<b>Total financial expenses</b>	<b>-58</b>	<b>-33</b>
<b>Financial result</b>	<b>601</b>	<b>692</b>

In the reporting year, a net gain of EUR 13 thousand for derivative instruments has been recognized (2007: net loss of EUR 4 thousand). For the net gains and losses of all other financial instruments reference is made to the overview above.

## 12. Taxes on income

The reported income taxes in the amount of EUR 213 thousand (2007: EUR 248 thousand) comprise exclusively taxes recorded by the Company's U.S. subsidiary in Seattle.

EUR thousand	2007	2008
Current tax expenses	40	64
Deferred tax expenses due to loss carryforwards	218	122
Deferred tax expenses due to temporary differences	-10	8
Allowance	0	19
<b>Total taxes on income</b>	<b>248</b>	<b>213</b>

Applying the local tax rate of 34% deferred tax expenses of EUR 14 thousand were calculated due to passive temporary differences between IFRSs and U.S. tax law for depreciation of tangible assets. Deferred tax income of EUR 6 thousand was calculated for active temporary differences between IFRSs and U.S. tax law in the valuation of liabilities. For deferred tax assets on tax loss carryforwards that had already been capitalized, deferred tax expenses of EUR 122 thousand were calculated for the reporting year. Due to better assessments, a correction had to be made for temporary differences from previous years. This correction had an impact on the tax loss carryforwards of the previous year leading to a potential increase of the capitalized deferred tax assets. This increase, however, was omitted because of the underlying time horizon of the calculation. An allowance of EUR 19 thousand was recorded instead.

Epigenomics, Inc. utilizes the deferred tax assets capitalized in the past. Deferred tax income was then calculated on its tax loss carryforwards as a consequence of the existing transfer price agreement between the German Epigenomics AG and its U.S. subsidiary. The usage of a cost plus method according to this agreement leads to a guaranteed annual profit for Epigenomics, Inc., so that a utilization of its tax loss carryforwards in the foreseeable future is sufficiently probable.

### Calculation of applicable tax charge:

	2007	2008
Corporate tax rate (incl. solidarity charge)	15.8%	15.8%
Trade tax rate	14.0%	14.0%
<b>Total applicable tax rate in Germany for the purpose of deferred taxes</b>	<b>29.8%</b>	<b>29.8%</b>

*Tax reconciliation:*

	2007	2008
<b>Operating result before taxes</b>	<b>-12,903</b>	<b>-12,058</b>
<b>Expected income tax</b>	<b>-3,845</b>	<b>-3,593</b>
loss carryforwards not capitalizable	4,286	4,171
foreign tax rate differential	-27	-16
tax effect from non-deductible operating expenses	24	26
effect from tax-free income	-26	-3
expenses for capital increase	-48	-234
other effects	-116	-138
<b>Total</b>	<b>248</b>	<b>213</b>
<b>Effective tax rate</b>	<b>-1.9%</b>	<b>-1.8%</b>

*13. Earnings per share*

The earnings per share (basic) are calculated by dividing the Group's net loss for the year by the weighted-average number of shares issued.

	2007	2008
Net loss for the year in EUR thousand	-13,151	-12,271
Weighted-average number of shares issued	17,807,258	26,007,110
Earnings per share (basic and diluted) in EUR	-0.74	-0.47

The outstanding stock options granted by the Company are antidilutive according to IAS 33.41 and 33.43 *Earnings per Share*. Therefore, the earnings per share (diluted) equal the earnings per share (basic). The number of shares issued as of the balance sheet date amounts to 26,710,886.

## Notes to the Group Balance Sheet

### Non-current assets

#### 14. Investment subsidies

In the reporting period, investment subsidies affecting the carrying values were received by Epigenomics AG in Germany in the amount of EUR 100 thousand (2007: EUR 93 thousand). This relates to a government investment grant for investments in tangible assets (“Investitionszulage”).

#### 15. Intangible assets

EUR thousand		Software	Licenses / patents	Goodwill	Development costs	Total intangible assets
Jan 1, 2007	Acquisition costs	652	5,236	3,351	0	9,239
	Additions	14	0	0	5	19
	Disposals	0	0	0	0	0
Dec 31, 2007	Acquisition costs	666	5,236	3,351	5	9,258
	Additions	2	211	0	83	296
	Disposals	-51	-786	0	0	-837
<b>Dec 31, 2008</b>	<b>Acquisition costs</b>	<b>617</b>	<b>4,661</b>	<b>3,351</b>	<b>88</b>	<b>8,717</b>
Jan 1, 2007	Accumulated amortization	410	1,580	726	0	2,716
	Additions	143	315	0	0	458
	Disposals	0	0	0	0	0
Dec 31, 2007	Accumulated amortization	553	1,895	726	0	3,174
	Additions	87	1,730	0	22	1,839
	Disposals	-50	-782	0	0	-832
<b>Dec 31, 2008</b>	<b>Accumulated amortization</b>	<b>590</b>	<b>2,843</b>	<b>726</b>	<b>22</b>	<b>4,181</b>
Dec 31, 2007	Carrying values	113	3,341	2,625	5	6,084
<b>Dec 31, 2008</b>	<b>Carrying values</b>	<b>27</b>	<b>1,818</b>	<b>2,625</b>	<b>66</b>	<b>4,536</b>

The licenses and patents listed represent mainly acquisition costs for acquired patents and exclusive rights of use to property rights of third parties. Those acquisition costs are usually caused by upfront payments. The majority of the licenses require the Company to pay additional annual minimum fees that are expensed immediately. The license contracts may usually be cancelled at short notice. However, some of those licenses are vital for the Company's business model.

In December 2008, the capitalized goodwill was tested for impairment in order to comply with IFRS 3 *Business Combinations* and IAS 36 *Impairment of Assets*. It had originated in the acquisition of Orca Biosciences (now: Epigenomics, Inc.) in 2001 and is assigned in content to the Company's cancer screening business as the relevant cash-generating unit. The Company's current business plan projections for the screening business were used for the test. According to this plan, future cash inflows will be generated in a partnering model from milestone payments, R&D payments and royalty income. The plans are based on the existing collaboration contracts with the Company's partners. Growth rates were anticipated in line with the industry standards. Due to the business model, the expected product life cycle and the underlying terms of the patents, cash flows were planned for a period of ten years. All future cash flows are measured by the net present value method. The appropriate discount rate, which has been applied in the reporting year, was 25%. No impairment had to be recognized.

In 2007, the Company has started to capitalize the expenditures which incurred in connection with the development of its RUO kits as the recognition criteria according to IAS 38.57 were met. The useful life of these capitalized development costs was defined as three years with regard to the expected product life cycles.

## 16. Tangible assets

EUR thousand		Fixtures/ leasehold improvements	Technical equipment	Other fixed assets	Total tangible assets
Jan 1, 2007	Acquisition costs	821	6,600	77	7,498
	Additions	28	-81	-1	-54
	Disposals	-3	-900	-1	-904
Dec 31, 2007	Acquisition costs	846	5,619	75	6,540
	Additions	0	164	1	165
	Disposals	-32	-945	-4	-981
<b>Dec 31, 2008</b>	<b>Acquisition costs</b>	<b>814</b>	<b>4,838</b>	<b>72</b>	<b>5,724</b>
Jan 1, 2007	Accumulated depreciation	675	4,722	51	5,448
	Additions	90	690	7	788
	Disposals	-3	-899	-1	-904
Dec 31, 2007	Accumulated depreciation	762	4,513	57	5,332
	Additions	33	628	6	667
	Disposals	-32	-932	-3	-967
<b>Dec 31, 2008</b>	<b>Accumulated depreciation</b>	<b>763</b>	<b>4,209</b>	<b>60</b>	<b>5,032</b>
Dec 31, 2007	Carrying values	84	1,106	18	1,208
<b>Dec 31, 2008</b>	<b>Carrying values</b>	<b>51</b>	<b>629</b>	<b>12</b>	<b>692</b>

*17. Financial assets*

EUR thousand		Securities held to maturity	Total financial assets
Jan 1, 2007	Acquisition costs	1,000	1,000
	Additions	0	0
	Disposals	0	0
Dec 31, 2007	Acquisition costs	1,000	1,000
	Additions		
	Disposals	-1,000	-1,000
<b>Dec 31, 2008</b>	<b>Acquisition costs</b>	<b>0</b>	<b>0</b>
Jan 1, 2007	Accumulated amortization	0	0
	Additions	0	0
	Disposals	0	0
Dec 31, 2007	Accumulated amortization	0	0
	Additions	0	0
	Disposals	0	0
<b>Dec 31, 2008</b>	<b>Accumulated amortization</b>	<b>0</b>	<b>0</b>
Dec 31, 2007	Carrying values	1,000	1,000
<b>Dec 31, 2008</b>	<b>Carrying values</b>	<b>0</b>	<b>0</b>

The financial assets at the beginning of the year in the amount of EUR 1,000 thousand, reported as securities held to maturity, represented exclusively a promissory note issued by a German special branch bank. This note has been redeemed in full by the issuer as specific contractual conditions were met.

### 18. Assets schedule

EUR thousand		Intangible assets	Tangible assets	Financial assets	Total assets
Jan 1, 2007	Acquisition costs	9,239	7,498	1,000	17,737
	Additions	19	-54	0	-35
	Disposals	0	-904	0	-904
Dec 31, 2007	Acquisition costs	9,258	6,540	1,000	16,798
	Additions	296	165	0	461
	Disposals	-837	-981	-1,000	-2,818
<b>Dec 31, 2008</b>	<b>Acquisition costs</b>	<b>8,717</b>	<b>5,724</b>	<b>0</b>	<b>14,441</b>
Jan 1, 2007	Accumulated depreciation /amortization	2,716	5,448	0	8,164
	Additions	458	788	0	1,246
	Disposals	0	-904	0	-904
Dec 31, 2007	Accumulated depreciation /amortization	3,174	5,332	0	8,506
	Additions	1,839	667	0	2,506
	Disposals	-832	-967	0	-1,799
Dec 31, 2008	Accumulated depreciation / amortization	4,181	5,032	0	9,213
Dec 31, 2007	Carrying values	6,084	1,208	1,000	8,292
<b>Dec 31, 2008</b>	<b>Carrying values</b>	<b>4,536</b>	<b>692</b>	<b>0</b>	<b>5,228</b>

Total depreciation and amortization of the reporting period of EUR 2,506 thousand includes extraordinary write-offs of EUR 1,580 thousand. These write-offs affect intangible assets in the amount of EUR 1,428 thousand and tangible assets in the amount of EUR 152 thousand. The predominant part of these write-offs is the outcome of a decision not to use the underlying technology anymore for the development of an IVD platform.

### 19. Deferred tax assets

In former years, deferred tax assets had been capitalized due to tax loss carryforwards of Epigenomics, Inc. (see also item 12 "Taxes on income"). At the balance sheet date, these deferred tax assets were valued at EUR 629 thousand. Due to taxable profits of the U.S. subsidiary in the reporting year, a utilization of EUR 149 thousand has been recognized.

EUR thousand	2007	2008
<b>Jan 1</b>	<b>985</b>	<b>778</b>
Deferred tax expenses	-208	-149
<b>Dec 31</b>	<b>778</b>	<b>629</b>

For the German parent company, deferred taxes arise as described in the following tables.

*Deferred tax assets*

EUR thousand	Dec 31, 2007	Dec 31, 2008
Tangible assets	155	0
Liabilities	21	25
<b>Total</b>	<b>176</b>	<b>25</b>

*Deferred tax liabilities*

EUR thousand	Dec 31, 2007	Dec 31, 2008
Intangible assets	1	20
Tangible assets	8	71
Cash and cash equivalents	0	2
Other current assets	421	0
Capital reserve	186	840
Other comprehensive income	296	433
Liabilities	5	0
<b>Total</b>	<b>917</b>	<b>1.366</b>

Since its inception through December 31, 2007, the Company's tax loss carryforwards in Germany amounted to approximately EUR 85 million (for corporate taxation) and to approximately EUR 84 million (for trade taxation). In addition, the Company expects to increase its cumulated tax losses significantly with the filing of its tax returns for 2008. As the deductibility of the tax loss carryforwards has been partially challenged by the German tax authorities in the past, it is not certain to which extent these carryforwards will lead to deferred tax income in the future.

Since all the aforementioned matters must be settled with the same fiscal authority, in accordance with IAS 12.71 *Income Taxes* et seq., a balancing of the respective tax income and expenses has been performed. As the current forecasts of the Company with regard to achieving the break-even point are still subject to significant uncertainty, valuation allowances have been recognized for all of the net deferred tax assets.



## Current assets

### 20. Inventories

EUR thousand	Dec 31, 2007	Dec 31, 2008
Consumables, raw materials, supplies	237	106
Finished goods	0	19
<b>Total inventories</b>	<b>237</b>	<b>125</b>

### 21. Trade receivables<sup>1</sup>

Trade receivables primarily include settlement receivables from development partners, customers and licensees. These receivables do not bear interest and are therefore not exposed to any interest rate risk. The carrying amounts of the receivables correspond to their fair values. The maximum default risk corresponded to the carrying value as of the balance sheet date.

EUR thousand	Dec 31, 2007	Dec 31, 2008
Trade receivables, gross	488	765
Allowance for bad debt	-49	-38
<b>Trade receivables, net</b>	<b>439</b>	<b>727</b>

At the balance sheet date, trade receivables in the amount of EUR 470 thousand were not due and receivables in the amount of EUR 257 thousand were past due but not impaired as there are no indications that debtors will not be able to meet their obligations.

EUR thousand	Dec 31, 2008
Trade receivables past due 1-30 days	251
Trade receivables past due 31-60 days	0
Trade receivables past due 61-90 days	6
<b>Trade receivables past due</b>	<b>257</b>

<sup>1</sup> In previous years, this balance sheet line had been named "Trade and other receivables". As a matter of fact, in the past, this line had only included "trade receivables" whereas "other receivables" had been reported under the balance sheet line "Other current assets". Therefore, it was decided to adjust the rather misleading name of this line. This name change has no impact on any previous years' numbers.

## 22. Marketable securities

All marketable securities in the amount of EUR 2,286 thousand as of December 31, 2008 (Dec 31, 2007: EUR 3,370 thousand) are recognized as financial instruments "available for sale" according to IAS 39.9 *Financial Instruments: Recognition and Measurement*.

Under the investment policy of the Company, each investment in securities underlies certain strict criteria. These include amongst others the limitation to securities nominated in euro currency only and an official capital market rating of the issuer or the securities not below "investment grade". However, the Company has not invested in any marketable securities during the last three reporting years.

All reported securities are underlying the usual market and interest risks. The interest rate risks are mostly price risks but for some securities there also is an interest rate cash flow risk. Currency risks are minimized by avoiding investments in securities nominated in currencies other than the euro.

The fair value of all marketable securities is identified by their stock exchange quotations at each relevant balance sheet date. All securities have been traded on active markets in the reporting year.

EUR thousand	Dec 31, 2007	Dec 31, 2008
Corporate bonds	2,325	2,098
Mortgage bonds	613	0
Debt certificates	432	188
<b>Total</b>	<b>3,370</b>	<b>2,286</b>

The investment strategy of the Company provides for an allocation of the various securities to different remaining maturities.

EUR thousand	Fair value Dec 31, 2007	in %	Fair value Dec 31, 2008	in %
<b>Time to maturity of marketable securities</b>				
< 1 year	613	18.2	485	21.2
1-2 years	490	14.5	0	0.0
2-5 years	811	24.1	779	34.1
> 5 years	1,024	30.4	834	36.5
Unlimited	432	12.8	188	8.2
<b>Total</b>	<b>3,370</b>	<b>100.0</b>	<b>2,286</b>	<b>100.0</b>

### 23. Cash and cash equivalents

Cash and cash equivalents increased to EUR 9,814 thousand at the balance sheet date (Dec 31, 2007: EUR 6,646 thousand). Approximately 84% of those funds were denominated in euro currency at the balance sheet date. The remainder is predominantly denominated in U.S. dollar currency. The total amount is allocated to three different banks.

EUR thousand	Dec 31, 2007	Dec 31, 2008
Time deposits	6,290	9,162
Bank accounts, petty cash, cheques	356	652
<b>Total</b>	<b>6,646</b>	<b>9,814</b>

### 24. Other current assets

EUR thousand	Dec 31, 2007	Dec 31, 2008
Receivables from tax authorities	877	605
Prepaid expenses	364	544
Claims based on granted projects	320	136
Interest receivables	95	82
Deposits	27	29
Advance payments	0	8
Excess payments	0	4
Deferred financing costs	1,414	0
Other	55	66
<i>thereof with a prospective maturity &gt; 1 year</i>	38	38
<b>Total</b>	<b>3,152</b>	<b>1,474</b>

## Equity

### 25. Notes to share categories and capital structure

As of December 31, 2008, the share capital of Epigenomics AG comprises exclusively common shares with equal rights and a par value of EUR 1.00 each. During the reporting year, the number of shares issued increased from 18,252,824 to 26,723,636 shares. A total of 8,458,062 new no-par value bearer shares were created by a capital increase entirely using Authorized Capital 2007 within a financing transaction in February 2008 at a price of EUR 1.60 each. This capital increase was registered with the commercial register Charlottenburg on February 7, 2008. A total of 12,750 new shares were created by the exercise of stock options.

Equity structure of Epigenomics AG as of December 31:

EUR	Dec 31, 2007	Dec 31, 2008	Variance
<b>Share Capital</b>	<b>18,252,824</b>	<b>26,723,636</b>	<b>8,470,812</b>
<b>Conditional Capital</b>	<b>1,430,988</b>	<b>4,089,326</b>	<b>2,658,338</b>
Conditional Capital I	26,258	13,508	-12,750
Conditional Capital III	139,625	139,625	0
Conditional Capital IV	617,426	617,426	0
Conditional Capital V	647,679	647,679	0
Conditional Capital VI	0	2,671,088	2,671,088
<b>Authorized Capital</b>	<b>8,458,062</b>	<b>2,671,088</b>	<b>-5,786,974</b>
Authorized Capital 2007	8,458,062	0	-8,458,062
Authorized Capital 2008/I	0	2,671,088	2,671,088

Conditional Capital I, III and IV cannot be used anymore to grant stock options as the underlying granting time frame has expired. However, new shares can still be created upon exercise of options from these older programs.

Conditional Capital V can be used to create new shares upon the exercise of stock options granted under the latest stock option program (06-10) of the Company.

Conditional Capital VI was resolved upon by the Annual General Shareholders' Meeting (AGM) on June 3, 2008. This Conditional Capital serves the purpose of granting shares to holders of convertible bonds issued on the basis of the Executive Board's authorization to issue convertible bonds and to the exclusion of subscription rights.

Until June 2, 2013, the Executive Board is authorized to issue, with the consent of the Supervisory Board, once or several times convertible bearer bonds in an aggregate nominal amount of up to EUR 25,000,000.00 with a maximum term of ten years and to grant conversion rights to the holders of convertible bonds for up to a total of 2,671,088 no-par value bearer shares in the Company representing a notional portion of the share capital of the Company of up to EUR 2,671,088.00 in total as specified in the terms and conditions of the convertible bonds.<sup>1</sup> Conditional Capital VI has been registered with the commercial register on June 17, 2008. Following this registration, the Company was served with a lawsuit filed by an individual shareholder challenging the aforementioned authorization.<sup>2</sup>

In February 2008, Authorized Capital 2007 was entirely used by the Executive Board to increase, with the consent of the Supervisory Board, the Company's share capital within the aforementioned financing transaction. In the AGM on June 3, 2008, the shareholders of the Company resolved upon creating another authorized capital ("Authorized Capital 2008/I") and the corresponding addition of Section 5 Paragraph 9 to the Company's Articles of Association. The Executive Board is authorized to increase, with the consent of the Supervisory Board, the share capital at any time or from time to time on or before June 2, 2013, by up to EUR 2,671,088.00 by issuing up to 2,671,088 new no-par value bearer shares in return for contributions in cash and/or in kind, whereby, in case of a capital increase against contribution in cash, shareholders have, in principle, a pre-emptive right<sup>3</sup>. The Authorized Capital 2008/I and the corresponding amendment of our Articles of Association were registered with the commercial register on June 17, 2008.

## 26. Capital reserve

In the reporting year, the capital reserve decreased from EUR 13,712 thousand (Dec 31, 2007) to EUR 3,567 thousand mainly due to the deduction of the net loss for the year 2007 (EUR 13,151 thousand). Offsetting effects came from the aforementioned capital increase (EUR 2,877 thousand, net), the current stock option expense accounting according to IFRS 2 *Share-based Payment* (EUR 120 thousand) and from the paid-in surplus of exercised employee stock options (EUR 9 thousand).

## 27. Other comprehensive income

The other comprehensive income arises from the revaluation of financial assets available for sale not affecting net income. The effective sale of revaluated financial assets available for sale leads to a recognition of the cumulated differences through profit or loss.

EUR thousand	2007	2008
<b>Balance as of January 1</b>	<b>610</b>	<b>993</b>
- adjustments from the sale of financial instruments available for sale	30	-23
- revaluation of available-for-sale financial instruments	353	482
<b>Balance as of December 31</b>	<b>993</b>	<b>1,452</b>

<sup>1</sup> For further details on the authorization to issue convertible bonds reference is made to the invitation to the Company's AGM on June 3, 2008, as published on the Company's website ([www.epigenomics.com/en/investor\\_relations/general\\_shareholders\\_meeting/](http://www.epigenomics.com/en/investor_relations/general_shareholders_meeting/)).

<sup>2</sup> For further details on the lawsuit reference is made to the corporate governance section in the consolidated management report of this annual report.

<sup>3</sup> For further details on the authorization to issue new shares reference is made to the invitation to the Company's AGM on June 3, 2008, as published on the Company's website ([www.epigenomics.com/en/investor\\_relations/general\\_shareholders\\_meeting/](http://www.epigenomics.com/en/investor_relations/general_shareholders_meeting/)).

## *28. Capital management*

The Group manages its capital to ensure that entities in the Group will be able to continue as a going concern while maximizing the long-term return to stakeholders. An optimization of the debt/equity ratio is always considered.

The capital structure of the Group consists of short-term debt, cash and cash equivalents, instruments available for sale and equity attributable to equity holders, comprising subscribed capital, capital reserve (including offset retained earnings) and other comprehensive income.

In 2008, the Group's equity ratio increased from 77.8% as of December 31, 2007, to 81.3% as of December 31, 2008. This increase is mainly attributable to the decrease in short-term liabilities.

The Company is not subject to any statutory capital requirements. However, the Company is obliged to issue new shares in connection with its existing stock option programs.

## Non-current liabilities

### *29. Liabilities from leasing contracts*

In the reporting year, the Company has closed an operating lease for lab equipment. The leasing contract has a remaining term until April 2011.

## Current liabilities

### 30. Deferred income

Payments received in advance for services to be rendered by Epigenomics AG in the future are recorded as deferred income. The payments received for commercial collaborations are recognized as revenue over the respective contractual terms. The payments received for granted projects are recognized as other income according to the percentage of completion method. There is no repayment obligation for Epigenomics.

EUR thousand	Dec 31, 2007	Dec 31, 2008
Payments for commercial collaborations	543	1,167
Payments for granted projects	94	87
<b>Total</b>	<b>637</b>	<b>1,254</b>

Deferred income in the amount of EUR 597 thousand as of December 31, 2008 (Dec 31, 2007: EUR 167 thousand), which will be released in the form of revenue recognition, has a duration exceeding twelve months. This corresponds to our usual licensing business cycle.

### 31. Other liabilities

EUR thousand	Dec 31, 2007	Dec 31, 2008
Payables due to staff	731	396
Payables due to tax authorities	170	178
Accrued audit fees	93	127
Liabilities from derivative instruments	71	85
Payables due to social security institutions	11	29
Accrued Supervisory Board fees	46	25
Liabilities from granted projects	0	13
Liabilities from financing activities	1,190	0
Other	42	34
<b>Total</b>	<b>2,354</b>	<b>887</b>

Liabilities from derivative instruments reflect the net present value at the balance sheet date of U.S. dollar forward contracts due on various dates in 2009 (EUR 58 thousand) and of an interest swap with a remaining term until April 2010 (EUR 27 thousand). Under certain conditions, the latter can also be terminated by the opposite partner on a short-term basis. Therefore, it is shown as a current liability.

### 32. Provisions

As of December 31, 2008, the provisions of the Company added up to EUR 481 thousand, a decrease of EUR 59 thousand compared to the reporting date of previous year. Substantially they were recognized for:

- possible obligations from licensing contracts, depending on outstanding decisions from patent courts;
- for uncertain liabilities due to employees in connection with the Employee's Invention Act in Germany and
- for other operating expenses which were uncertain at the reporting date regarding their exact amounts or the point in time when they will incur.

While a utilization of the other provisions is largely expected within the next twelve months, a utilization of the licensing and the payroll provisions could lie in more than twelve months' time.

Statement of changes in current provisions:

EUR thousand	Licensing provisions	Payroll provisions	Provision for granted projects	Other provisions	Total
<b>January 1, 2008</b>	<b>209</b>	<b>206</b>	<b>57</b>	<b>68</b>	<b>540</b>
Utilization	0	0	0	-49	-49
Reversal	-209	0	-57	-13	-279
Additions	188	22	0	59	269
<b>December 31, 2008</b>	<b>188</b>	<b>228</b>	<b>0</b>	<b>65</b>	<b>481</b>



### 33. Notes to financial instruments

AC = Amortized Cost  
 FV Rec. Eq. = Fair Value Recognized in Equity  
 FV Rec. PL = Fair Value Recognized in Profit or Loss

#### Primary financial instruments

in EUR thousand	Valuation principle	Carrying amount	Fair value	Carrying amount	Fair value
				as of Dec 31, 2008	
		as of Dec 31, 2007			
<b>Assets</b>					
<b>Loans and receivables</b>	<b>AC</b>	<b>3,591</b>	<b>3,591</b>	<b>1,045</b>	<b>1,045</b>
Trade receivables		439	439	727	727
Other current assets		3,152	3,152	318	318
<b>Financial assets available for sale</b>	<b>FV Rec. Eq.</b>	<b>3,370</b>	<b>3,370</b>	<b>2,286</b>	<b>2,286</b>
Marketable securities		3,370	3,370	2,286	2,286
<b>Financial assets held to maturity</b>	<b>AC</b>	<b>1,000</b>	<b>987</b>	<b>0</b>	<b>0</b>
Financial assets		1,000	987	0	0
<b>Cash and cash equivalents</b>	<b>n/a</b>	<b>6,646</b>	<b>6,646</b>	<b>9,814</b>	<b>9,814</b>
<b>Liabilities</b>					
<b>Financial liabilities measured at amortized cost</b>	<b>AC</b>	<b>3,845</b>	<b>3,845</b>	<b>1,508</b>	<b>1,508</b>
Trade liabilities		1,562	1,562	1,027	1,027
Liabilities from leasing contracts		0	0	66	66
Other current liabilities		2,283	2,283	415	415

#### Derivative financial instruments

in EUR thousand	Valuation principle	Carrying amount	Fair value	Carrying amount	Fair value
				as of Dec 31, 2008	
		as of Dec 31, 2007			
<b>Liabilities</b>					
<b>Financial liabilities held for trading</b>	<b>FV Rec. PL</b>	<b>71</b>	<b>71</b>	<b>85</b>	<b>85</b>
Interest rate swap		71	71	27	27
Currency forward contracts		0	0	58	58

## Notes to the Group Cash Flow Statement

### *34. Operating activities*

Cash flow from operations is derived indirectly on the basis of the net loss for the year before taxes on income. Cash comprises bank deposits and cash in hand. Cash equivalents are defined as instruments being convertible on a short-term basis to a known amount of cash and carrying a very low risk of changes in value.

### *35. Investing activities*

Cash flow from investing activities is ascertained in respect of payment.

For information on the reported proceeds from investment grants please refer to “Investment Subsidies” (item 14).

### *36. Financing activities*

Cash flow from financing activities is ascertained in respect of payment.

## Risks and Risk Management

### *37. General*

For a comprehensive overview of the risks the Company is facing reference is made to the “Opportunities and Risk Report” section of the Group management report 2008.

### *38. Liquidity risk*

The liquidity risk of Epigenomics results from the Group’s potential inability to meet its financial liabilities, i.e. not paying its suppliers, creditors or lenders.

To secure the Company’s liquidity, Epigenomics constantly monitors the capital markets and undertakes all necessary efforts to raise fresh capital early before the Group runs out of liquidity. Short-term liquidity is ensured by maintaining internal cash forecasts and a corresponding strategy of managing time deposits with the Company’s house banks.

Epigenomics has a strict cost management in place to avoid unnecessary spending. On the procurement side it always tries to reduce and minimize purchase prices by closing favorable contracts and negotiating all relevant conditions.

### *39. Foreign currency exchange risk*

The Group constantly faces a foreign currency exchange risk through the fluctuations between the euro and the U.S. dollar and always tries to mitigate or to eliminate this risk as far as possible. The Group mainly uses derivative financial instruments in the shape of forward contracts to minimize this risk. These instruments are recognized at fair value on the Group balance sheet as short-term assets or short-term liabilities. Changes in fair value are charged to profit or loss as the Company currently does not meet the requirements of IAS 39 *Financial Instruments: Recognition and Measurement* regarding hedge accounting.

As of December 31, 2008, the Group had already covered its anticipated needs for U.S. dollars until the third quarter of 2009 by forward contracts. After the balance sheet date, it has also covered the U.S. dollar needs for the rest of 2009 so that the foreign currency exchange risk for the next twelve-month period is reduced to a valuation risk regarding the related derivative contracts.

#### *40. Credit risk*

The Company's overall credit risk is low. Securities have only been acquired under careful observation of the Company's investment policy, i.e. a strict selection by the credit ratings of the issuers has been conducted. However, the worldwide financial market crisis of 2008 has shown, that even top-rated issuers can suddenly face a threatening situation or even collapse. Additionally, 2008 has shown that there is a clear risk of illiquid markets.

Trade receivables basically concern renowned commercial partners with acceptable ratings. Whenever possible, payments are collected upfront. In all cases, the maximum amount at risk can be derived from the carrying values.

#### *41. Interest rate risk*

The Group holds interest-bearing financial instruments in the form of cash and cash equivalents (daily and time deposits), of securities and of an interest rate swap contract.

As the Group's time deposits have usually maturities of up to a maximum of 180 days, the interest rate risk of these financial instruments can be considered negligible.

However, the securities held by the Group with maturities of more than one year are subject to an interest rate risk as the terms and conditions for interest payments depend on the development of the long-term interest rates on the capital markets. In a worst-case scenario, the Group will receive no interest payments at all from the issuers of these securities but in no case it will have a negative interest income (i.e. it will not pay interest). The remaining securities with a maturity of less than one year bear a fixed interest rate and the underlying risk can be considered negligible at the balance sheet date as the bond is expected to be repaid by the end of February 2009.

Further, the Group faces an interest rate risk via the interest rate swap contract as it has the obligation to pay a fixed rate and receives a variable rate of interest, again depending on the development of the long-term interest rates on the capital markets. In a worst-case scenario, the Group will pay interest of EUR 30 thousand and will receive no interest income at all. The swap contract will terminate in April 2010.

## Information on Stock Option Programs

### *42. Expired stock option programs*

As of the balance sheet date, the Epigenomics Group (via Epigenomics AG) had four fixed stock option programs in place. Details of the three programs 2000, 01-05 and 03-07 can be found in the Company's prospectus for the capital increase dated January 22, 2008. This document is available on the Company's website. Those three programs are all expired at the balance sheet date, i.e. no stock options can be granted from those programs in the future. In general, the rights under all three programs are such that option holders can obtain shares in the Company by exercising their options once all exercise hurdles have been surpassed. In order for options to be exercisable, the stock price must have appreciated by at least 10% versus the stock price at grant date and the statutory waiting period of two years as well as vesting must have been completed. If employees leave the Company before the options are vested these forfeit without compensation.

### *43. Current stock option program*

A fourth stock option program ("06-10") was introduced in 2006 and approved by the Annual General Shareholders' Meeting on July 10, 2006. The Company's share capital was therefore conditionally increased by up to 3.95% of the share capital registered before the capital increase, i.e. by up to EUR 647,679.00 by issuance of up to 647,679 bearer shares of common stock with an accounting par value of EUR 1.00 each (Conditional Capital V). The Executive Board of the Company is authorized until the expiration (December 31, 2010) to issue subscription rights with respect to shares out of the stock option program 06-10 in one or more annual tranches in favor of beneficiaries according to the conditions of this program, once the Conditional Capital V becomes effective by registration in the commercial register. In case of Executive Board members being beneficiaries, only the Supervisory Board can grant such options.

Each individual subscription right entitles the beneficiary to subscribe to one bearer share of common stock of the Company with a par value of EUR 1.00 each against payment of the exercise price. Beneficiaries of the program are the Company's Executive Board members ("group 1"; 69.5% of the total volume) and its employees ("group 2"; 30.5% of the total volume).

The subscription rights in every tranche shall vest for the group-2-beneficiaries as follows: one-third of the subscription rights issued in one tranche shall vest one year after the issuance of the subscription rights of such tranche; a further one-third of the subscription rights issued in one tranche shall vest two years after the issuance of the subscription rights of such tranche; the final one-third of the subscription rights issued in one tranche shall vest three years after the issuance of the subscription rights of such tranche.

The subscription rights of every tranche shall vest completely or partially for group-1-beneficiaries, if and to the extent that the Supervisory Board of the Company declares such vesting of subscription rights vis-à-vis a group-1-beneficiary in compliance with the rules set out hereafter. The declaration of vesting of subscription rights vis-à-vis a group-1-beneficiary by the Company's Supervisory Board requires a corresponding prior resolution by the Supervisory Board. The Supervisory Board adopts its decision regarding the "if" and the extent of the vesting of subscription rights of a group-1-beneficiary at its free discretion taking into account the individual services of the individual beneficiary and the development of the Company. The Supervisory Board can declare the complete or partial vesting of subscription rights issued in one tranche in favor of group-1-beneficiaries at any time after the issuance of these subscription rights. In case the Supervisory Board does not decide on the vesting vis-à-vis one or more of the group-1-beneficiaries, the subscription rights of every tranche shall vest for group-1-beneficiaries in the same way as for group-2-beneficiaries (see above).

Subscription rights of each tranche can be exercised for the first time after their vesting as described before and after expiration of the statutory waiting period. The statutory waiting period starts with the issuance of the subscription rights of a tranche and ends two years after the issuance of the subscription rights of such tranche. The restriction of the exercise of the subscription rights to certain exercise periods and the subscription rights being subject to the compliance with all exercise conditions remain unaffected by the expiration of the waiting period.

The term of the subscription rights of every tranche begins with the issuance of the subscription rights of such tranche and ends with the expiration of seven years after the issuance of the subscription rights of such tranche.

The subscription rights can only be exercised against payment of the exercise price to the Company. The exercise price corresponds to the average stock exchange closing price, increased by 10%, of the 20 stock exchange trading days preceding the issuance of the subscription rights in the Exchange Electronic Trading (XETRA) system, in no case, however, less than the final stock exchange price of the share on the day the subscription rights were issued ("market value" or "fair market value"). Furthermore, the subscription rights regarding a tranche can only be exercised in case the price of the Company's share has reached or surpassed the payable exercise price at least once within the period between the issuance of the subscription rights of this tranche and the exercise of these subscription rights (performance target).

Any subscription rights of a beneficiary that have not yet vested expire without compensation in any case upon termination of the employment or work contract with the beneficiary, irrespective of the reason for such termination. The expiration date is the day on which the employment or work contract ends.

The subscription rights granted to the beneficiaries under the stock option program 06-10 are nontransferable. In case subscription rights are not or cannot be exercised until the end of their term, they expire without compensation. The same applies for vested subscription rights.

The new shares shall participate in the profit from the beginning of the fiscal year in which they are issued.

#### 44. Development of stock options in the reporting year

In 2008, a total number of 30,000 stock options were granted under the Company's stock option program 06-10 to employees of the Company. Each option right entitles the holder to subscribe to one bearer share of common stock with a par value of EUR 1.00 each in return for payment of the exercise price. The exercise price for each of the new rights was fixed at the average closing price of the 20 trading days before the grant date. The aggregate proceeds to the Company if these options were exercised and shares were issued would amount to EUR 63,205.

##### Details of stock options granted in 2008:

Expiry date	April 1, 2015	October 1, 2015	Total 2015
Number	25,000	5,000	30,000
Share price at grant date (in EUR)	1.84	2.31	1.92
Exercise price (in EUR)	2.02	2.54	2.11
Historical volatility at grant date	57.76%	55.40%	57.37%
Risk-free interest rate	3.85%	2.72%	3.66%
Aggregate proceeds if shares are issued (in EUR)	50,500	12,705	63,205

A total number of 203,682 stock options can still be granted to the Company's employees and Executive Board members from the stock option program 06-10.

	Options issued as of Dec 31, 2007	Options issued in 2008	Options forfeited in 2008	Options cancelled in 2008	Options exercised in 2008	Options issued as of Dec 31, 2008
<b>Option holder</b>						
Geert Walther Nygaard	180,000	0	0	0	0	180,000
Oliver Schacht, Ph.D.	159,363	0	0	0	12,750	146,613
<b>Total Executive Board</b>	<b>339,363</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>12,750</b>	<b>326,613</b>
Other option holders	756,303	30,000	41,250	158,003	0	587,050
<b>Total options</b>	<b>1,095,666</b>	<b>30,000</b>	<b>41,250</b>	<b>158,003</b>	<b>12,750</b>	<b>913,663</b>
Average exercise price (in EUR)	4.66	2.11	6.47	4.50	1.76	4.60
Average share price at exercise (in EUR)					1.88	

At December 31, 2007, a total number of 293,226 option rights was held by the former Executive Board members Dr. Kurt Berlin and Christian Piepenbrock, now included in the table above under "Other option holders".

The number of options issued as of December 31, 2008, includes 374,001 exercisable rights (December 31, 2007: 368,786).

*Terms of outstanding options:*

Term	Weighted-average exercise price in EUR as of Dec 31, 2007	Options issued as of Dec 31, 2007	Weighted-average exercise price in EUR as of Dec 31, 2008	Options issued as of Dec 31, 2008
2008	3.20	27,655		0
2009	4.53	21,772	4.53	17,472
2010	4.53	47,334	4.53	46,994
2011	4.58	246,005	4.53	234,200
2012	7.31	26,020	7.30	25,340
2013	5.57	121,880	5.48	112,660
2014	4.48	605,000	4.47	446,997
2015		0	2.11	30,000
<b>Total</b>		<b>1,095,666</b>		<b>913,663</b>

## Other Information

### 45. Information on the Executive Board and the Supervisory Board of the Company and their remuneration

Members of the Executive Board of the Company during the reporting year were:

- Geert Walther Nygaard, Berlin (D), Chief Executive Officer
- Dr. Kurt Berlin, Stahnsdorf (D), Chief Scientific Officer (until August 31, 2008)
- Christian Piepenbrock, Berlin (D), Chief Operating Officer (until April 30, 2008)
- Oliver Schacht, Ph.D., Seattle, WA (U.S.A.), Chief Financial Officer;  
Chief Executive Officer of Epigenomics, Inc.

In 2008, the total remuneration of the members of the Executive Board amounted to EUR 1,284 thousand (2007: EUR 1,344 thousand), comprising EUR 747 thousand in fixed compensation (2007: EUR 859 thousand), EUR 236 thousand in bonus payments (2007: EUR 383 thousand) and EUR 301 thousand in other compensation payments (2007: EUR 102 thousand). No stock options were granted to the members of the Executive Board in 2008 while in 2007, stock options with a fair value at granting date of EUR 514 thousand had been granted to the Company's Executive Board members.



Members of the Supervisory Board of the Company during the reporting year were:

- Prof. Dr. Dr. h.c. Rolf Krebs, Mainz (D), Chairman
- Prof. Dr. Dr. Uwe Bicker, Bensheim-Auerbach (D), Deputy Chairman
- Günther Frankenne, Berg/Neumarkt (D)
- Ann Clare Kessler, Ph.D., Rancho Santa Fe, CA. (U.S.A.)
- Heino von Prondzynski, Einsiedeln (CH)
- Prof. Dr. Günther Reiter, Pfullingen (D)

In 2008, total remuneration of the members of the Supervisory Board amounted to EUR 155 thousand (2007: EUR 158 thousand) plus out-of-pocket expenses amounting to EUR 29 thousand (2007: EUR 25 thousand).

Further details to the composition of the Executive Board and the Supervisory Board and their compensation in the reporting year can be found in the "Compensation Report" section of the Group management report 2008.

#### *46. Other financial obligations*

For the Epigenomics Group, other financial obligations arise from a total of two leases at the Berlin and Seattle locations:

- a) For the Berlin location at Kleine Präsidentenstrasse 1, there is a fixed-term lease with a term expiring on February 28, 2010. Until this date, a total rent of approximately EUR 380 thousand (undiscounted) has to be paid.
- b) For the Seattle location, there is a fixed-term lease with a term expiring on November 30, 2009. Until this date, a total rent of USD 440 thousand (undiscounted) has to be paid.

In the reporting period and in previous years, Epigenomics acquired numerous exclusive licenses to third-party intellectual property. This means that there are some obligations to pay minimum license fees in years to come. Additionally, Epigenomics has the obligation to reimburse most of those third parties for costs incurred in connection with the maintenance and the prosecution of the licensed rights. Those costs are mainly charges for patent attorneys or office actions and are difficult to forecast regarding their amounts and timing. The expected amount due to various licensors (including reimbursements for patent prosecution) stands at approximately EUR 675 thousand for the years 2009 and 2010. However, most of these agreements could be terminated by Epigenomics at short notice. There is only one case in which Epigenomics is under a fairly long-term binding obligation. However, this payment obligation will not exceed EUR 20 thousand per year.

Once Epigenomics starts to generate product revenue with third parties, which is generated with the help of this licensed intellectual property, then in some cases license fees that are above and beyond and which correspond to a percentage of such revenue must be paid to the licensors. Consequently, the potential amount of the obligations is difficult to quantify, since the significant share of the variable license fees is dependent on the type and composition of future revenue.

Due to contracts with third parties, at the balance sheet date, Epigenomics had payment obligations of EUR 80 thousand for services and goods to be received in 2009. Additional payment obligations of more than USD 2.1 million could arise from various contracts with providers of tissue samples in the course of the ongoing PRESEPT Study. However, as delivery dates and effective delivery quantities are to some extent uncertain, the future payments resulting from those contracts could also be significantly lower.

#### *47. Information on the auditors of the Company*

As in the previous years, UHY Deutschland AG had been chosen as the Company's auditing firm for the financial year 2008. During the reporting year, a total amount of EUR 142 thousand has been expensed for miscellaneous services of this auditing firm for Epigenomics AG. Details are shown in the following table:

in EUR thousand	2007	2008
Costs for annual audit	96	99
Costs for critical reviews of quarterly reports	27	28
Other confirmation and valuation services	176	15
<b>Total</b>	<b>299</b>	<b>142</b>

The costs disclosed for the annual audits are related to the audits on the individual financial statements of Epigenomics AG according to German GAAP as well as on the individual financial statements of Epigenomics, Inc. and on the consolidated financial statements for the Epigenomics Group, both according to IFRSs. Other confirmation services occurred partially for services in connection with the capital increase and partially in connection with granted projects and have in these latter cases been reimbursed by the sponsor.

#### *48. Statement of the Executive Board and the Supervisory Board of Epigenomics AG pursuant to Section 161 of the German Stock Corporation Act (Aktiengesetz) with respect to the German Corporate Governance Code*

In December 2008, the Executive Board and the Supervisory Board of the Company issued the declaration of conformity in accordance with Section 161 of the German Stock Corporation Act (Aktiengesetz). The declaration has been published on the Company's website ([www.epigenomics.com](http://www.epigenomics.com)) and can also be taken from the Group management report 2008.

#### *49. Information on other transactions with related parties*

At the reporting date, the Company's liabilities due to members of its Executive Board amounted to EUR 174 thousand (Dec 31, 2007: EUR 384 thousand) and the liabilities due to members of its Supervisory Board amounted to EUR 46 thousand (Dec 31, 2007: EUR 177 thousand).

After his retirement as Epigenomics's CSO in August 2008, Dr. Kurt Berlin entered into a consulting agreement with the Company for the calendar years 2008 and 2009. Under the terms of this agreement, in 2008, Dr. Berlin offered his expertise and services to the Company in scientific matters on 43 consulting days for a total amount of EUR 36 thousand. Additionally, he received a one-time bonus of EUR 40 thousand (net in each case). From his total remuneration an amount of EUR 56 thousand gross is shown as liability at December 31, 2008.

He serves as chairman of Epigenomics' Scientific Advisory Board and is continuing to advise Epigenomics on scientific, technological, licensing and IP-related matters as a consultant throughout 2008 and 2009 on ten days per calendar quarter. The consulting agreement can not be terminated before June 30, 2009.

In previous years, the Company had reported transactions with Epiontis GmbH as "related party transactions". As the Company's stake in Epiontis has been diluted repeatedly to now less than 13% and the Company simultaneously has lost all of its formerly already limited influence on Epiontis, the criteria for a related party status according to IAS 24.9 *Related Party Disclosures* are no longer met.

#### *50. Information on material events after the end of the reporting period*

For material nonadjusting events after the balance sheet date reference is made to the "Supplementary Report" section of the Group management report 2008.

#### *51. Cleared for publication*

These consolidated financial statements have been approved and cleared for publication by the Executive Board of the Company on February 27, 2009.

Berlin, February 27, 2009

The Executive Board

## Responsibility Statement

To the best of our knowledge, and in accordance with the applicable reporting principles, the consolidated financial statements give a true and fair view of the assets, liabilities, financial position and profit or loss of the Group, and the Group management report includes a fair review of the development and performance of the business and the position of the Group, together with a description of the principal opportunities and risks associated with the expected development of the Group.

Berlin, February 27, 2009

The Executive Board

## Auditors' Report

"We have audited the consolidated financial statements prepared by Epigenomics AG, Berlin, comprising the balance sheet, the income statement, statement of changes in equity, cash flow statement and the notes to the consolidated financial statements, together with the Group management report for the business year from January 1 to December 31, 2008. The preparation of the consolidated financial statements and the Group management report in accordance with IFRS, as adopted by the EU, and the additional requirements of German commercial law pursuant to § (Article) 315a Abs. (paragraph) 1 HGB and supplementary provisions of the articles of incorporation are the responsibility of the parent company's management. Our responsibility is to express an opinion on the consolidated financial statements and on the Group management report based on our audit.

We conducted our audit of the consolidated financial statements in accordance with § 317 HGB and German generally accepted standards for the audit of financial statements promulgated by the Institut der Wirtschaftsprüfer (Institute of Public Auditors in Germany–IDW). Those standards require that we plan and perform the audit such that misstatements materially affecting the presentation of the net assets, financial position and results of operations in the consolidated financial statements in accordance with the applicable financial reporting framework and in the Group management report are detected with reasonable assurance. Knowledge of the business activities and the economic and legal environment of the Group and expectations as to possible misstatements are taken into account in the determination of audit procedures. The effectiveness of the accounting-related internal control system and the evidence supporting the disclosures in the consolidated financial statements and the Group management report are examined primarily on a test basis within the framework of the audit. The audit includes assessing the annual financial statements of those entities included in consolidation, the determination of entities to be included in consolidation, the accounting and consolidation principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements and Group management report. We believe that our audit provides a reasonable basis for our opinion.

Our audit has not led to any reservations.

In our opinion, based on the findings of our audit, the consolidated financial statements comply with IFRS, as adopted by the EU, the additional requirements of German commercial law pursuant to § 315a Abs. 1 HGB and supplementary provisions of the articles of incorporation and give a true and fair view of the net assets, financial position and results of operations of the Group in accordance with these requirements. The Group management report is consistent with the consolidated financial statements and as a whole provides a suitable view of the Group's position and suitably presents the opportunities and risks of future development.

Furthermore, not intended to qualify our opinion, we point out that the financial statements are prepared on a going concern basis of the Group. The Executive Board derives the positive prognosis for the Group's continued existence from a detailed financial and earnings plan for the business years 2009 and 2010 with the result that the Group will most probably be able to continue its business activity during the present and coming business year, with adherence to the payment obligations.

In this regard, we refer to the explanations regarding financial risks in the consolidated management report, in particular to the section "Financial Opportunities and Risks" and "Outlook on financial situation". In consideration of the fresh liquid resources in the amount of EUR 5.2 million created by means of a capital increase before preparation of the consolidated financial statements in February 2009, the Group will be reliant on the allocation of fresh financial resources at the latest by the end of the business year 2010, as the resulting annual deficits in 2009 and 2010 will, according to plan, exceed the liquid resources on December 31, 2008."

Berlin, February 27, 2009  
UHY Deutschland AG  
Wirtschaftsprüfungsgesellschaft

(Lauer)  
Wirtschaftsprüfer

(Dr. Peters)  
Wirtschaftsprüferin

## Profit and Loss Statement 2008 of Epigenomics AG (according to HGB)

The Profit and Loss Statement of Epigenomics is prepared according to Section 275 Paragraph 2 of the German Commercial Code.

	2007 (EUR thousand)	2008 (EUR)
<b>Total income</b>	<b>4,439</b>	<b>4,179,551.15</b>
<b>Sales revenue</b>	<b>2,341</b>	<b>1,951,803.47</b>
<b>Changes in inventories</b>	<b>226</b>	<b>633,129.12</b>
<b>Other operating income</b>	<b>1,872</b>	<b>1,594,618.56</b>
<b>Cost of materials</b>	<b>-1,163</b>	<b>-1,531,935.92</b>
a) Expenses for raw materials, supplies and purchased goods	-944	-891,777.82
b) Expenses for purchased services	-220	-640,158.10
<b>Personnel costs</b>	<b>-5,306</b>	<b>-5,019,749.07</b>
a) Wages and salaries	-4,706	-4,457,570.70
b) Social security contributions	-600	-562,178.37
<b>Depreciation and amortization</b>	<b>-1,061</b>	<b>-2,340,413.06</b>
a) On tangible and intangible assets	-1,061	-2,340,413.06
<b>Other operating expenses</b>	<b>-12,030</b>	<b>-9,421,190.81</b>
<b>Other interest and similar income</b>	<b>903</b>	<b>976,340.77</b>
<i>thereof from affiliated companies</i>	210	262,118.14
<b>Write-down of securities held as current assets</b>	<b>-355</b>	<b>-491,530.00</b>
<b>Interest and similar expenses</b>	<b>-30</b>	<b>-30,001.93</b>
<b>Result from ordinary business activities</b>	<b>-14,603</b>	<b>-13,678,928.87</b>
<b>Net loss for the year</b>	<b>-14,603</b>	<b>-13,678,928.87</b>

## Balance Sheet of Epigenomics AG as of December 31, 2008 (according to HGB)

The Balance Sheet of Epigenomics is prepared according to Section 266 of the German Commercial Code.

<b>ASSETS</b>	Dec 31, 2007 (EUR thousand)	Dec 31, 2008 (EUR)
<b>A. Non-current assets</b>	<b>12,691</b>	<b>5,891,243.54</b>
<b>I. Intangible assets</b>	<b>3,445</b>	<b>1,844,366.68</b>
1. Franchises, trademarks, patents, licenses and similar rights and licenses to such rights	3,445	1,844,366.68
<b>II. Tangible assets</b>	<b>910</b>	<b>559,829.37</b>
1. Leasehold improvements	94	50,587.06
2. Technical equipments and machines	802	500,930.54
3. Other equipment, furniture and fixtures	13	8,311.77
<b>III. Financial assets</b>	<b>8,336</b>	<b>3,487,047.49</b>
1. Shares in affiliated companies	3,487	3,487,047.49
2. Loans to affiliated companies	3,849	0.00
3. Non-current securities	1,000	0.00
<b>B. Current assets</b>	<b>11,827</b>	<b>14,083,448.30</b>
<b>I. Inventories</b>	<b>347</b>	<b>967,560.19</b>
1. Raw materials, supplies and production materials	121	105,937.20
2. Work in progress	226	840,363.37
3. Finished products and goods	0	19,259.62
4. Prepayments	0	2,000.00
<b>II. Receivables and other current assets</b>	<b>1,676</b>	<b>1,241,491.91</b>
1. Trade accounts receivable	356	369,002.78
2. Other current assets	1,319	872,489.13
<b>III. Securities</b>	<b>3,370</b>	<b>2,285,920.00</b>
1. Other securities	3,370	2,285,920.00
<b>IV. Cash on hand and cash in banks</b>	<b>6,434</b>	<b>9,588,476.20</b>
<b>C. Prepaid expenses</b>	<b>306</b>	<b>208,062.37</b>
<b>Total assets</b>	<b>24,824</b>	<b>20,182,754.21</b>
<b>LIABILITIES AND SHAREHOLDERS' EQUITY</b>	Dec 31, 2007 (EUR thousand)	Dec 31, 2008 (EUR)
<b>A. Shareholders' equity</b>	<b>15,622</b>	<b>15,498,372.12</b>
<b>I. Subscribed capital</b>	<b>18,253</b>	<b>26,723,636.00</b>
<i>Conditional capital: € 4,089,326</i>	<i>1,431</i>	
<b>II. Capital reserves</b>	<b>3,690</b>	<b>2,453,664.99</b>
<b>III. Retained earnings</b>	<b>8,282</b>	<b>0.00</b>
1. Other retained earnings	8,282	0.00
<b>IV. Net loss for the year</b>	<b>-14,603</b>	<b>-13,678,928.87</b>
<b>B. Accruals and provisions</b>	<b>2,570</b>	<b>1,189,290.13</b>
1. Accruals and provisions for staff	325	298,921.96
2. Other accruals and provisions	2,245	890,368.17
<b>C. Payables</b>	<b>6,163</b>	<b>2,241,212.40</b>
1. Deferred income	313	494,350.00
2. Trade accounts payable	905	372,788.96
3. Liabilities due to affiliated companies	4,506	1,109,659.82
4. Other liabilities	439	264,413.62
<b>D. Deferred income</b>	<b>468</b>	<b>1,253,879.56</b>
<b>Total liabilities and shareholders' equity</b>	<b>24,824</b>	<b>20,182,754.21</b>

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## Glossar

- A Assay.** Chemical reactions that allow detection or quantification of substances or biomarkers in samples.
- B Biochip.** Microarray. Technology for the simultaneous measurement of multiple biomarkers.
- Biomarker.** A characteristic that is objectively measured and evaluated as an indicator of normal biologic or pathogenic processes or pharmacologic responses to a therapeutic intervention.
- Biopsy.** Sample of tissue from a living body extracted for diagnostic purposes.
- Bronchial Lavage.** Flushing of part so of the lung with a saline solution in order to wash out cells for inspection by a pathologist.
- Bronchoscopy.** Visual inspection of the airways with an endoscope
- C CE marking.** The CE marking is a mandatory safety mark on many products placed on the market in the European Economic Area (EEA). By affixing the CE marking, the manufacturer assures that the item meets the essential requirements of all applicable EU directives.
- Clinical proof of concept.** Demonstration that a diagnostic or therapeutic procedure (concept) can in principle be applied with success.
- Colonoscopy.** Invasive endoscopic examination of the large colon and the end section of the small bowel with a CCD camera or a fiber optic camera on a flexible tube passed through the anus. Frequently used to diagnose colorectal cancer and other colon diseases.
- Cross-licensing agreement.** Contract between two parties, that gives each party access to the patents of the other party.
- CT.** Computer tomography. Diagnostic imaging procedure that allows three-dimensional reconstruction of the body structure by use of serial x-ray images.
- D DNA.** Deoxyribonucleic acid. The carrier of genetic information for all complex organisms. DNA consists of four different bases bound to a sugar phosphate backbone: adenine (A), cytosine (C), guanine (G), thymine (T). The genetic information is encoded in the sequence of the four bases.
- DNA methylation.** Natural biological process by which a chemical methyl group is added stably to cytosine, one of the four bases of the DNA. DNA methylation serves the regulation of genes and the stability of the genetic information.
- E Endoscope.** Optical device for the inspection of body cavities and minimally invasive surgery. See also colonoscopy.
- Endoscopy.** Visual inspection of body cavities by use of an endoscope. See also colonoscopy.
- F False-positive rate.** Percentage of healthy individuals, falsely identified as sick due to the imprecision of a diagnostic procedure.
- FDA.** Food and Drug Administration. U.S. Government agency responsible for the approval of drugs and medical devices (e.g. IVD tests).
- FOBT.** Fecal Occult Blood Test. Test that detects blood in stool, a possible indicator of colorectal cancer.
- I Immunological FOBTs.** Tests, that detect human blood in a stool sample by the use of antibodies.
- Incidence.** Number of new cases per year in a specific disease indication.
- In vitro.** In a test tube.
- IVD.** In vitro diagnostic.
- IVD platform.** One or more instruments or devices by means of which an in vitro diagnostic test can be performed and the results analyzed.
- L LDT.** Laboratory-developed test. Assay for a biomarker developed within a diagnostic laboratory following certain quality standards (CLIA) that can be offered – with certain restrictions – by that laboratory in the U.S. without prior regulatory clearance by the FDA. Also known as “homebrew” test.
- Lead marker.** Strongest biomarker of a panel; further biomarkers are selected to increase performance of the panel but would be insufficient without the lead marker.
- M Methylated Sept9 DNA.** DNA of the Sept9 gene that at specific cytosine positions shows the pattern of methylgroups typical for colorectal cancer.
- “GSTP1.”** DNA methylation biomarker GSTP1, i.e. the use of methylated DNA of the GSTP1 gene as a biomarker.
- Milestone payment.** One-time payment between contractual parties upon reaching important goals within a collaboration.
- Molecular classification test.** Diagnostic test that, based on the analysis of DNA or RNA allows the more precise classification of a disease in clinically or pathologically relevant subgroups.
- Molecular diagnostics.** Diagnostics based on genetic and epigenetic information.
- Monitoring.** The tracing of potential recurrence or assessment of progression of a disease.
- “PITX2.** DNA methylation biomarker PITX2, i.e. the use of methylated DNA of the PITX2 gene as a biomarker.
- “SEPT9.** DNA methylation biomarker SEPT9, i.e. the use of methylated DNA of the SEPT9 gene as a biomarker.
- N Nonexclusive licensing model.** Strategy for the commercialization of patents by which several licensees in a geographic region obtain the rights to use one or more patents for the same application.
- O Oncology.** The branch of medicine that studies tumors (cancer) and seeks to understand their development, diagnosis, treatment, and prevention.
- P PCR.** Polymerase chain reaction. Method to multiply a section of the DNA in a test tube.
- PET.** Positron Emission Tomography. Diagnostic imaging procedure, by which the distribution of a slightly radioactive substance in an organism is visualized to map biochemical and physiological processes.
- PIPE financing.** Private Investment in Public Equity. Selling of shares from authorized capital to private investors without making a public offering and under exclusion of subscription rights. Under German law limited to up to 10% of the share capital within twelve months.
- Prognosis.** Prediction of how a patient’s disease will progress, and the chance of recovery.
- PSA.** Prostate-specific Antigen. A biomarker currently used to screen for prostate cancer.
- R Reagents.** Chemical substances needed for the performance of an assay.
- Reference laboratory.** Centralized diagnostic laboratory that provides testing services for routine and specialty applications.
- Research market.** Market for laboratory equipment and supplies not intended for therapeutic or diagnostic use in humans or animals.
- RNA.** Ribonucleic acid. Molecule build of similar components as DNA that mainly as an information carrier is involved in the use of genetic information to direct the synthesis of proteins. Compared to DNA, RNA is chemically and biologically considerably less stable.
- RT PCR.** Real-time PCR. PCR in which the amplification of a DNA segment is continuously measured.
- RUO.** Research-Use-Only. Label for products only intended for research applications. (also: research products)
- S Screening.** The systematic and preventive mass screening of an asymptomatic population for early detection of disease.
- Sensitivity.** The measure of a test’s ability to accurately detect the presence of a disease. For example, a sensitivity of 90% means that out of 100 patients which actually have the disease, on average 90 are correctly diagnosed.
- Specificity.** The measure for a test’s ability to exclude a disease if it is truly not present. For example, a specificity of 90% means that out of 100 healthy people ten are falsely identified as having the disease.
- T Test kit. Test reagent kit.** A set of reagents, consumables and processing instructions necessary to perform a diagnostic laboratory test.
- Test panel.** Combination of different biomarkers in a diagnostic test.
- Tumor.** A mass of excess tissue that results from abnormal cell division.
- V Validation.** Establishing documented evidence that a process or system, when operated within established parameters, can perform effectively and reproducibly and meet its predetermined specifications and quality attributes.

# Corporate Calendar 2009

## Annual Report 2008

Reporting period: January 1 – December 31, 2008  
Press Conference and Analyst Meeting  
in Frankfurt/Main  
Tuesday, March 31, 2009

## 3-Month Report 2009

Reporting period: January 1 – March 31, 2009  
Monday, May 11, 2009

## Annual General Shareholders' Meeting 2009 in Berlin

Monday, May 11, 2009

## 6-Month Report 2009

Reporting period: January 1 – June 30, 2009  
Tuesday, August 11, 2009

## 9-Month Report 2009

Reporting period: January 1 – September 30, 2009  
Tuesday, November 10, 2009

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# Opportunities and Outlook\* —

2009 / 2010 – First product launches, decisive clinical data, further strategic partners

## Colorectal cancer program

- First diagnostic laboratories in Europe and the United States expected to launch laboratory-developed tests for *m*SEPT9
- Our IVD industry partner Abbott launches the first IVD blood test for colorectal cancer in Europe
- PRESEPT Study demonstrates performance and health economic benefit of *m*SEPT9 testing in screening population

## Lung cancer program

- Further clinical data support clinical utility of our biomarkers in lung cancer screening and diagnosis
- We launch our first IVD product in Europe to aid the diagnosis of lung cancer

## Prostate cancer program

- Clinical opinion leaders and patients get access to our prognostic prostate cancer test in early access program
- We further leverage value of our prognostic biomarker *m*PITX2 through partnerships with IVD and pharma companies

## Partnering

- Further IVD development and commercialization partnerships for diagnostic products will solidify and grow future revenue stream
- Further R&D collaborations in personalized medicine with partners in pharma and biotech industries will leverage our expertise, biomarkers and technology through short-term revenue and long-term product opportunities

\*Forward looking statements; please note our legal disclaimer on page 125

