

BioCentury

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Volume 20 • Number 50 • Page A1 of 22

Regulation

Opioid REMS under gun

BioCentury This Week

Cover Story

Opioid REMS Under Gun — An FDA panel's thumbs-down vote on Zohydro ER challenges the agency's classwide opioid REMS, as well as what it should do with a product that met existing safety and efficacy standards.

Strategy

Puzzle Pieces — Teva's new management expects to achieve sustainable growth by globalizing key functions to change its cost structure, regionalizing its product offerings, and using BD to amass capabilities incrementally. [A5](#)

Russian Push — Takeda is building out Nycomed's infrastructure in Russia in preparation for expected reimbursement changes that would make the market more able to pay for innovator drugs. [A9](#)

Emerging Company Profile

Mining for Host Factors — Haplogen is screening haploid human cells to identify new host factors required for bacterial or viral infection, which it hopes will lead to anti-infectives with less potential for resistance. [A10](#)

Freezing Out AD — Alzinova's Alzheimer's vaccine targets AD-associated beta amyloid

oligomers, a target the company expects to yield a stronger protective immune response than other vaccine candidates. [A11](#)

Finance

Sinfully Good — Sofinnova Partners has made good money in three areas it says are scorned as "cardinal sins" among LPs: venture, life sciences and Europe. It's now unveiled its first fund with a focus on all three. [A12](#)

A Deep Well — Counting the \$275 million Infinity and Sarepta raised last week, biotech companies have pulled in more than \$1.7 billion in follow-ons this quarter, more than twice what was raised in 4Q11. [A14](#)

Ebb & Flow — Maple Leaf windfall for YM. Pain has enough money, thank you. Herkulean return from Pronova. Also: Alexza; Ariad; BG Medicine; Biotie; Celldex; Clavis; Oncolytics; Rigel; Acura; Isis; Somaxon, et al. [A16](#)

Featured links this week [A13](#)

Stock charts & tables [A22](#)

Company index [A8](#)



BioCentury 100™ Indicators

Week ended 12/14/12

PRICES	VOLUME
2940.63	702.7M shrs
up 1%	up 20%

By Michael J. Haas
Senior Writer

This month's negative FDA panel review of Zohydro ER from **Zogenix Inc.** turned into a referendum on the classwide REMS for extended-release and long-acting opioids the agency promulgated in July. Whether or not FDA approves the compound anyway will say a lot about how the agency plans to treat drugs in this class going forward.

The panel's votes present FDA with two dilemmas, one general to the drug class and one specific to Zohydro ER.

The broad dilemma is whether FDA should revisit the REMS and create a stronger one — after the agency had already declined to do so based on its view that this would put excessive limits on patient access to needed drugs.

The specific dilemma is whether it should follow the panel's recommendation. *See next page*

Pathway to Asia

The 10th Annual BIO Asia International Conference in Tokyo offers access to robust representation of companies from Asia.

Please see announcement following A22.

BioEquity Savings

Now's the time to capture early registration deals for the 14th Annual BioEquity Europe, convening in Stockholm. Please see A18.

This Week in SciBX

Translating Autism. — McGill researchers have used a small molecule to correct an eIF4E-mediated translational error and an associated autistic phenotype in mice. Please see SciBX Table of Contents on A7.

BioCentury
THIS WEEK

HEALTHCARE RESET

What's on the Table
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Please See Program Notes on A12

Emerging Company Profile

Haplogen: Mining for host factors

By Chris Cain
Senior Writer

Haplogen GmbH is screening haploid human cells to identify new host factors required for bacterial or viral infection, which it hopes will lead to the development of anti-infectives with less potential for resistance.

Haplogen was founded to commercialize a screening system developed in the lab of one of the company's scientific founders, Thijn Brummelkamp, at the **Whitehead Institute for Biomedical Research**.

In work published in *Science* in 2009, Brummelkamp and his team provided the first proof of concept that new host factors required for bacterial or viral infection could be identified by mutagenizing and screening haploid cells.

First the team used retroviral insertional mutagenesis to generate a library of gene knockouts in a chronic myelogenous leukemia cell line haploid for all chromosomes with the exception of chromosome 8. Then they exposed the collection to a variety of viruses and toxins, including influenza A virus and cytolethal distending toxin (CDT), which is produced by many bacterial gastrointestinal pathogens.

The screen identified transmembrane protein 181 (TMEM181) as a new host factor required for uptake of *Escherichia coli* CDT. It also identified solute carrier family 35 UDP-galactose transporter A2 (SLC35A2) and cytidine monophosphate N-acetylneuraminic acid synthetase (CMAS) as new host factors required for influenza A infection.

Brummelkamp improved the efficiency of the approach and also introduced high throughput sequencing in subsequent work describing the platform in *Nature Biotechnology* in 2011. This led to the identification of 12 human genes important for the toxic effects of four different CDTs.

More recently, Brummelkamp and academic collaborators used the platform to identify a host protein, Niemann-Pick disease type C1, required for cellular entry

Haplogen GmbH

Vienna, Austria

Technology: Haploid human somatic genetics for target identification

Disease focus: Infectious

Clinical status: Preclinical

Founded: 2010 by Thijn Brummelkamp, Giulio Superti-Furga, Sebastian Nijman, Georg Casari and Gustav Ammerer

University collaborators: Research Center for Molecular Medicine of the Austrian Academy of Sciences (CeMM)

Corporate partners: Evotec AG

Number of employees: 13

Funds raised: Undisclosed

Investors: Undisclosed

CEO: Georg Casari

Patents: None issued

by Ebola virus (see *SciBX: Science-Business eXchange*, Sept. 8, 2011).

Haplogen licensed the screening technology from the Whitehead and has exclusivity in the area of infectious disease. CEO Georg Casari told BioCentury the platform can be used to identify targets that he thinks have less potential for resistance than anti-infectives that act directly, and noted that some degree of safety is built into the screen.

"It is more difficult and rare for the virus to evade an agent that is acting on a host factor, and our platform can do two things at the same time — it can identify components that are vital to the virus, but it also excludes things that are vital to the cell," he said.

Casari added that Haplogen has made improvements to the published platform, and now can screen additional haploid cell lines with distinct cell types.

He said the demonstrated reliability of Haplogen's platform now has set it apart from competitors, which include **3-V Biosciences Inc.** 3-V is developing novel

antiviral therapeutics targeting host cell factors required for viral infection, but has not disclosed details of its technology.

Haplogen is also collaborating with the **Research Center for Molecular Medicine of the Austrian Academy of Sciences (CeMM)** to generate a bar coded collection of knockout cell lines that can be used in future studies.

In addition to his role as CEO, Casari is director of IP and technology transfer at CeMM, which provided seed funding to Haplogen. Brummelkamp is an adjunct principal investigator at CeMM, and in 2011 he moved from the Whitehead to the **Netherlands Cancer Institute** to become a group leader.

Last month, the company signed its first partnership, with **Evotec AG**, to discover and develop small molecule antivirals against an undisclosed target.

"We focus our internal team largely on the platform and on target discovery, and when it comes to capabilities like medicinal chemistry, we make use of external resources," Casari said. "This is why the partnership with Evotec makes a lot of sense for us, instead of duplicating our know-how, we focus on what we each do best."

He said Haplogen's screening platform has potential in other disease areas, including cancer and metabolic diseases. The company is looking for pharma partners to explore these indications.

Haplogen hopes to select its first lead compound series in the next year.

COMPANIES AND INSTITUTIONS MENTIONED

Evotec AG (Xetra:EVT), Hamburg, Germany

Haplogen GmbH, Vienna, Austria

The Netherlands Cancer Institute, Amsterdam, the Netherlands

3-V Biosciences Inc., Menlo Park, Calif.

Research Center for Molecular Medicine of the Austrian Academy of Sciences (CeMM), Vienna, Austria

Whitehead Institute for Biomedical Research, Cambridge, Mass.

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