Pharmaceutical BIOPROCESSING

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News

Highlighting the latest news in Pharmaceutical Bioproccessing

Sanofi to launch large-scale production of artemisinin

The pharmaceutical company has announced a collaboration with PATH to produce artemisinin using a pioneering semisynthetic bioprocessing method

Sanofi and PATH, a not-for-profit global health organization, are to launch the production of semisynthetic artemisinin at one of Sanofi's Italian sites. The companies plan to produce 35 tons of the compound in 2013, followed by 50–60 tons per year from 2014 onwards.

Artemisinin, a sesquiterpene endoperoxide, is a key component of artemisinin-based combination therapies, an important antimalaria therapeutic. The natural, plant-derived supply of this compound – isolated from the plant *Artemisia annua* – is unstable, which highlights the importance of establishing a steady supply chain of synthetically produced product.

President and CEO of PATH, Steve Davis, commented on their collaboration with Sanofi: "Taking lifesaving innovation to scale requires many things, but it begins with strong partnerships and keeping a close ear to what's most needed on the ground. That's why I'm extremely pleased we've partnered with Sanofi in the scale up of semisynthetic artemisinin, a key ingredient in the treatment for malaria."

The semisynthetic method that will be utilized in Sanofi's production line was initially developed by Jay Keasling (University of California, Berkeley, CA, USA). This research was funded by the Bill and Melinda Gates foundation in collaboration with Amyris Inc. and Sanofi with the aim of developing "a new commercial-scale alternative manufacturing process to produce a complementary source of artemisinin."

In the initial research, recently published online in *Nature*, Keasling describes how *Saccharomyces cerevisiae* can be genetically engineered to produce high quantities of artemisinic acid. Keasling and colleagues then present their method to convert artemisinic acid to artemisinin via a photochemical reaction.

The two processes – first the production of artemisinic acid through fermentation, followed by the synthetic transformation of this compound to artemisinin via photochemistry – will be carried out at two separate sites. The first stage will be executed by Huvepharma, in Bulgaria, and the second at Sanofi's Garessio site, in Italy.

Sanofi explain that the artemisinin will be produced using a "no-profit, no-loss

The editorial team welcomes suggestions for timely, relevant items for inclusion in the news. If you have newsworthy information, please contact Gino D'Oca, Managing Commissioning Editor

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production model", which should help maintain the low price of this therapeutic in developing countries. Davis commented on the importance of a steady and affordable

supply of high-quality artemisinin, stating that it is: "a critical part of PATH's efforts to ultimately eradicate malaria and advance health equity."

Sources: PATH Press Release: www.path.org/news/pr130411-ssart-launch.php; Paddon CJ, Westfall PJ, Pitera DJ et al. High-level semi-synthetic production of the potent antimalarial artemisinin. Nature 496(7446), 528-532 (2013).

CHO cell line shows potential in eluding apoptosis

In research recently published online in Biotechnology Progress, a group of researchers from Genentech (San Francisco, CA, USA) describe their research on a Bax/Bak-deficient CHO cell line. The cell line demonstrates potential as a host for the production of therapeutic proteins on an industrial scale.

The cell line has 5758585747w7w5878476858856868 designed been to 25887908t657662074070434246823789 avoid apoptosis, which 67-08457289 frequently observed in is cell lines producing large-scale amounts of therapeutic proteins. In their research, Andrew Snowden and colleagues describe a Bax/Bakdeficient CHO cell line that is more

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resistant to apoptosis - demonstrating the ability to withstand high concentrations of chemicals such as sodium butyrate, a known apoptosis-inducing agent. Such cells showed no reduction in titer, viability or growth. In addition, the team describe the cell line achieving higher titers than parental CHO lines - due to the ability to reach a higher cell density.

The researchers demonstrate that their cells have more mitochondria, which they suggest contributes to their growth rate. The authors conclude that the traits shown by the cells "render Bax- and Bakdeficient cells a potentially attractive host for production of therapeutic proteins at industrial scale."

Source: Misaghi S, Qu Y, Snowden A, Chang J, Snedecor B. Resilient immortals, characterizing and utilizing Bax/Bak deficient Chinese hamster ovary (CHO) cells for high titer antibody production. Biotechnol. Prog. doi:10.1002/btpr.1722 (2013) (Epub ahead of print).

Finding high-risk manufacturers: US FDA call for 'Decision Support Solution'

In a recent 'request for information', the US FDA has called for a system that will allow data mining to highlight pharmaceutical bioprocessing plants that are most likely to be producing unsafe products.

The FDA explains that inspections outside the USA increased by 10% last year, relying on inspectors from outside the country. As explained in the request for information document; they are looking for a system that can carry out "real-time evaluation, priority setting, and reporting to support decision making for the selection of facilities and sites for inspections". The plan is to establish a 'Drug Quality Data Domain' that would inform the Office of Scientific Investigations and Office of Manufacturing and Product Quality, who collectively decide which facilities to inspect.

The system would analyze data from various FDA resources; such as reports for good clinical practice, bioequivalence, risk evaluation, mitigation strategies, and pre- and post-approvals among others.

As the supply chain for pharmaceutical bioprocessing becomes more complex, becoming ever more global, it is more difficult for the FDA to monitor the safety of such products. This system should ensure that the greater risk plants are inspected first.

Source: US FDA. Request for Information/Sources Sought for the Implementation of a Decision Support Solution to Support Core Regulatory Work Processes: www.fbo.gov/index?s=opportunity&mode=form&id=dc038c0d0813ef885b5878a17a97f6a3&tab=core&_cview=1

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INDUSTRY NEWS

Companies to share expertise in production of antibody–drug conjugates

In a recent press release, Goodwin Biotechnology (GBI) and Coldstream Laboratories have announced their agreement to collaborate in developing and manufacturing biopharmaceuticals.

GBI is a contract manufacturing organization specializing in the production of antibody-drug conjugates, monoclonal antibodies and recombinant proteins. Coldstream Laboratories is a 'speciality manufacturer', producing sterile injectable drugs from their facility in Lexington (KY, USA) – with a focus on highly toxic compounds.

It has been agreed that GBI will use Coldstream's facility for "analytical testing, formulation, liquid or lyophilized fill and finish, storage and shipment of manufactured highly potent bioconjugates." Muctarr Sesay, GBI Vice President of Process Development, explained that this will allow the production of a wide range of their products: "These manufacturing activities may be performed for non-good manufacturing practice (GMP) proof-ofconcept and process development work, as well as manufacturing to support both GLP Tox and cGMP ... Our filling batch sizes will vary from tens of non-GMP vials for use in non-clinical, proof-of-concept studies to thousands of cGMP-compliant vials to enable human clinical trials."

Eric Smart, President and CEO of Coldstream Laboratories, commented on the collaboration: "Our FDA-inspected facility is well suited for manufacturing potent, cytotoxic products. Our skilled team of experts uses this highly sophisticated facility to safely and efficiently manufacture sterile, potent, drug products. This capability, coupled with the bioconjugation expertise of GBI, will help advance patient care through the delivery of sophisticated potent therapies." "This capability, coupled with the bioconjugation expertise of Goodwin Biotechnology, will help advance patient care through the delivery of sophisticated potent therapies."



Source: GBI Press Release: www.goodwinbio.com/GBI-Coldstream-PR-25Apr13

Company expands to include new UK-based cell banking facility

Fujifilm Diosynth Biotechnologies have recently announced the commissioning of a new mammalian cGMP cell banking facility at their Billingham site (UK). The facility will be available to their customers as either a stand alone service or part of a full development program.

Fujifilm Diosynth Biotechnologies produce a range of biopharmaceuticals, including recombinant proteins, monoclonal antibodies and larger molecules, using a range of production systems – from microbial and mammalian, to insect cell lines.

The company plan to commission another cGMP manufacturing facility on the same site, which will primarily use single-use technologies. This facility is expected to be 'on-line' at the end of 2013.

Steve Bagshaw, Fujifilm Diosynth Biotechnologies managing director, commented on this expansion: "This is the next step in our strategy to grow our services in the contract development and manufacturing organization field, becoming a world-class player across both microbial and mammalian cell culture platforms, offering a full life cycle support for our customers."

Source: Fujifilm News Release: Fujifilm Diosynth Biotechnologies commissions new cell banking facility at Billingham, UK Site: www.fujifilmdio-synth.com/pdfs-uploaded/fujifilm_cbf.pdf

All stories written by Alice O'Hare.