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Creating markets & marketing strategies

Newsletter

December 15, 2016

Dear Regina,

Welcome to BioMarketing Insight's monthly newsletter.

Last month I covered "The Economics of Pharmaceutical Pricing: The Supply Chain." If you missed last month's article, click here to read it. This month's newsletter will cover, The First Human to Receive the CRISPR, Gene Editing Therapy.

Read on to learn more about this topic and other current news. The next newsletter will be published in the new year on January 15, 2017.

We encourage you to share this newsletter with your colleagues by using the social media icons at the top, or by simply forwarding this newsletter or use the link at the bottom of this newsletter. Should you or your colleagues want to join my mailing list, click on the icon below or scan the QR code.

Please email me, Regina Au, if you have questions, comments or suggestions.

Sincerely,
Regina Au
Principal, New Product Planning/
Strategic Commercial Consultant
BioMarketing Insight

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What Are the Next Game Changing Drugs in Cancer Therapy?

I am pleased to announce that my article on "What Are the Next Game Changing Drugs in Cancer Therapy?" that covers immuno-oncology drugs (Checkpoint Inhibitors and CAR-T Therapy) has been published in Pharma IQ. To read the article, click here.

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Executive Judge at Suffolk University Entrepreneur Presentations

I was an executive judge for the Entrepreneurship program executive presentations at Suffolk University Business School on December 7, 2016. Students presented their analysis and recommendations for a company as if they were presenting to senior management in growing the business. As judges we critiqued their presentation and gave feedback.

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The First Human to Receive the CRISPR, Gene Editing Therapy

The race to be the first country to use the CRISPR, gene editing tested in humans is official. Last month, it was reported that Lu You, an oncologist at Sichuan University in Chengdu, China injected the first patient with a PD-1 knockout engineered T-cells, using the CRISPR-Cas9 for an aggressive form of metastatic non-small cell lung cancer, in a phase I dose escalation clinical trial at West China Hospital, Chengdu.

The trial will enroll a total of ten patients, each will receive either two, three or four injections. As a phase I trial, patients will be monitored for six months to determine the safety profile for any serious adverse effects. Dr. Lu's team will also monitor the patients beyond the six months to determine whether there is any benefit from the treatment.

"The technology to be able to do this is incredible," says Naiyer Rizvi of Columbia University Medical Center in New York City. Antonio Russo of Palermo University in Italy notes that antibodies that neutralize PD-1 have successfully put lung cancer in check, boding well for a CRISPR-enabled

attack on the protein. "It's an exciting strategy," he says. "The rationale is strong."

This past June, an advisory committee at the National Institutes of Health (NIH) approved a proposal to use CRISPR-Cas9 to help augment cancer therapies using a patient's T cells. The trial is also designed to test whether CRISPR is safe to use in a small number of people. It will be funded by a US$250-million immunotherapy foundation formed by former Facebook president Sean Parker. The University of Pennsylvania will manufacture the edited cells, and in addition, will recruit and treat patients along with other centers from California and Texas.

This trial will enroll 18 patients with various types of cancers and perform three CRISPR edits on them: 1) the first edit will insert a gene for a protein engineered to detect cancer cells and instruct the T cells to target them; 2) the second edit removes a natural T-cell protein that could interfere with this process; and 3) the third edit, a defensive one, will remove the gene for a protein that identifies the T cells as immune cells and prevent the cancer cells from disabling them. The researchers will then infuse the edited cells back into the patient. The trial is anticipated to start in 2017.

In November, a team from Salk Institute in California announced that they had partially restored vision to rats suffering a form of retinitis pigmentosa, a significant cause of human blindness, by correcting the defective gene as published in Nature.

The Salk scientists were able to efficiently edit non-dividing cells in the eye. CRISPR has previously been most effective in dividing cells such as those in the skin and gut but most cells in an adult mammal are non-dividing.

Silence Therapeutics, a UK company, has used CRISPR to add genes to mice, to produce new proteins in their liver for 200 days with no apparent adverse effects. Ali Mortazavi, chief executive, said the study showed that "in vivo" gene editing would be possible, as well as the "ex vivo" applications in which target cells are extracted, edited and put back into the body. The theory would be that clinicians would use genome editing for permanent genetic changes and use alternative RNA-based technologies for transient treatments.

The Unknowns

While this is cutting edge technology and very exciting in possibly curing diseases, there are still a number of issues that need to be addressed in order for this technology to be commercialized and avoid any long-term consequences that could result from genome editing.

The following issues need to be addressed:

1) Moral perspective: The scientific community around the world have discussed and are trying to address this issue. Here is the main topics of discussion from the Nuffield Council on Bioethics, in the UK:

1. Science as a moral enterprise - in the pursuit of scientific knowledge, that will benefit society by improving the conditions of human existence and the environment.
2. Intervening in the genome - it has significant and distinctive implications due to the role of the genome in determining biological processes and passing on changes to future generations.
3. Moral conservatism - concerns that deliberate human intervention to direct complex biological processes may go beyond conventional treatments for disease. Or that science and technologies such as genome editing are moving too quickly for processes of critical reflection (e.g. law, regulation, cultural practices) to keep pace.
4. Moral norms and human rights - this may prevent the use of the technology due to human rights or prevent state from intervening in the use of genome editing where there is no legitimate reason for doing so.
5. Welfare and risk - suggests a measurable set of consequences by which to judge and compare different proposed initiatives. The expected benefits of genome editing, the possible harms it may lead to, and the risks associated with not doing it, should be calculated in this risk. Where the possible consequences of an action may lead to serious and irreversible harm, a precautionary approach should be favored.
6. Social justice - The benefits and harms such as genome editing may not necessarily be distributed equitably among all people. Demographic factors may disproportionately affected how genome editing is used. Special consideration to possible negative effects that could cause discrimination, injustice or disadvantage in society needs to be addressed.
7. Governance and democracy - Many people want clear limits that distinguish between morally acceptable and unacceptable uses of genome editing, since everyone's perspectives and values can greatly

vary and affect people's judgment on these issues. Democratic procedures that take account of the range of views will have an important role to play in developing regulatory and practical ways forward.

2) Improving the CRISPR tool: CRISPR-Cas9 has tremendously advanced gene editing, but there are still some issue to iron out. Feng Zhang from the Broad Institute in Massachusetts, who also worked on the CRISPR/Cas9 system, discovered another enzyme Cpf1 that will help overcome some of the difficulties researchers have encountered by using a one strand system for a simpler design, using staggered cuts or "sticky end" for easier insertion of a new gene after the old one is removed, and when Cpf1 hones in on a gene, it actually makes the cut off to the side or farther down the DNA strand which could be "potentially useful" in preserving the target site for subsequent rounds of editing.

3) Scalability: The process of extracting, genetically modifying and multiplying cells is "a huge undertaking and not very scalable", says Rizvi. "Unless it shows a large gain in efficacy, it will be hard to justify moving forward." He doubts it will be superior to the use of antibodies, which can be expanded to unlimited quantities in the clinic.

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Closing Thoughts

Since the CRISPR technology has proven to be viable, this field has exploded with practically everyone using this technology to edit genes involved with various diseases and the fastest that anyone has gotten this technology into humans for clinical trials. It's a very competitive race as to who will be the first to successfully cure diseases using this method which will go down in history as being one of the most disruptive technology.

But before, we get too far ahead, the moral and safety issues both short and long-term as discussed above still needs to be solidified before anything gets out of control and major restrictions hinders the

advancement of this technology. Proceed with caution is always the best policy.

More research is needed to address the issues with the CRISPR technology, in making it a more precise tool both editing and avoiding on- and off-target consequences as in the example with CRISPR- Cpf1. We will get there sooner than other technologies.

Scalability is always an issue with these types of technology similar to CAR-T cells. Here, combination therapy maybe very useful such as checkpoint inhibitors, which are more scalable and you may want a drug that is transient with inhibiting T-cells that interfere with engineered protein for a limited period of time. The concern for permanent consequences decreases.

This is a very exciting time and glad I'm here to witness it. I will continue to report the progress as it unfolds. Should you have any questions, feel free to email me here.

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