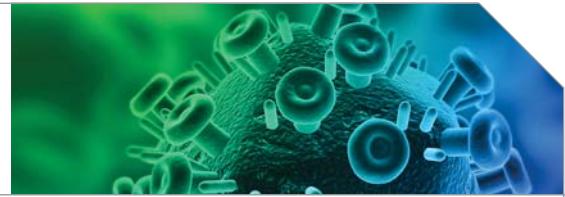


Emory Case Study

HIV/Aids drugs



In the battle against HIV/AIDS and other deadly viruses, Emory University researchers are on the frontlines. Emory professors and researchers, Doctors Dennis Liotta, Raymond Schinazi and Woo-Baeg Choi, co-developed two of the major drugs in the HIV/AIDS arsenal: 3TC and FTC. Emory University, on their behalf, applied for and received patents for both of these drugs. These break-through discoveries, made in the early 1990s, are used by approximately 80% of all HIV/AIDS patients who are receiving treatment.

These wonder drugs became the subject of litigation and patent disputes until an out-of-court settlement put all of the issues to rest. Emory University supported their researchers and went to extraordinary lengths to protect their Intellectual Property by financing millions of dollars of legal support required. As a result of Emory's efforts, they were able to retain their Intellectual Property and their researchers were able to continue their life's work of finding progressive treatments, and hopefully a vaccine and cure for HIV/AIDS.

DISPUTE OVERVIEW

3TC was the subject of duplicate patent claims. Both BioChem Pharmaceuticals and Emory University developed very similar technology, lamivudine, also known as 3TC. BioChem had won the international patent race for 3TC, based on being the first to file, which is the determining factor for Intellectual Property ownership. In the U.S. however, based on the first to invent rules, Emory was the rightful owner of domestic patent rights to 3TC. BioChem had licensed their international patents for 3TC to British drug maker, Glaxo who then attempted to invalidate Emory's U.S. patent rights.

FTC had initially been licensed to Burroughs Wellcome and Triangle Pharmaceuticals, a company founded by one of the inventors of FTC, both of whom initiated clinical trials of the drug. Shire Pharmaceuticals also later licensed FTC from Emory after it lost a patent dispute with the University. Burroughs Wellcome was still in the clinical trial phase of FTC when Glaxo acquired the company. As part of the acquisition, Glaxo returned the license of FTC to Emory in favor of their pursuit of 3TC as an HIV treatment.

During the trial period and prior to the merger, Burroughs Wellcome had filed patents to treat the Hepatitis B virus with FTC. Emory had previously filed in the U.S. for the Hepatitis B treatment and filed suit against Glaxo, on the basis that Burroughs Wellcome had misappropriated Emory's inventors' property and that the intellectual property that Burroughs Wellcome had used for their patent was not their own. Glaxo also was refusing to return to Emory the clinical trial data for studies conducted under the Wellcome license to FTC.

Resolution

After six years of legal debate involving upwards of 40 attorneys at one point in the trial, the lawsuit and counterclaim were settled out of court.

- Glaxo received an undisclosed payment in exchange for granting exclusive worldwide rights to Emory and Triangle for the test data and Intellectual Property related to FTC.
- Emory retained the rights to both 3TC and FTC, thereby securing the intellectual property of their inventors they had sought all along to protect.
- Glaxo and Shire obtained exclusive license from Emory to 3TC.
- Triangle Pharmaceuticals was able to keep its license to FTC, which is now commercialized by Gilead Sciences as a result of their purchase of Triangle.

As a result of Emory University's involvement and support of its researchers, its Intellectual Property is intact, their researchers are still happily in their employ, they have functional, ongoing relationships with their defendants and counterclaimants and are able to facilitate and cultivate continued research that is impacting lives both in the U.S. and worldwide. Emory University continues to be a recognized leader in worldwide HIV/AIDS research, with more than 100 faculty members drawn from diverse departments contributing to Emory's Center for AIDS Research.



Innovation And Patent Details

FTC and 3TC are used as part of the treatment plan for most HIV/AIDS sufferers and the World Health Organization (“WHO”) recommends the use of either of these drugs as part of a first-line treatment regimen. These drugs are part of a class known as Nucleoside Reverse Transcriptase Inhibitors (“NRTIs”) that help prevent or delay the HIV virus from replicating and infecting other cells. In combination with other HIV treatment drugs, they help reduce drug-resistance, bolster the body’s immune activity and can help slow the rate of other infections that prey on those who are immune deficient.

INVENTION/INNOVATION NAME

3TC (lamivudine) - marketed as Epivir®, Epivir HBV®

FTC (emtricitabine) - marketed as Emtriva®

INSTITUTION WHERE INVENTION/INNOVATION WAS DEVELOPED

Emory University

NAME(S) OF INVENTOR(S)/INNOVATOR(S) – TITLE – ADVANCED DEGREES HELD

DENNIS LIOTTA, PhD: Department of Chemistry, Chair;
Vice President for Research, Emory University

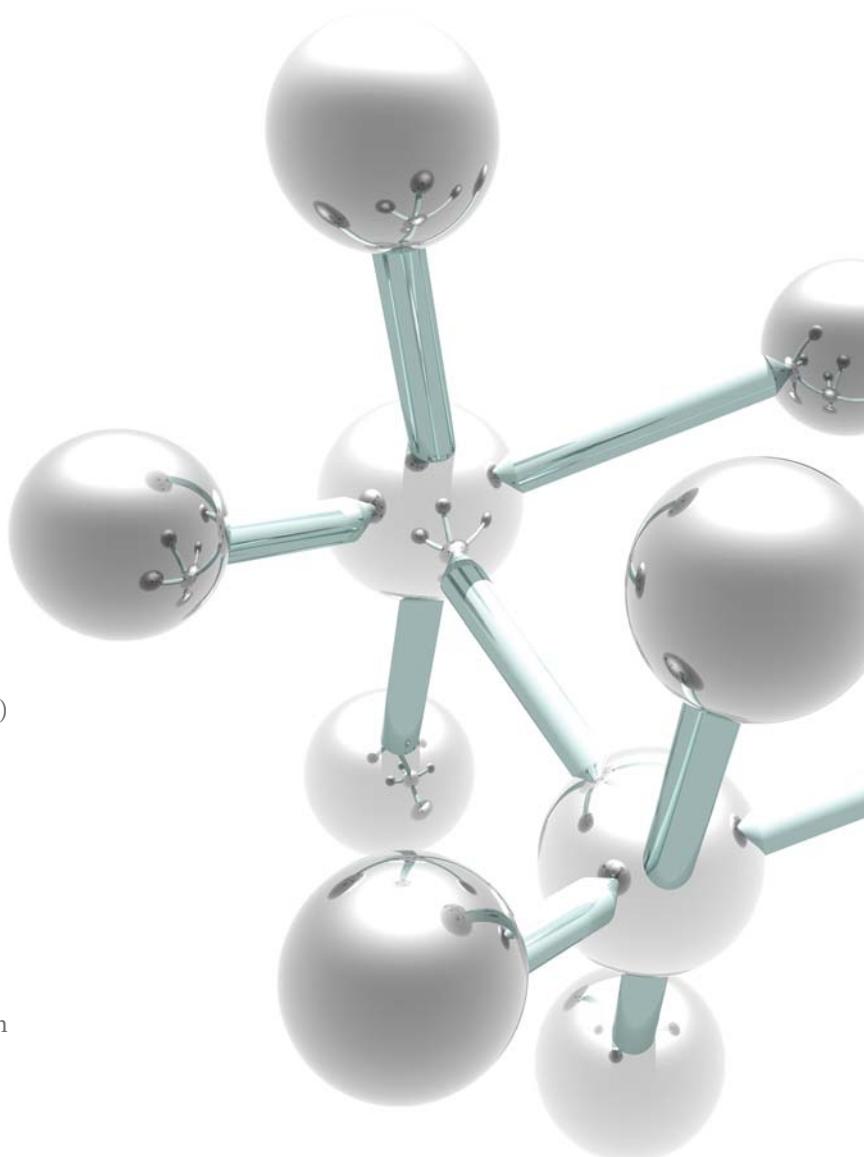
RAYMOND SCHINAZI, PhD: Professor of Pediatrics
and Chemistry; Director, Emory University Laboratory of
Biochemical Pharmacology, Department of Pediatrics

WOO-BAEG CHOI, PhD: Post-Doctorate Researcher, Emory
University (at time of patent); Founder, FOB Synthesis (current)

REVENUE GENERATED (IF APPLICABLE)

FTC: Gilead has seen combined revenues from the individual sale of Emtriva® and the sale of Truvada® (a fixed dose combination of Emtriva® and Viread®) of over \$3 billion since it acquired the license to Emtriva® as part of its acquisition on Triangle Pharmaceuticals.

3TC: Glaxo SmithKline has seen revenues for Epivir® grow from \$315 million in 1996 to nearly quadruple that a decade later resulting in annual sales in excess of \$1.1 billion.



Innovation And Patent Details Continued

PATENT NUMBER(S), DATES ISSUED, PATENT HOLDER'S NAME

[Emory Patents: 3TC]

PATENT 5,204,466: Method and compositions for the synthesis of BCH-189 and related compounds; the present invention relates to a method of preparing BCH-189 and various analogs of BCH-189 from inexpensive precursors with the option of introducing functionality as needed. This synthetic route allows the stereoselective preparation of the biologically active isomer of these compounds, .beta.-BCH-189 and related compounds. Furthermore, the stereochemistry at the nucleoside 4' position can be controlled to produce enantiomerically-enriched .beta.-BCH-189 and its analogs.

Filed: February 1, 1990

Inventors: Dr. Dennis C Liotta, Dr. Woo-Baeg Choi

Assignee: Emory University

Commercial Name: Epivir®

PATENT 5,539,116: Method and compositions for the synthesis of BCH-189 and related compounds; the present invention relates to a method of preparing BCH-189 and various analogs of BCH-189 from inexpensive precursors with the option of introducing functionality as needed. This synthetic route allows the stereoselective preparation of the biologically active isomer of these compounds, .beta.-BCH-189 and related compounds. Furthermore, the stereochemistry at the nucleoside 4' position can be controlled to produce enantiomerically-enriched .beta.-BCH-189 and its analogs.

Filed: February 10, 1993

Inventors: Dr. Dennis C Liotta, Dr. Woo-Baeg Choi

Assignee: Emory University

Commercial Name: Epivir®

[Emory Patents: FTC]

PATENT: 5,210,085: Method for the synthesis, compositions and use of 2'-deoxy-5-fluoro-3'-thiacytidine and related compounds; the present invention relates to a method of preparing the antiviral compounds 2'-deoxy-5-fluoro-3'thiacytidine (FTC) and various prodrug analogues of FTC from inexpensive precursors with the option of introducing functionality as needed; methods of using these compounds, particularly in the prevention and treatment of AIDS; and the compounds themselves. This synthetic route allows the stereoselective preparation of the biologically active isomer of these compounds and related compounds.

Filed: February 22, 1991

Inventors: Dr. Dennis C Liotta, Dr. Raymond F Schinazi, Dr. Woo-Baeg Choi

Assignee: Emory University

Commercial Names: Coviracil®, Emtriva®

PATENT: 5,814,639: Method for the synthesis, compositions and use of 2'-deoxy-5-fluoro-3'-thiacytidine and related compounds; The present invention relates to a method of preparing the antiviral compounds 2'-deoxy-5-fluoro-3'thiacytidine (FTC) and various prodrug analogues of FTC from inexpensive precursors with the option of introducing functionality as needed; methods of using these compounds, particularly in the prevention and treatment of AIDS; and the compounds themselves. This synthetic route allows the stereoselective preparation of the biologically active isomer of these compounds and related compounds.



Filed: February 16, 1993

Inventors: Dr. Dennis C Liotta, Dr. Raymond F Schinazi, Dr. Woo-Baeg Choi

Assignee: Emory University

Commercial Names: Coviracil®, Emtriva®

[Biochem Patents]

PATENT 5,047,047: 2-substituted-5-substituted-1,3-oxathiolanes with antiviral properties; methods and compositions for preventing or treating human immunodeficiency virus (HIV) infections characterized by 2-substituted-5-substituted-1,3-oxathiolanes.

Filed: February 8, 1989

Inventors: Dr. Bernard Belleau, Dr. Nghe Nguyen-Ba

Assignee: BioChem International

PATENT 5,151,426: 2-substituted-5-substituted-1,3-oxathiolanes with antiviral properties; methods and compositions for preventing or treating human immunodeficiency virus (HIV) infections characterized by 2-substituted-5-substituted-1,3-oxathiolanes.

Filed: June 17, 1991

Inventors: Dr. Bernard Belleau, Dr. Nghe Nguyen-Ba

Assignee: BioChem International

PATENT 5,466,806: Processes for preparing substituted 1,3-oxathiolanes with antiviral properties; Disclosed are processes for preparing compounds of the formula (I) and pharmaceutically acceptable salts or esters thereof: ##STR1## wherein R.sub.2 is a purine or pyrimidine base or an analogue

or derivative thereof; and Z is S, S.dbd.O or SO.sub.2. The invention also relates to intermediates of use in the preparation of these compounds.

Filed: March 29, 1993

Inventors: Dr. Bernard Belleau, Dr. Tarek Mansour, Dr. H.L. Allan Tse, Colleen A. Evans, Dr. Haolun Jin, Dr. Boulos Zacharie, Dr. Nghe Nguyen-Ba

Assignee: BioChem International

PATENT 5,684,164: Processes for preparing substituted 1,3-oxathiolanes with antiviral properties; Disclosed are processes for preparing compounds of the formula (I) and pharmaceutically acceptable salts or esters thereof: ##STR1## wherein R.sub.2 is a purine or pyrimidine base or an analogue or derivative thereof; and Z is S, S.dbd.O or SO.sub.2. The invention also relates to intermediates of use in the preparation of these compounds.

Filed: June 6, 1995

Inventors: Dr. Bernard Belleau, Dr. Tarek Mansour, Dr. H.L. Allan Tse, Colleen A. Evans, Dr. Haolun Jin, Dr. Boulos Zacharie, Dr. Nghe Nguyen-Ba

Assignee: BioChem International

Emory University professors, Dr. Dennis Liotta and Post-Doctorate Researcher Woo-Baeg Choi developed the break-through HIV treatment 3TC. Although not credited on the 3TC patents (466 & 166), Dr. Raymond Shinazi was actually the one who envisioned the idea to synthesize BCH-189. Shinazi later became a hands-on collaborator with the development of FTC. These break-through discoveries, made in the early 1990s are used by approximately 80% of all HIV/AIDS patients who are receiving treatment. Emory University, on their behalf, applied for and received patents for 3TC and FTC.

Both FTC and 3TC went through legal skirmishes to preserve the Emory inventors' rights in their work and in support of their researchers, Emory University financed millions of dollars for the legal support required.

Dispute Details

FTC CONTROVERSY

FTC is actually a fluorinated version of 3TC and is less expensive to produce than other HIV/AIDS therapies.

FTC was another result of the improvement process of the BHC-189 compound and had initially been licensed to Burroughs Wellcome and Triangle Pharmaceuticals, a company founded by one of the inventors of FTC, both of whom commenced clinical trials of the drug. Shire Pharmaceuticals also later licensed FTC from Emory after it lost a patent dispute with the University.



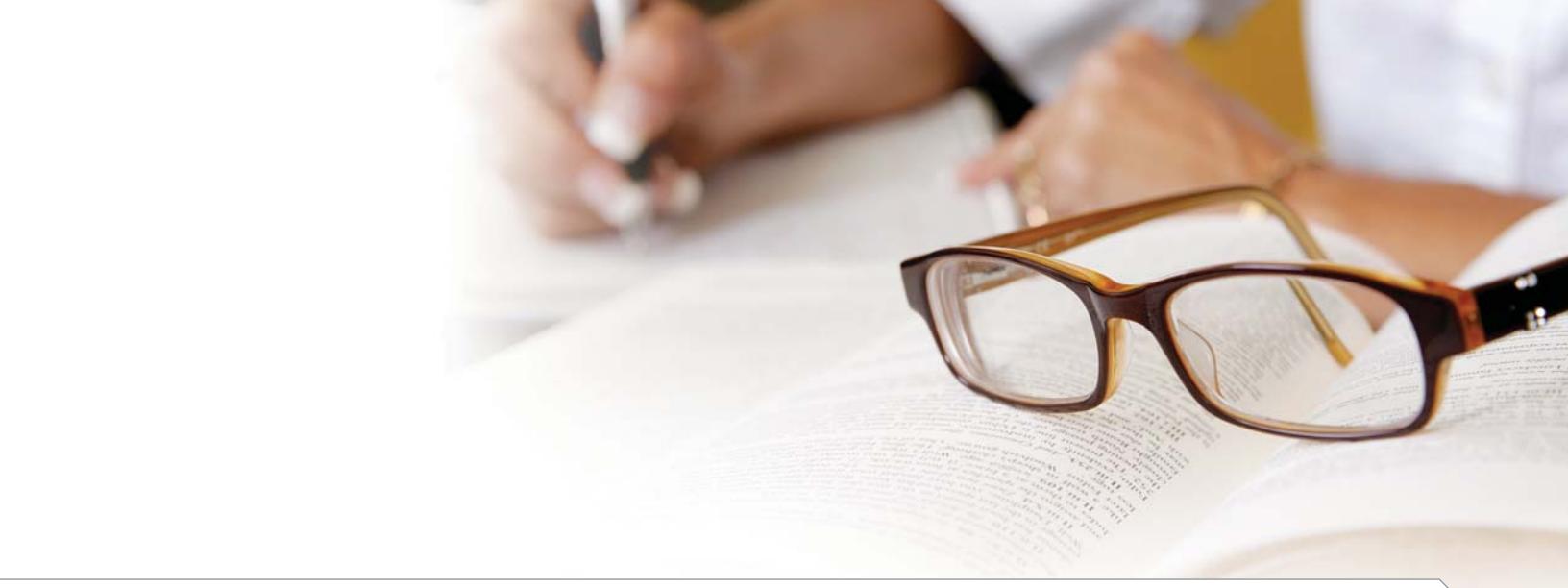
Burroughs Wellcome was still in the clinical trial phase of FTC when the company was acquired by Glaxo. As part of the merger, Glaxo returned the license of FTC back to Emory, in favor of their pursuit of 3TC. During the trial period, prior to the merger, Burroughs Wellcome had filed patents to treat the Hepatitis B virus with FTC. Part of Glaxo's purpose in the merger was to acquire Wellcome's patent portfolio.

Emory had prior filed in the U.S. for the Hepatitis B treatment and filed suit against Glaxo, on the basis that Wellcome had misappropriated Emory's inventors' property and that the intellectual property that Burroughs Wellcome had used for their patent was not their own. Glaxo also was refusing to return to Emory the clinical trial data for studies conducted under the Wellcome license to FTC.

3TC CONTROVERSY

Both BioChem Pharmaceuticals and Emory University developed very similar technology, lamivudine, also known as 3TC, which was an improved synthesis of the BHC-189 compound. BioChem had won the international patent race for 3TC, based on being first to file, which is the determiner for international intellectual property ownership. In the U.S. however, based on first to invent rules, Emory was the rightful owner of domestic patent rights to 3TC. BioChem had licensed their international patents for 3TC to British drugmaker, Glaxo who then attempted to invalidate Emory's U.S. patent rights.

Importantly, during the litigation process, Emory did not seek an injunction to stop sales of the life-prolonging drug, not wanting to impact any HIV/AIDS sufferers while they pursued protection of the rights of their inventors.



UNIVERSITY INVOLVEMENT

Early on, Emory and its researchers recognized the importance of HIV/AIDS research. Research was conducted in different departments all over the campus prior to 1997, when the Emory Center for AIDS Research began to integrate efforts from all corners of the University, encourage interdisciplinary research and raise the profile of the study of HIV/AIDS.

Emory understood the significance of the break-through innovations developed by their researchers, and went to great lengths, financial and otherwise, to preserve their inventors' rights in their intellectual property. When called upon, Emory aggressively and proactively defended its researchers, utilizing the legal system as well as the tenets of the U.S. Patent Office.

LEGAL FILINGS/PROCEEDINGS

Emory University v Glaxo Wellcome, Inc., et al 7/23/96 Counter Claims by Glaxo Wellcome & BioChem Pharmaceuticals v Emory University

Plaintiff Assertions: Emory filed suit against Glaxo Wellcome and BioChem Pharma for patent infringement.

Damages Sought: Unspecified

Filed: July 23, 1996

Defendant Assertions: Glaxo, et al fought to establish BioChem's patent rights in the U.S., despite BioChem's Canadian location. For research conducted outside of the U.S., specific deadlines for patent filing exist.

Counterclaim: Glaxo's counterclaim was similar to its defense, based on their claims of the precedence of BioChem's patents and claimed Emory's patent is invalid.

AWARDS/LEGAL RULINGS

After six years of legal debate involving upwards of 40 attorneys at one point in the trial, the lawsuit and counterclaim were settled out of court. As a result:

- Emory and Triangle were granted exclusive worldwide rights for the test data and Intellectual Property related to FTC. Emory retained the rights to both 3TC and FTC, thereby securing the Intellectual Property of their inventors they had sought all along to protect.
- Glaxo and Shire obtained exclusive license from Emory to 3TC.
- Triangle Pharmaceuticals was able to keep its license to FTC, which is now commercialized by Gilead Sciences as a result of their purchase of Triangle.
- Glaxo received an undisclosed payment from Emory and Triangle

PERTINENT DOCUMENTS

None of the case filings related to this case are accessible, and the parties involved kept the settlement of the dispute confidential.

IMPLICATIONS OF CASE

Although Emory University had to be prodded initially to pursue patents for the discoveries of Liotta, Schinazi and Choi, once they were onboard, they remained fully committed to what would turn out to be six long, expensive years of legal wrangling.

When the patent disputes began, Emory could not have known whether or not they would emerge victorious, but they have been amply rewarded for their diligence with a half-billion dollar royalty buyout from Gilead, as well as an ongoing royalty stream from 3TC sales by Glaxo SmithKline. By siding with their inventors and staying the course, Emory was vindicated on all fronts and its researchers were able to continue their work to eradicate HIV/AIDS on a global scale.

Analysis

STATEMENTS FROM INVENTORS

“Everyone was intrigued but skeptical about our work - no one realized the importance of what we had found, the NIH didn’t believe us – even my own administration didn’t believe us. We pushed Emory University very hard to file a patent to protect these inventions. Emory finally did, and received the rewards less than 10 years later.”

- Dr. Raymond Schinazi

“Suddenly, we had an incredibly versatile method for making these compounds and we could run through a study very quickly, while our friends in industry who were trying to move these same compounds forward were slugging it out and having a very difficult time.”

- Dr. Dennis Liotta

In contrast, IP Advocate’s case studies of Restasis® at the University of Georgia, extra-cellular matrix at Purdue and the PET/CT scanner at the University of Pittsburgh show what can happen when a university is at odds with their inventor. The University of Georgia’s preference to side with a licensee instead of their researcher resulted in a loss estimated in the hundreds of millions of dollars. Purdue lost on appeal, pocketed no damages and lost an invaluable researcher whose work continues to change the world. The University of Pittsburgh spent millions on a legal dispute with their inventor and came away with nothing but a smear on their reputation.

Emory University’s conduct in this case is reflected in its results: their intellectual property is intact, their researchers still happily in their employ, they have functional, ongoing relationships with their defendants and counterclaimants and are able to facilitate and cultivate continued research that is impacting lives both in the U.S. and worldwide.

FUTURE ACTIVITY ANTICIPATED

By 2006, the World Health Organization estimated there were more than 40 million people around the world living with HIV/AIDS, 25 million of which are using a daily drug therapy pioneered by the Emory researchers.

Emory University continues to be a recognized leader in worldwide HIV/AIDS research, with more than 100 faculty members drawn from diverse departments contributing to Emory’s Center for AIDS Research. The large financial reward reaped by Emory and the inventors has been reinvested in a large part, by all parties, into HIV/AIDS research.

- Emory invested in a Global Health Institute, a new chemistry building, additional lab space, science programs for undergraduates, scholarships for science majors and additional faculty.
- Dr. Liotta has formed iThemba, from the Zulu word “hope”, a drug discovery company based in South Africa, which he says is a “natural hotbed for AIDS research”.
- Dr. Schinazi serves as director of the Virology/Drug Discovery Core at Emory’s Center for AIDS Research (CFAR) where he oversees over 100 researchers working toward both a cure and preventative measures for HIV/AIDS.

Both Dr. Liotta and Dr. Schinazi still serve as professors and researchers at Emory University.