

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

TET SYSTEMS GMBH & CO. KG,

Plaintiff,

v.

ISIS PHARMACEUTICALS, INC.,

Defendant.

Civil Action No. _____

JURY TRIAL DEMANDED

COMPLAINT FOR PATENT INFRINGEMENT AND JURY DEMAND

Plaintiff TET Systems GMBH & Co. KG (“TET” or “Plaintiff”), by and through its undersigned counsel, Gibbons P.C., as for its Complaint against Defendant Isis Pharmaceuticals, Inc. (“Isis” or “Defendant”), alleges as follows:

OVERVIEW

1. TET was founded by prominent academic researchers, two of whom -- Dr. Hermann Bujard and Dr. Manfred Gossen -- invented and patented a system to modify cells for replicating viruses.
2. Using the invention made by Dr. Bujard and Dr. Gossen, higher cells and entire organisms can be used as hosts in assays, or screening tests, that control target gene expression via external stimuli.
3. In particular, cell-based screening assays can be useful in discovering and profiling the activity of chemical compounds versus medically-relevant targets, including, for example, antiviral activity against the Hepatitis virus.

4. TET's patented technology has proven to be so commercially valuable that academic institutions, pharmaceutical companies and other drug development companies worldwide, of varying sizes, license its use from TET.

5. Indeed, ~85% of the world's leading pharmaceutical companies license TET's patented technology, and its broad usage is demonstrated by more than 9,000 publications in peer-reviewed journals.

6. Drs. Bujard and Gossen and the TET System have been recognized in numerous peer-reviewed scientific journals throughout the world.

7. TET brings this action for patent infringement under 35 U.S.C. § 271 *et seq.*, as a result of Isis' unauthorized and willful use of TET's patented technology.

THE PARTIES

8. TET is a corporation organized and existing under the laws of Germany, having its principal place of business at Im Neuenheimer Feld 582, 69120 Heidelberg, Germany.

9. TET is the owner, by assignment, of all rights, title and interest in Drs. Bujard and Gossen's inventions, including all rights, title and interest in United States Patent No. 5,464,758, entitled "Tight Control of Gene Expression in Eucaryotic Cells by Tetracycline-Responsive Promoters" ("the '758 Patent") and United States Patent No. 6,914,124 entitled "Tetracycline-Regulated Transcriptional Activator Fusion Proteins" ("the '124 Patent") (collectively referred to as the "TET System").

10. On information and belief, Isis is a corporation organized and existing under the laws of Delaware, having its principal place of business at 2855 Gazelle Court, Carlsbad California, 92010.

JURISDICTION AND VENUE

11. This Court has original jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

12. This Court has personal jurisdiction over Isis by virtue of, *inter alia*, Isis' continuous and systematic business contacts with the State of Delaware, including Isis' incorporation in Delaware, its partnerships with other pharmaceutical and biomedical companies incorporated in Delaware, and its extensive intellectual property sale and licensing programs as described on its website as generating over \$400 million to date involving, on information and belief, companies including other Delaware corporations.

13. Venue is proper in this district under 28 U.S.C. §§ 1391(b), 1391(c) and 1400(b).

THE TET SYSTEM

14. The '758 Patent was duly and legally issued by the United States Patent and Trademark Office on November 7, 1995. A copy of the '758 Patent is attached hereto as Exhibit 1.

15. The '124 Patent was duly and legally issued by the United States Patent and Trademark Office on July 5, 2005. A copy of the '124 Patent is attached hereto as Exhibit 2.

16. Claims of the '124 Patent cover, *inter alia*, certain fusion proteins which activate transcription.

17. Claims of the '758 Patent cover, *inter alia*, a two component system consisting of hybrid polynucleotide molecules encoding a transactivator fusion protein and a transcription unit, which is responsive to the transactivator fusion protein.

18. When polynucleotide molecules encoding the fusion protein and the responsive transcription unit, respectively, are inserted into suitable vectors and transfected into a cell, they

can provide accurate and reproducible control of expression of a gene of interest using tetracycline or a tetracycline analogue as the controlling effector molecule.

19. This allows users to utilize that cell and its progeny to screen new drug compounds.

20. The HepAD38 cell line is a cell line within the scope of the claims of the '758 Patent, as described in paragraphs 17-19 above.

21. Claims of the '758 Patent also cover, *inter alia*, a method of using the cell transfected with a vector containing the hybrid polynucleotide molecule in a tetracycline or a tetracycline analogue medium as a means of controlling gene expression.

22. This enables users to determine the activity of compounds in the presence of stimuli, on the activity of viral proteins, required for replication and/or pathogenicity.

23. Using the HepAD38 cell line is within the scope of the claims of the '758 Patent, as described in paragraphs 21-22 above.

24. Claims of the '758 Patent further cover, *inter alia*, a kit that provides the novel reagents of the invention for convenient use by companies to set up an assay system useful to identify the activity of compounds to evaluate their potential use as drugs.

25. The TET System has been recognized in the scientific literature as a broadly and successfully applied system for controlled gene expression in eukaryotes, i.e., organisms made up of cells that possess a membrane-bound nucleus containing genetic material.

26. TET's novel technology allows users to control the activity of a target gene both *in vivo* and *in vitro*. The TET System has been applied in cultured cells, as well as in a wide spectrum of organisms, from animals and plants to various unicellular systems.

27. The advantages of the TET System have provided scientists with new insights into complex biological processes of development, disease and behavior.

28. One example involves cell lines in which the Hepatitis B viral (“HBV”) genome was placed under the TET System control. This led to the discovery of new antiviral compounds and also proved useful for testing antiviral drugs against Hepatitis viruses.

29. TET has commercially embodied features claimed in the ‘758 and ‘124 Patents.

ISIS’ INFRINGING ACTIVITIES

30. Isis is a biomedical pharmaceutical company that describes itself as “the leading company in antisense drug discovery and development.” See <http://www.isispharm.com/about-isis>.

31. TET has recently discovered that Isis has been using HepAD38 cells and the TET System without a license or other consent from TET including Isis’ admission that it “acquired the HepAD38 cell line on July 22, 2010” and “the cell line was used in August and September of 2010.”

32. In fact, Isis’ infringing conduct is fully described in two (2) published patent applications, namely WO 2012/145674 and US 202/295961.

33. Isis’ infringing use of the TET System occurred before the expiration of the ‘758 and ‘124 Patents.

34. Isis is and has been aware of the ‘758 and ‘124 Patents.

COUNT I: DIRECT INFRINGEMENT UNDER 35 U.S.C. § 271(a)

35. TET realleges paragraphs 1 to 34 as if fully set forth herein.

36. In violation of 35 U.S.C. § 271(a), and as evidenced above, Isis has infringed, literally or under the doctrine of equivalents, each of the elements of one or more claims of the ‘758 and ‘124 Patents, without license from TET, by, *inter alia*, growing out the purchased cells,

thus reproducing the claimed DNA and protein compounds and using such newly created cellular material in the TET System as described by the '758 and/or '124 Patents.

37. Upon information and belief, Isis' infringement has been knowing and willful.

ISIS' OTHER HARM TO TET

38. TET realleges paragraphs 1 to 37 as if fully set forth herein.

39. As a direct and proximate cause of Isis' infringing acts, TET has been injured in its business and property rights, and has suffered injury and damages for which it is entitled to relief under 35 U.S.C. § 284.

PRAYER FOR RELIEF

WHEREFORE, TET respectfully requests of this Court the following relief:

(a) A judgment and decree that Isis has infringed one or more claims of the '758 and/or '124 Patents;

(b) An award of damages for Isis' infringement, which should be trebled pursuant to 35 U.S.C. § 284;

(c) That this case be declared "exceptional" and award TET its reasonable attorney fees, expenses, and costs in this action pursuant to 35 U.S.C. § 285; and

(d) Such other and further relief as the Court may deem just and proper.

Dated: October 14, 2013

Respectfully submitted,

GIBBONS P.C.

/s/ Christopher Viceconte

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JURY DEMAND

TET hereby demands a jury on all issues so triable in this action.

Dated: October 14, 2013

GIBBONS P.C.

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