SUMMARY

TROVAN, KANO STATE CIVIL CASE - STATEMENT OF DEFENSE

In its Statement of Defense, Pfizer denies each and every material allegation contained in the plaintiff's Statement of Claim; and states its belief that the Kano State civil lawsuit has no merit and is both frivolous and a gross abuse of the legal process 11 years after the fact.

Background on Meningococcal Meningitis Epidemics

Meningococcal meningitis is a bacterial infection that causes the inflammation of the tissues that cover the brain and spinal cord. Advanced bacterial meningitis can lead to brain damage, coma and death. Survivors can suffer long term complications, including, but not limited to, hearing loss, mental retardation, paralysis and seizures.

Meningitis epidemics strike impoverished countries in sub-Saharan Africa, where crowded living conditions and dry climates contribute to the spread of disease. They occur in seasonal cycles (between November and June) during the dry season. The cyclical impact of the disease has earned this area of Africa the name the 'Meningitis Belt'.

The 1996 outbreak was the most serious meningitis epidemic ever recorded in Nigeria. It took the lives of almost 12,000 people over a six-month period, and significantly strained the country's healthcare system. The severity of the epidemic was evidenced in the fatality rate, which was as high as 20% in the first weeks. Eventually, as reported in one source, it decreased to 10.7%.

Defendants' Response to 1996 Epidemic in Nigeria

Pfizer intervened in the 1996 meningitis epidemic in Nigeria by setting up and conducting the investigative Trovan study at the Infectious Disease Hospital (IDH) in Kano. The company's contribution, however, went beyond the clinical trial. Pfizer donated over N18 million to Kano State in medicines, equipment and materials to help fight the concurrent epidemics involving associated diseases, such as cholera and measles, ongoing at the time. Kano State acknowledged the donations in writing.

Defendants Made No Misrepresentations About Intentions

Pfizer did not misrepresent or conceal any facts in its decision to come to Nigeria. In fact, the company's intent was clear from the beginning. Pfizer's long-term goal was to bring a life saving, innovative, and cost-effective form of antibiotic that could be used effectively in a meningitis epidemic in a developing country.

At the time of the Kano clinical trial, Trovan was in late stage development and had been tested clinically in more than 5,000 patients in both oral and intravenous forms. Pre-clinical studies demonstrated that Trovan had excellent activity against all meningitis pathogens and penetrated very well into the cerebrospinal fluid (CSF) to effectively treat the disease. Trovan had also been tested on children in two pharmacokinetic (dosing) studies. The drug's oral form avoided the use of intravenous administration or

intramuscular injections, which are difficult to administer in an epidemic setting, can be painful to those receiving the drugs, and can lead to the spread of other diseases if sterile needles are not used.

Defendants Obtained Approvals from Relevant Government Agencies

Before conducting the Trovan clinical study in Kano, Pfizer sought and obtained all necessary approvals from relevant federal and state government agencies in Nigeria. In that regard, Pfizer has more than 12 letters between the company and the U.S. FDA as well as Nigeria's NAFDAC (National Agency for Food and Drug Administration and Control), Ministry of Health, Ministry of Finance, and Kano State's Ministry of Health, discussing and approving the study.

An approval letter from NAFDAC obtained in March 20, 1996, states that (1) "We have been supplied with adequate information about the drug and its proposed investigational use by the sponsor" and (2) "The drug may be legally used by investigators in Nigeria."

Approval was also obtained from Kano State's Ministry of Health. Dr. A. Dogunro met with Ms. Lawan Gadanya at the Kano State Ministry of Health, discussed the study's protocol and explained that Trovan was an investigational new drug. Ms. Gadanya gave her approval for the study. In a letter from Kano's Ministry of Health and Social Services to Pfizer, Ms. Gadanya stated that: "Approval is also hereby given for your staff to participate in treating patients at our hospitals."

Prior to commencing the study, Pfizer also participated in a series of meetings with Nigerian officials.

Defendants Engaged In Legal and Ethical Conduct

Pfizer conducted the Kano clinical trial using the best medical knowledge available at the time, and always acted in the best interests of the approximately 200 children involved (half were treated with Trovan and half with Ceftriaxone). The protocol approved by Nigerian authorities anticipated risks and detailed procedures to manage those risks.

Trovan's positive performance in the 1996 Kano clinical trial confirmed results from earlier studies of this particular drug and the class of drugs it belongs to, quinolones. At the time of the Kano study, Trovan was in late stage development and had been tested clinically in more than 5,000 patients in the United States, Europe and elsewhere both in oral and intravenous forms. Results of those studies demonstrated Trovan to be effective against several types of bacteria known to cause meningitis, to have excellent activity against all meningitis pathogens, and to penetrate very well into the cerebrospinal fluid (CSF) to effectively treat the disease. In addition, Trovan had been administered to children in two pharmacokinetic (dosing) studies that showed the medicine to behave similarly in adults as it did in children. At least five scientific articles published prior to 1996 also express support for the use of quinolones in children as "medically indicated and ethically justified." Prior to the Trovan study in 1996, Pfizer was ready to start formal meningitis trials in children around the world. The pediatric meningitis study was eventually conducted and the investigators found Trovan to be an effective antibiotic for the treatment of pediatric meningitis and raised no new safety concerns.

At Kano's Infectious Disease Hospital (IDH), parents or guardians of potential study participants were explained the details of the trial, including that participation was voluntary. Local Nigerian nurses explained orally to patients' parents and/or guardians in Hausa the details of the clinical trial. Oral consent was obtained before any patient was admitted into the study, and at no point were the parents or guardians separated from the children.

Children who participated were given a series of tests and physical exams to ensure that the clinical diagnosis of meningitis was consistent with laboratory results. Patients were randomized to receive either Trovan or Ceftriaxone and were given a bracelet and a pink identification card both stating which drug he or she had received. Patients were treated with either Trovan or Ceftriaxone for five consecutive days and they were monitored in the hospital or out-patient clinics, depending on the status of each patient's heath. Dr. Isa Dutse, the Nigerian doctor who served as Principal Investigator, performed rounds twice daily in the clinics and was assisted by Nigerian residents from Bayero Teaching Hospital.

The fact is that results of the trial plainly proved that Trovan helped saved lives. With a survival rate of 94.4%, Trovan was at least as effective as the best treatment available at Kano's IDH. The overall survival rate in Nigeria was less than 90%.

Patients in the Trovan study already had serious symptoms of meningitis before they were treated, and it is well documented that advanced meningitis can lead to brain damage, coma and death. In fact, deaths were associated with every treatment available at Kano's IDH, but all clinical evidence points to the fact that any deaths occurring during the Trovan clinical study were the direct result of the illness and not the treatment provided to patients. Survivors of meningitis can suffer the very same long term complications unjustly and erroneously attributed to the Trovan clinical trial including, but not limited to, hearing loss, mental retardation, paralysis and seizures.

At the end of the trial, any child who required additional attention was transferred to a local Kano hospital for continued care at Pfizer's expense. Four weeks after concluding the study - on May 15, 1996 - a follow-up exam of study participants was conducted by Pfizer. No unusual side effects, unrelated to meningitis, were observed by the patients who returned for the exam.

Copies of records showing the sex, age, diagnosis, date of admission, date of discharge or death - as well as other records - were left with IDH.

The results of the study also point to the efficacy of the comparator drug, Ceftriaxone, at the doses administered. After the initial dose of 100 mg/kg dose, subsequent doses of Ceftriaxone were reduced to 33 mg/kg to diminish the significant pain resulting from the intramuscular injection. At the reduced dosage level, the amount of the drug was still approximately 620 times the level required to kill the meningitis bacteria.

A clinical study of Ceftriaxone sponsored by Doctors Without Borders in 2003 confirms that a total dose of 100 mg/kg, significantly lower than the one used in the Trovan study in Nigeria, was effective in treating epidemic meningococcal meningitis.

Conduct and Practices of Defendants Had No Adverse Effect on Patients

In relation to the abrupt and short interruption of the study at the insistence of Dr. Idris Mohammed, Pfizer contends that Dr. Mohammed had no statutory authority to act with respect to the 1996 Trovan trial. Even so, he was provided a copy of the protocol at the start of the study, which he approved. Dr. Mohammed's action was overruled and later condemned in writing by Nigeria's Ministry of Health as an "action totally indefensible," and "an act of bad faith, ill-motivated, and lack[ing] merit." Pfizer continued the treatment after the Kano State government gave its authorization to do so.

Ethical Committee Clearance to Conduct Investigative Study Not Required Under Nigerian Law

Pfizer contends that there was no regulation or law in Nigeria requiring ethical committee approval before conducting a clinical trial or investigative study. Therefore, there was no need to obtain what the law did not require. In addition, there was no formal ethics committee sitting at either Kano's IDH or at the nearby Bayero Teaching Hospital. There were, however, numerous other forms of approval by local physicians and government officials authorizing the study to go forward including, but not limited to, the head of the IDH and Dr. Idris Mohammed. At no time was patient care compromised in any way.

Source of Allegations

Many of the allegations in the Kano state civil case are rooted in a Government Report that is unconstitutional - and to Pfizer's knowledge never published - which documents Dr. Idris Mohammed's failed attempts to permanently stop the Trovan study.

Dr. Nasidi, Chairman of the Investigation Committee that issued the Government Report, was an individual who not only had expressed opposition to the Trovan study but was also very close to Dr. Mohammed. In perhaps the most egregious abuse of power, Dr. Nasidi gave evidence to the committee, effectively acting as both a witness and judge in his own investigation.

The Statement of Defense also recounts 20 points cited in the Government Report later ignored in the report's conclusion, including public statements of support for the study's protocol, important statistics about efficacy of the Trovan clinical trial, the cited participation of Kano State Ministry of Health staff in the drug management, contradictory witness accounts, and repeated instances of government approval of the trial.

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