

TRIBUNE WATCHDOG Compromised care

Company paid psychiatrist nearly \$500,000 to promote an antipsychotic, despite its own doubts about his practices

Doctor's lucrative ties to drug manufacturer

By Christina Jewett PROPUBLICA
and Sam Roe TRIBUNE REPORTER

Executives inside pharmaceutical giant AstraZeneca faced a high-stakes dilemma.

On one hand, Chicago psychiatrist Dr. Michael Reinstein was bringing the company a small fortune in sales and was conducting research that made one of its most promising drugs look spectacular.

On the other, some worried that his research findings might be too good to be true.

As Reinstein grew irritated with what he perceived as the company's slights, a top executive outlined the scenario in an e-mail to colleagues.

"If he is in fact worth half a billion dollars to (AstraZeneca)," the company's U.S. sales chief wrote in 2001, "we need to put him in a different category." To avoid scaring Reinstein away, he said, the firm should answer "his every query and satisfy any of his quirky behaviors."

Putting aside its concerns, AstraZeneca would continue its relationship with Reinstein, paying him \$490,000 over a decade to travel the nation promoting its best-selling antipsychotic drug, Seroquel. In return, Reinstein provided the company a vast customer base: thousands of mentally ill residents in Chicago-area nursing homes.

During that period, Reinstein also faced accusations that he over-medicated and neglected patients who took a variety of drugs. But his research and promotional work went on, including studies and presentations examining many of the antipsychotics he prescribed on his daily rounds.

The AstraZeneca payments, filed



Chanile Hayes says Dr. Michael Reinstein told her taking the anti-psychotic drug Seroquel would help her lose weight. Instead, she says, she went from 140 pounds to nearly 300 pounds within two years and developed diabetes. She is among thousands suing the drug's maker. ABEL URIBE/TRIBUNE PHOTO

as exhibits in a federal lawsuit, highlight the extent to which a leading drug company helped sustain one of the busiest psychiatrists working in local nursing facilities.

In an interview and in response to written questions, Reinstein said industry payments he has received for speeches and other engagements have had no bearing on his research results or patient care. He said he does not "accept any money from corporations to study their medications. This eliminates any possible conflicts of interest."

But he does receive money from the Uptown Research Institute, a for-profit business that conducts

industry- and government-funded studies on psychotropic drugs to help mentally ill patients.

Reinstein's office in Uptown is adjacent to the research institute, which is owned by John Sonnenberg, a clinical psychologist who describes Reinstein as "a mentor of mine" and "brilliant."

Sonnenberg said drugmakers and others pay his institute to do research, and the group, in turn, pays Reinstein a consulting fee of "under \$2,000 a month" and has for years. A decade ago, Sonnenberg said, Reinstein was an active researcher for the institute but since then has served only as an adviser.

"My research organization is separate from him, financially and organizationally," Sonnenberg said.

While payments from drugmakers to researchers are legal, critics have long argued that they should be publicly disclosed. Legislation to make Illinois one of a handful of states to require disclosure died in Springfield this year but is included in the U.S. House and Senate versions of health care reform proposals.

"We need to know that we can fully trust the relationship we have with our doctor and that another, more lucrative relationship with

industry does not outweigh it," Sen. Herb Kohl, D-Wis., who is pushing for such reform, said in an interview.

Health professionals who have encountered Reinstein have had similar concerns. When he gave promotional presentations about various medications at Grasmere Place nursing home in Chicago, case manager Staci Burton recalled that she was pleased to get free lunches. But she said she wondered why Reinstein put his patients on twice as many drugs as other psychiatrists who treated residents.

"I was thinking, 'Why are you using so many medications?'" Burton, who worked at the facility from 2004 to 2006, said in an interview. "(His patients) would have symptoms, they'd have all these side effects, and their doctor was not listening."

Psychotropics to lose weight?

Chanile Hayes, a South Side resident, says she came under Reinstein's care at a psychiatric hospital after she suffered a nervous breakdown nearly 10 years ago. She found it odd, she said, when Reinstein told her that taking Seroquel would help her lose weight.

"I couldn't understand why he wasn't taking it because he was a plus-sized man himself," said Hayes, now 37. She is one of thousands of people nationwide suing AstraZeneca on allegations it concealed Seroquel's links to weight gain and diabetes.

While she is a plaintiff in New York state, a federal suit is playing out in Orlando, Fla. Reinstein is not a defendant in either case, but

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Orlando plaintiffs have cast him as a key figure: an influential promoter of Seroquel who was financially backed by AstraZeneca. They allege that Reinstein has claimed that the antipsychotic drug helps patients lose weight.

Hayes said she went from 140 pounds to nearly 300 within two years of taking the drug and later developed diabetes.

Reinstein has done studies, funded by AstraZeneca and two other drugmakers, that found that various medications, including Seroquel, carry an unexpected yet welcome side effect: They help some patients shed pounds.

That claim runs counter to established research that links so-called atypical antipsychotic drugs, such as Seroquel, to considerable weight gain. Drugs in this class, approved for schizophrenia and bipolar disorder, can have other serious side effects that include spastic movement disorders and seizures and can cause premature death among the elderly.

A Seroquel flier dated 1999 features a photograph of Reinstein on the cover. Inside, Reinstein describes one patient losing weight and no longer needing insulin shots because his diabetes had improved so much.

In a 2001 promotional telecast to 5,000 physicians nationwide, Reinstein said he had "jokingly kind of suggested to AstraZeneca" that the drug could be used for "taking away excessive appetite."

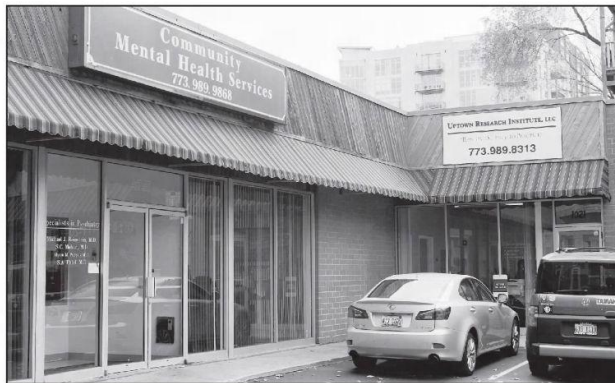
"There's actually some nurses in some of our facilities who have actually requested (Seroquel) because they noticed it really did suppress the appetite, and they wanted to lose weight themselves," Reinstein said, according to a transcript of the speech, sponsored by AstraZeneca and broadcast from Somerset Place, a Chicago nursing home.

Two years after the speech, the Food and Drug Administration, armed with mounting research, asked AstraZeneca to warn patients of Seroquel's diabetes risk. The drug's label now cautions that the medication is linked to diabetes and weight gain — with nearly four times more patients gaining weight on Seroquel than on a placebo.

In his response to reporters, Reinstein characterized Seroquel as "generally weight neutral, although some patients gain weight and others lose weight."

"I would never recommend" that patients take antipsychotics "to lose weight," he wrote.

AstraZeneca spokesman Tony Jewell said plaintiffs have not proved that Seroquel was respon-

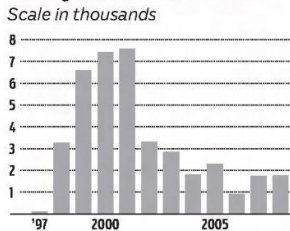


Dr. Michael Reinstein's office is next to the Uptown Research Institute, which pays him a consulting fee of "under \$2,000 a month," according to its owner. **ALEX GARCIA/TRIBUNE PHOTO**

Drug's key backer

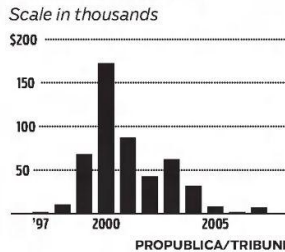
Over the course of 10 years, Dr. Michael Reinstein wrote nearly 40,000 Seroquel prescriptions. During that time the drug's maker, AstraZeneca, paid him \$490,000 to promote the drug.

SEROQUEL PRESCRIPTIONS



SOURCE: Tribune and ProPublica reporting

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sible for their injuries. He said the company, based in London, provided appropriate safety data about Seroquel to the FDA.

Chanile Hayes, who said she saw Reinstein during visits to his office, questioned why he prescribed her the drug: "How could you tell me that it would help me lose weight if it doesn't help (people) lose weight?"

At AstraZeneca, early doubts

In the corporate halls of AstraZeneca, the company's scientific staff also questioned Reinstein's work.

Copies of e-mails filed as part of the Seroquel litigation in Orlando reveal executives' misgivings about a Reinstein study involving patients on high doses of the drug. The results that came back were too rosy for AstraZeneca's own executives to accept.

One called Reinstein's conclusion that patients experienced no adverse effects "suspect" and "hard to believe." Executives "decided that we would ... try to distance

ourselves from this study," according to e-mails from John Tumas, an AstraZeneca publications manager.

Reinstein presented his findings in 2001 at the annual meeting of the American Psychiatric Association, the profession's most high-profile gathering. At least three researchers have subsequently cited his study in medical journals.

During a deposition for the Orlando case, Reinstein said he was unaware of any criticism from AstraZeneca about his research.

But he had some criticisms of his own, according to an internal company e-mail filed in federal court. Reinstein vented to an AstraZeneca employee in 2001, saying the firm was giving him the "run around." He also complained that the company did not help present his research findings or include him in high-profile studies.

Within days, Reinstein wrote a letter to AstraZeneca's CEO in the U.S., identifying him and four doctors he works with as "the largest prescribers of Seroquel in the world." He said his travel expenses weren't paid upfront and called for

"new leadership" in Seroquel's marketing.

Reinstein's complaints caused a stir.

In a strongly worded 2001 e-mail, Georgia Tugend, the U.S. brand manager for Seroquel, told colleagues that research conducted by Reinstein and his partners "is often criticized by their peers in psychiatry."

Some scientists have "significant and numerous issues ... with the quality of research this group has produced in the past," Tugend wrote, yet Reinstein's group persists in "demanding research grants from us."

At one point, according to an e-mail from an AstraZeneca executive, Reinstein and his partners had "blatantly threatened" to switch patients to a Seroquel competitor. Reinstein later denied that accusation during a deposition, testifying that he "cannot imagine" making such a threat.

Malcolm May, AstraZeneca's U.S. sales director, reacted to Reinstein's discontent by saying that the company should be careful not to alienate a psychiatrist worth up to a half-billion dollars to the firm.

"I am not suggesting we kowtow to his whims, nor to support any unethical behavior," May wrote in 2001 in an e-mail to fellow AstraZeneca executives. "I am suggesting ... we need to be more responsive to his opinion and needs."

May continued: "It seems we are annoying possibly our most important single customer, and that is not acceptable. ... My concern is that Dr. Reinstein could be looking for a trigger to leave our fold. That would be disastrous for our Seroquel business in the short and long term."

May's message did not cite a basis for the half-billion-dollar estimate. Reached by phone, May said he did not recall sending the e-mail.

Court documents show that AstraZeneca continued to pay Reinstein to promote Seroquel until 2007. A Reinstein ledger lists hundreds of payments beginning in 1997. The payments, in increments from \$10 to \$20,000, totaled \$490,000.

During that period, Reinstein ordered Seroquel for as many as 1,000 Chicago-area Medicaid patients per year at a total cost of \$7.6 million to taxpayers, records show.

AstraZeneca spokesman Jewell said the company wasn't paying Reinstein to prescribe its drug but rather to make promotional speeches. Reinstein and AstraZeneca mutually declined to renew their ties in 2008, but Jewell would not say why.

Reinstein said in an interview that some AstraZeneca officials

were critical of him only after his complaint to the firm's U.S. chief executive.

Today, Reinstein said, he gets money from the maker of a dissolvable form of clozapine, another antipsychotic that he often prescribes. He said he receives less than \$25,000 per year to be in the manufacturer's speakers bureau, which drug companies commonly set up to promote their products.

In his deposition last year, Reinstein himself expressed surprise about some of his research results, saying one study's findings were "hard for me to believe" — in line with concerns expressed at AstraZeneca. When asked about another study in which patients lost weight on Seroquel, he said the results could have been affected by a change in the nursing home's cook or possible problems with the scales.

In all, Reinstein has published at least eight research articles, mostly about antipsychotic drugs. He has been cited in at least 20 others. The Uptown Research Institute is now working on eight studies involving psychotropics, said Sonnenberg, the owner.

Sonnenberg said studies by his institute "are highly scrutinized for accuracy and credibility" by the drugmakers, third-party ethics review boards and, potentially, the FDA.

Dr. Jerome Kassirer, a professor at Tufts University School of Medicine and a former editor of the New England Journal of Medicine, read the AstraZeneca e-mails at the request of ProPublica and the Tribune. He concluded that editors of medical journals should investigate Reinstein's published studies.

"Once you know that he has done a study that has been discredited," Kassirer said, "you have to ask yourself about all other studies done."

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