OxyContin goes global — “We’re only just getting started”

By Harriet Ryan, Lisa Girion and Scott Glover • Dec. 18, 2016

OxyContin is a dying business in America.

With the nation in the grip of an opioid epidemic that has claimed more than 200,000 lives, the U.S. medical establishment is turning away from painkillers. Top health officials are discouraging primary care doctors from prescribing them for chronic pain, saying there is no proof they work long-term and substantial evidence they put patients at risk.

Prescriptions for OxyContin have fallen nearly 40% since 2010, meaning billions in lost revenue for its Connecticut manufacturer, Purdue Pharma.

So the company’s owners, the Sackler family, are pursuing a new strategy: Put the painkiller that set off the U.S. opioid crisis into medicine cabinets around the world.
A network of international companies owned by the family is moving rapidly into Latin America, Asia, the Middle East, Africa and other regions, and pushing for broad use of painkillers in places ill-prepared to deal with the ravages of opioid abuse and addiction.

Visit the site

**Mundipharma China**

Mundipharma is courting Chinese patients with a campaign encouraging people to take medications as their physicians prescribe.

In this global drive, the companies, known as Mundipharma, are using some of the same controversial marketing practices that made OxyContin a pharmaceutical blockbuster in the U.S.

In Brazil, China and elsewhere, the companies are running training seminars where doctors are urged to overcome “opiophobia” and prescribe painkillers.
They are sponsoring public awareness campaigns that encourage people to seek medical treatment for chronic pain. They are even offering patient discounts to make prescription opioids more affordable.

U.S. Surgeon General Vivek H. Murthy said he would advise his peers abroad “to be very careful” with opioid medications and to learn from American “missteps.”

“I would urge them to be very cautious about the marketing of these medications.” — Vivek H. Murthy, U.S. Surgeon General

“I would urge them to be very cautious about the marketing of these medications,” he said in an interview. “Now, in retrospect, we realize that for many the benefits did not outweigh the risks.”

Former U.S. Food and Drug Administration commissioner David A. Kessler has called the failure to recognize the dangers of painkillers one of the biggest mistakes in modern medicine. Speaking of Mundipharma’s push into foreign markets, he said, “It’s right out of the playbook of Big Tobacco. As the United States takes steps to limit sales here, the company goes abroad.”

“It’s right out of the playbook of Big Tobacco.” — David A. Kessler, former commissioner
Some Mundipharma representatives and promotional material have downplayed the risk that patients will become addicted to their opioid medications. Those claims recall the initial marketing of OxyContin in the U.S. in the late 1990s when Purdue deceived doctors about the drug’s addictiveness.

Purdue and three executives pleaded guilty in 2007 to federal charges of misbranding drugs and were ordered to pay $635 million. The Drug Enforcement Administration said in 2003 that the company’s “aggressive, excessive and inappropriate” marketing “very much exacerbated” abuse and criminal trafficking of OxyContin.

Purdue was a small New York City pharmaceutical firm when brothers Mortimer and Raymond Sackler, both psychiatrists, bought it in 1952. The spectacular success of OxyContin has generated nearly $35 billion in revenue over the last two decades and made the Sacklers one of the nation’s wealthiest families. Three generations of the family now help oversee Purdue and the Mundipharma associated foreign corporations.

Family members declined to be interviewed for this article, as did executives who run their international companies.

In a statement, Mundipharma International, which is based in Cambridge, England and responsible for European operations, said it was “mindful of the risk of abuse and misuse of opioids” and was “drawing on the experiences and
insights of the US in tackling this issue.”

Mundipharma said those efforts include seeking regulatory approval in Europe for a formulation of OxyContin already sold in the U.S. that deters certain forms of abuse and introducing another opioid painkiller, Targin, with similar abuse-deterrent properties.

“Mundipharma is committed to developing prescription medicines for healthcare professionals to treat patients in pain safely and responsibly,” the statement said.

Promotional videos for Mundipharma, which feature smiling people of many ethnicities, suggest the companies regard OxyContin’s U.S. success as merely a beginning.

“We’re only just getting started,” the videos declare.

“Opiophobia” around the globe

Joseph Pergolizzi Jr. is a Florida doctor with an array of business ventures. He runs a pain management clinic and co-founded a drug research company. He invented a non-prescription pain-relieving cream he sells on cable television and he serves as an expert for a mail-order nutritional supplements company. He also talks up opioids to foreign doctors for Mundipharma.

In April, Pergolizzi was in Rio de Janeiro at a cancer pain seminar sponsored by the company. For an hour, Pergolizzi lectured the gathered physicians in English about the use of opioids in cancer patients and those with what he called “the death sentence of chronic pain.”

Brazil had stepped up its use of painkillers in recent years, he said, but “you are still low” compared with the U.S., Canada and Europe.
“I think unfortunately you may not have all the tools you need to properly address pain,” he said, according to a video of the seminar posted online by Mundipharma.

Consultants like Pergolizzi are key to helping Mundipharma overcome one of its greatest obstacles to selling painkillers abroad: Doctors’ aversion to prescribing narcotics.

Consultants like Pergolizzi are key to helping Mundipharma overcome one of its greatest obstacles to selling painkillers abroad: Doctors’ aversion to prescribing narcotics. For generations, physicians have been taught that opioid painkillers are highly addictive and should be used sparingly and primarily in patients near death.

Mundipharma executives and consultants call this “opiophobia” and top company officials have said publicly that success in new markets depends on defeating this mind-set. Speeches like Pergolizzi’s portray painkillers as a modern approach endorsed by leading experts in the U.S.

Mundipharma presented Pergolizzi to the Brazilian group as a professor at the Johns Hopkins and Temple University medical schools. Medical journal articles published in 2015 and 2016 with funding from Mundipharma or in collaboration with its scientists have identified him variously as a faculty member at Johns Hopkins, Temple and Georgetown University medical schools.

In fact, he is an adjunct professor at Johns Hopkins and he has not been affiliated with Georgetown since 2010 or Temple since 2014, according to
school officials.

Asked to explain, Pergolizzi said by email that he was having “paperwork issues” at Temple “which I am rectifying with their full cooperation” and was “in discussions” with Georgetown about an adjunct position.

“I have never intentionally misrepresented ... my university affiliations,” he wrote in another email.

A Temple spokesman said the university had “no reason to believe he will have any future relationship” with the school, and a Georgetown spokeswoman said, “We are not in discussions with that gentleman.”

Government records indicate that Purdue and other U.S. pharmaceutical firms have paid Pergolizzi more than $1 million since 2013 for consulting
work, speaking engagements and other services as well as travel reimbursements. The records do not include any payments he may have received from foreign pharmaceutical firms such as Mundipharma. In his Rio presentation, he clicked quickly past a slide listing 16 drug companies for which he had done work.

After Purdue launched OxyContin in the U.S. in 1996, the company ran similar training seminars for specialists — known in pharmaceutical marketing as “key opinion leaders” — in the pain field. Doctors were invited to all-expenses paid weekends in resort locations like Boca Raton, Fla., and Scottsdale, Ariz. The company found that doctors who attended seminars in 1996 wrote more than twice as many prescriptions as those who didn’t, according to a company analysis.

Several thousand of these specialists signed on to the Purdue “speakers bureau,” which paid them to make speeches about opioids at medical conferences and at hospitals.

Dr. Barry Cole, a Reno psychiatrist and pain management specialist, started giving speeches about OxyContin for Purdue the year the drug hit the market. In recent years, he moved to the company’s international operation in a consulting role he described in an online resume as a “pain ambassador,” teaching the use of opioids to doctors in Colombia, Brazil, South Korea, the Philippines, China and Singapore.

“Any side effect is reversible when treatment is discontinued, and there is no permanent damage to the body,” Cole told a 2014 conference of pain specialists in Veracruz, Mexico, according to an account of the presentation published on Mexican health websites.

In an interview with The Times, Cole said he made the foreign presentations despite having developed deep misgivings about the use of OxyContin and
similar drugs in the U.S. Witnessing the opioid epidemic unfold, seeing the
effect of opioids on his patients and reading scientific literature about the
drugs, he said, led him to conclude by about 2010 that painkillers were too
dangerous for most chronic pain patients.

“We thought we could just get away with putting everybody on opioids, and it
would be hunky-dory,” Cole said. “And it didn’t work and it had darker
consequences than any of us were predicting.”

He defended his work promoting opioids to foreign doctors, saying terminally
ill patients were dying in pain in many places he visited. He said he never
shied away from questions about abuse and had no way of knowing whether
his talks led doctors to prescribe more opioids.

“You show up, do a presentation and then you get back on the plane and are
gone,” he said. He said he stopped making appearances for Mundipharma
last year.

One “key opinion leader” who attended Cole’s seminars was Ricardo
Plancarte Sanchez, a Mexico City pain doctor who holds a position at
Mexico’s national cancer institute.

Plancarte now speaks at Mundipharma seminars in Mexico. In an interview,
he said his aim was to help “demystify the use of opioids in chronic pain” and
that he was not paid for his appearances.

“We need to work more to educate so that people use analgesics more,”
Plancarte said.

He said he was not concerned Mexico would see large-scale abuse and
addiction.

“If we educate our doctors as well as our patients, there will be better use of
the drugs than in the United States,” he said.

‘Talking about big money’

Untreated pain is a global scourge. Each year millions with terminal cancer and end-stage AIDS die in needless agony, according to the United Nations. The problem is most acute in the poorest countries.

Stefano Berterame, an officer of the U.N.-affiliated International Narcotics Control Board in Vienna, works to increase access to opioids in countries with shortages. He said most of the global problem could be solved with “very cheap morphine” but that selling it held little allure for multinational drug companies.

“It’s not very profitable,” he said. “Companies prefer to market expensive preparations.”

Purdue charges hundreds of dollars a bottle for a month’s supply of OxyContin in the U.S. Generic morphine, which provides similar pain relief, can cost as little as 15 cents a day.

Mundipharma is not alone in seeking new markets for opioids outside American borders. In the last year, two other manufacturers, Teva and Grunenthal, each bought drug companies in Mexico.

Mundipharma sells drugs for a range of conditions, including asthma, cancer, and arthritis, but the core of its product line is opioid painkillers. In its global expansion, Mundipharma is looking to countries with wealth, health benefits or large emerging middle classes. And it is pursuing patients healthy enough to be customers for a long time.

“If your market is only cases of terminal cancer, then your market is relatively limited...,” Berterame said. “If you enlarge the market to also chronic pain,
then you are talking about big money.”

‘Rebel against the pain’

Seeking new patients in Spain, Mundipharma chose ambassadors guaranteed to attract attention: Naked celebrities.

A string of topless actors, musicians and models looked into the camera and told fellow Spaniards to stop dismissing aches and pains as a normal part of life.

“Don’t resign yourself,” Maria Reyes, a model and former Miss Spain, said in the 2014 television spot.

“Chronic pain is an illness in and of itself,” the pop singer Conchita added.

The one-minute ad was part of a nationwide campaign developed and financed by Mundipharma to raise awareness of chronic pain — Rebélate contra el dolor (Rebel against the pain).
The ads do not recommend a specific treatment or medication, but do urge sufferers to see a healthcare professional — thousands of whom have been trained by the company in the use of opioids.

The campaign is part of a strategy to redefine back pain, joint aches and other common conditions as a distinct malady — chronic pain — that doctors and patients should take seriously.

Chronic pain patients, who fill prescriptions month after month and often year upon year, have been the driver of billion-dollar sales for Purdue in the U.S. University of North Carolina researchers analyzed the medical records of patients taking OxyContin at strengths of 30 milligrams or more— common doses for the drug — and found that more than 85% were diagnosed with chronic pain of one type or another.

In Spain, painkiller use is on the rise. Company sales were up seven-fold since
2007, a Mundipharma executive said in a 2014 interview with an industry blog.

Spanish pain specialist Cesar Margarit, a consultant for Mundipharma, said the celebrity ads performed a public service by propelling patients who were “shy in recognizing they suffer from pain” to seek treatment.

“You have celebrities saying, ‘I have chronic pain.’ [Patients] say, ‘OK, if they can say that, I can too,” Margarit said. “The impact in Spain was a very big one.”

A Spanish-language promotional video titled “Dolor Cronico Camapana 2014” shows people discussing pain and where it might afflict them with graphic illustrations. (Instituto Mundipharma)

The company removed the “Rebel against the pain” spots from its YouTube channel this fall — after The Times submitted questions to the company about the chronic pain campaign. A spokeswoman said the videos were taken down because the program was inactive.
Around the world, Mundipharma companies cite statistics suggesting there is a great unmet need for their products. Opening an office in Mexico in 2014, Mundipharma officials declared that 28 million citizens were suffering from chronic pain. In Brazil, the company cited a figure of 80 million. In Colombia last year, a company news release said 47% of the population — about 22 million people — were afflicted by “this silent epidemic.”

![Bar chart showing OxyContin sales from 2008 to 2015. The y-axis represents sales in billions, with a peak of $3.5 billion in 2010.]
A 2011 survey in the Philippines designed and paid for by the company concluded that the “government should recognize chronic pain as a specific health problem” and should improve access to pain medications.

Health authorities in the U.S. say opioids are not the solution to chronic pain. The Centers for Disease Control and Prevention said this year there is “insufficient evidence” that the drugs relieve pain in patients who take them for more than three months.

Up to 24% of people on the drugs long-term become addicted, the CDC said.

Some Mundipharma representatives abroad have suggested publicly that painkiller risk is overblown. As public health officials in the U.S. were issuing their latest warning about painkiller abuse last year, a Mundipharma executive was quoted in a Seoul newspaper saying that Korean doctors “worry too much” about addiction.

“But many studies have shown that it’s almost impossible for those with chronic or severe pain to become addicted to narcotics, as long as the drug is used for pain relief,” Lee Jong-ho told the Korea Herald. Lee could not be reached for comment.

Willem Scholten, a retired World Health Organization official Mundipharma has paid to speak at medical conferences, said President Obama, public health officials and the media have “exaggerated” the U.S. prescription opioid crisis. The surge in addiction and death was largely due to recreational abuse, he said.
“The problem is a lot of crime,” Scholten, a Dutch pharmacist, said in an interview. “If [other countries] make good regulations, they won’t have similar problems.”

He said that “there is hardly any evidence” that pain patients abuse medications.

Sharon Walsh, a University of Kentucky addiction expert who advises the FDA on risks from pain drugs, called the assertions “completely untrue.”

“That is exactly the same thing they were teaching U.S. physicians when they launched OxyContin in this country,” said Walsh, who runs the university’s Center on Drug and Alcohol Research.

‘The Google of the pharma industry’

Mundipharma’s operations in the developing world are run out of a sleek Singapore office with a Silicon Valley feel. There are bean bag chairs, a “chill-out zone” and a tea bar, and employees are encouraged to think of the company as a nimble, creative start-up — “the Google of the pharma industry,” in the words of one executive.

After introducing OxyContin in the U.S., Purdue’s Canadian affiliate and Mundipharma’s Australian company began promoting the painkiller in those countries. In the last decade and a half, both have seen U.S.-style problems, including criminal trafficking, addiction and death.

Mundipharma turned its focus to the developing world in 2011, as U.S. sales began their drop. Rapidly modernizing countries are expected to spend more than $20 billion on pain medicines by 2020, according to QuintilesIMS Institute for Healthcare Informatics.

Mundipharma expanded first in Asia, then Latin America and then the
Middle East and Africa, ultimately having a presence in 122 developing markets.

The high cost of brand-name medications remains a barrier in many developing countries, but Mundipharma has sought ways to adjust. In Brazil, the company started a program this year that offers patients discounts on the cost of pills. Purdue used coupons in the U.S. that offered patients a free initial prescription for OxyContin. About 34,000 coupons were redeemed before the company terminated the program as concerns about abuse grew, according to a Congressional report.

Revenues for Mundipharma Emerging Markets, the Singapore-based company that oversees developing world operations, have risen 800% over the last five years to about $600 million annually. A Mundipharma spokeswoman said that growth included revenue from deals the companies have made with other manufacturers to sell non-opioid products.

Raman Singh, head of Mundipharma Emerging Markets, has said publicly that pain treatment in Asia is 1/50th of what it should be. Half the company’s worldwide sales in the developing world, which include products other than painkillers, already come from China, according to Mundipharma, and China is central to the Mundipharma’s global strategy.
As the head of Mundipharma Emerging Markets, Raman Singh, right, has overseen 800% sales growth in the developing world. Tennis star Caroline Wozniacki, left, is a Mundipharma brand ambassador for the antiseptic Betadine. (Suhaimi Abdullah / Getty Images)

The Chinese government has pledged that all 1.4 billion citizens will have health insurance by the close of the decade, and the company is working quickly to establish itself as the market leader in pain medications. Since 2011, Mundipharma has hired more than a thousand employees, most of them sales representatives, and now has a presence in 300 cities.

Thousands of Chinese doctors have attended training seminars about Mundipharma’s drugs, and it claims a 60% share of the cancer pain market. Mundipharma has sponsored clinical trials of OxyContin and Targin at hospitals across the country.

There remains, however, a deep-seated fear of opioids stemming from
Chinese defeats in the 19th century Opium Wars that left millions addicted. Under strict government regulations, patients can purchase OxyContin only from a hospital or other medical institution, and can receive no more than a 15-day supply. Relatively few Chinese use Mundipharma’s painkillers for chronic pain because of their high price.

Mundipharma’s operation in China, headquartered in a Beijing skyscraper, has expanded rapidly since 2011.

(Jonathan Kaiman/Los Angeles Times)

Mundipharma is courting Chinese patients with a campaign encouraging people to take medications as their physicians prescribe. In one animated video on the company’s website, an elderly cancer patient who expresses fear about becoming addicted to painkillers is corrected by his nurse.

“You will not be addicted if you follow the doctor’s instructions,” she tells him. The video was removed from the site this fall at around the time The
Times asked company officials about it. Asked why, a company spokeswoman said “programs and campaigns change frequently and content is updated often.”

In China, where there are nearly 3 million registered drug abusers, the government has forced addicts into boot-camp style treatment that human rights advocates have described as prisons. Treatment is rudimentary or unavailable in many parts of the developing world.

UNC researcher Nabarun Dasgupta, who has advised federal health authorities and the WHO on prescription opioid abuse, said the wide use of painkillers in those countries “sounds like a recipe for disaster” because “a certain percent [of users] will go on to need addiction treatment.”

“A certain percent [of users] will go on to need addiction treatment.” — Nabarun Dasgupta, University of North Carolina researcher

Mundipharma Emerging Markets said in a statement, “We attach great importance on promoting our pain medicines in a balanced and responsible manner so that the correct physicians are prescribing the correct medicines to the correct patients.”

‘A big deal’

Public health officials in Europe worry far less about painkiller addiction than their American counterparts. Government
health systems in many countries track prescriptions, making it more difficult than in the U.S. to obtain large amounts of opioid medication for abuse or criminal trafficking.

But when a team of international researchers recently conducted the first large-scale survey of drug abuse in Europe, they found what the lead investigator described as a significant problem with prescription opioid abuse.

Painkiller abuse rates are similar to the U.S. in the early 2000s “before the epidemic really got going,” Scott Novak, a scientist at the nonprofit RTI International in North Carolina, said in an interview.

In Spain, 18% of those surveyed acknowledged abusing painkillers in the course of their life, according to the study published in August. Across Europe, people with prescriptions were eight times as likely to abuse the drugs.

“They are potentially at the precipice of a major public health problem if prescribing increases,” Novak said.

Mundipharma International took issue with that conclusion. The company said in a statement that painkiller abuse is less of a problem in Europe than in the U.S., in part because of stricter pharmacy regulation and government health systems. Mundipharma said that it was conducting a study of abuse in Britain and Germany and that initial results “suggest that in these countries abuse of prescription opioids is less than 1%.”

In one European country — Cyprus — OxyContin abuse is an acknowledged problem. Mundipharma began marketing the painkiller in 2008 on the Mediterranean island of 1 million. Government health coverage made the
medication cheaper than heroin and addicts began crushing and snorting the pills.

Officers responding to overdoses knew little of the U.S. experience with painkillers. Stelios Sergides, a superintendent with the Cyprus National Police, said that the first time he heard the word OxyContin, he had to look it up online.

Since 2013, authorities have linked six deaths to the drug.

“It’s a big deal, a big deal,” Sergides said.
Mundipharma said it was “deeply disturbed” by the deaths in Cyprus and suggested the blame rested with a rehab center which used OxyContin to treat heroin addiction, a practice the company does not recommend.

Police in Cyprus are investigating doctors suspected of overprescribing and working with public health officials to get addicts into rehab. Last year, 59 people requested treatment.

“We are worried, of course, because of the numbers, especially the treatment demand,” Sergides said.

In the Mundipharma’s Cyprus office, managing director, Menicos M. Petrou, called OxyContin “an excellent product” and said he had been honored to meet members of the Sackler family during visits to a factory on the island.

“If people misuse drugs, most of the time there is little a pharmaceutical company can do,” he said.

Times staff writers Hector Becerra, Marisa Gerber and Brittny Mejia in Los Angeles and special correspondent Jessica Meyers and news assistants Nicole Liu and Yingzhi Yang in The Times’ Beijing bureau contributed to this report.

Additional credits: Lily Mihalik and Evan Wagstaff.