REPLIDYNE INC
Form 8-K
September 17, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of
The Securities Exchange Act of 1934
Date of Report (Date of earliest event reported) September 17, 2007 (September 17, 2007)

REPLIDYNE, INC.
(Exact name of registrant as specified in its charter)

Delaware	**000-52082**	**84-1568247**
(State or other jurisdiction of incorporation or organization)	*(Commission File Number)*	*(I.R.S. Employer Identification No.)*

1450 Infinite Drive, Louisville, Colorado	**80027**
(Address of principal executive offices)	*(Zip Code)*

303-996-5500
(Registrant s telephone number, including area code)
Not Applicable
(Former name, former address and former fiscal year, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

INFORMATION TO BE INCLUDED IN THE REPORT

Section 7 Regulation FD

Item 7.01 Regulation FD Disclosure.

Replidyne, Inc. (the Company) announced today that it will be presenting 21 posters relating to three of its research pipeline programs at the 47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held at the McCormick Place conference center in Chicago, Illinois. The posters will describe previously unpublished data related to faropenem medoxomil, the Company s Phase III clinical program for community-acquired respiratory tract infections; REP8839, the Company s Phase II topical antibiotic initially targeted for the treatment of impetigo, the most common bacterial skin infection in children; and REP3123, the Company s product candidate to treat *Clostridium difficile* (*C. difficile*) related diseases, a major cause of morbidity among the elderly and hospitalized patients.

REP3123 Presentations

On September 17, 2007 at the All New Antimicrobial Agents session of the ICAAC, the Company s Chief Scientific Officer, Nebojsa Janjic, described details of the Company s *C. difficile* program. The presentation introduced REP3123, highlighting key preclinical findings, including its ability to inhibit growth, halt toxin production and prevent spore-formation of the Gram-positive *C. difficile* bacterium without inhibiting other key organisms that are essential for normal intestinal functioning.

The Company will present the following *C. difficile* posters on Thursday, September 20, 2007 at 10:00 AM, Room E253D:

Poster F1-2112, titled Novel Inhibitors of Methionyl tRNA Synthestase from *Clostridium difficile*: Identification and Synthesis of REP3123.

REP3123 is a novel antibacterial agent that inhibits growth of *C. difficile* by inhibiting an essential enzyme called methionyl t-RNA synthetase (MetRS) that prevents the organism from synthesizing proteins. The research work shows that REP3123 has an *in vitro* microbiological profile that is competitive with vancomycin and metronidazole currently used to treat *C. difficile* associated disease (CDAD).

Poster F2113, titled REP3123 is a Potent and Selective Inhibitor of Methionyl tRNA Synthetase from *Clostridium difficile*.

The objective of the study was to characterize the interaction of REP3123 with the isolated MetRS enzyme from *C. difficile*, define its potency of inhibition under standard conditions and compare its ability to inhibit MetRS enzymes from other bacteria and humans. REP3123 is an inhibitor of the MetRS enzyme from *C. difficile* and most Gram-positive bacteria, which is consistent with its narrow spectrum of inhibition of bacterial growth. It is a limited inhibitor of the human MetRS enzyme from both cellular mitochondria and cytoplasm. These data help establish that MetRS is the target enzyme for REP3123 inhibition of bacterial growth. The limited inhibition of human MetRS predicts little protein synthesis inhibition in the bacterial host.

Poster F1-2114, titled Co-Crystal Structure of REP3123 Bound to *Clostridium difficile* Methionyl tRNA Synthetase.

This study determined the three-dimensional structure of *C. difficile* MetRS (CDMetRS) in combination with REP3123 by X-ray crystallography. Knowing the three-dimensional structure of REP3123 bound to CDMetRS will allow further study related to how REP3123 inhibits CDMetRS. This understanding will also facilitate design of the next generation of MetRS inhibitors.

Poster F1-2115, titled Spectrum of Activity of REP3123 against Aerobic Bacterial Pathogens.

REP3123 is a narrow spectrum antibacterial agent with activity against Gram-positive aerobes, including resistant strains, but limited or no activity against Gram-negative aerobes. The limited activity against enteric Gram-negative organisms suggests that REP3123 is unlikely to disturb the ecological balance of intestinal aerobes. The potent activity of REP3123 against vancomycin-resistant enterococci suggests that the agent is unlikely to promote intestinal colonization with these organisms. Based on the outcome of studies conducted to date, further studies are believed to be warranted to evaluate REP3123 as a novel agent for the treatment of CDAD.

Poster F1-2117, titled *In vitro* Activity of REP3123 against *Clostridium difficile* and Other Anaerobic Intestinal Bacteria.

The objective of the study was to evaluate the activity of REP3123 and comparator agents against 50 strains of *C. difficile* and 233 other common Gram-positive and Gram-negative intestinal anaerobic bacterial organisms. REP3123 demonstrated activity against *C. difficile* and limited activity against other friendly intestinal strains and warrants further clinical evaluation for treatment of CDAD.

Poster F1-2118, titled REP3123: A Narrow Spectrum Antibacterial Agent that Inhibits Growth and Prevents Sporulation in *Clostridium difficile*.

In contrast to vancomycin and metronidazole at sub-minimum inhibitory concentrations, REP3123 was effective in preventing vegetative cells of *C. difficile* from producing spores. Because *C. difficile* infection is thought to be initiated via ingestion of spores, REP3123 may be a useful agent in treating CDAD and reducing outbreaks and relapse rates. REP3123 is a novel agent with antibacterial activity against *C. difficile* and further studies will be needed to evaluate its ability to treat CDAD in a clinical setting.

Poster F1-2119, titled REP3123 Inhibits Toxin Production in *C. difficile*.

REP3123 inhibited growth and toxin production in *C. difficile* broth cultures. REP3123 was found to be more potent against *C. difficile* broth cultures compared to vancomycin and metronidazole. REP3123 inhibited *de novo* toxin production in high cell density, stationary phase cultures of *C. difficile.* REP3123 has the potential to be a superior therapeutic agent compared to currently used antibiotics against CDAD with the added benefit of quickly disarming the disease-causing bacteria.

Poster F1-2120, titled Efficacy of Novel MetRS Inhibitors in a *C. difficile* Hamster Model.

In a hamster model, REP3123 exhibited superior efficacy to vancomycin for the treatment of CDAD. Unlike vancomycin, the hamster survived for the duration of the study suggesting that REP3123 may provide protection from relapse or re-infection. REP3123-treated animals had a healthy gastrointestinal appearance at study termination. These data suggest that REP3123 is a promising new agent for the treatment of CDAD and superior to current standard therapy based upon efficacy results in this animal (hamster) model.

Faropenem Presentations

The Company will present the following Faropenem posters on Monday, September 17, 2007 at 12:00 PM, Hall D:

Poster E-256, titled Comparison of the Bactericidal Activities of Faropenem, Ertapenem, Amoxicillin, Cefixime, Cefuroxime and Moxifloxacin against *Streptococcus pneumoniae*.

In this study, both experimental and mathematical models were used to evaluate differences between time and concentration dependent killing properties of faropenem medoxomil and other agents against two strains of *S. pneumoniae*. Faropenem medoxomil exhibited the most pronounced bactericidal effects against *S. penumoniae* when compared with moxifloxacin, amoxicillin, cefuroxime, cefixime and ertapenem, even at the minimum inhibitory concentration (MIC). In the mathematical model the maximal kill rates (k-max, h-1) were 2.4 for faropenem medoxomil, 1.4 for ertapenem, amoxicillin, cefuroxime and moxifloxacin, and 0.7 for cefixime. Much lower concentrations of faropenem medoxomil were required for 3log kill within six hours when compared with the other agents. These results suggest that faropenem medoxomil should be an effective agent for the treatment of infections caused by *S. pneumoniae*.

Poster E-257, titled Comparative Ability of Faropenem to Select for Resistant Mutants of *S. pneumoniae*.
The objective of the study was to evaluate the ability of faropenem medoxomil and other agents to select for resistant strains of *S. pneumoniae* in the laboratory. Faropenem medoxomil had low MICs for all strains of *S. pneumoniae* isolates tested, including strains resistant to penicillin and macrolides. Faropenem medoxomil failed to select for resistant mutants of *S. pneumoniae* even after 50 daily subcultures in contrast to the macrolides and quinolones that selected for mutants with higher MICs. Development of resistance following the launch of a new antibacterial agent is always a concern. Some antibiotics seem to select for resistant bacteria more quickly than others. These *in vitro* study results suggest that faropenem medoxomil is unlikely to select for resistant isolates of *S. pneumoniae* in the clinical setting.

Poster E-258, titled Comparative Ability of Faropenem to Select for Resistant Mutants in *H. influenzae*.
The aim of the study was to evaluate the ability of faropenem medoxomil and other agents to select for resistant strains *H. influenzae* in the laboratory. Faropenem medoxomil, unlike the macrolides and quinolones, did not select for resistant mutants in any of the six strains of *H. influenzae* tested in this study even after 50 days. Development of resistance following the launch of a new antibacterial agent is always a concern. Some antibiotics seem to select for resistant bacteria more quickly than others. These *in vitro* study results suggest that faropenem has a low likelihood of resistance selection when the drug is introduced into the clinical setting.

Poster C2-200, titled Antimicrobial Resistance Patterns among *Streptococcus pneumoniae* Isolated from Children in the U.S. 2005-2006 Faropenem Surveillance Study.
The objective of the study was to determine the prevalence of resistant strains of *S. penumoniae* collected from U.S. children during the 2005-2006 respiratory season and determine the activity of faropenem medoxomil and other agents against recent clinical isolates. Penicillin-resistant and multi-drug resistant strains of *S. pneumoniae* remain prevalent among U.S. isolates from children aged 14 years or less during 2005-2006 despite widespread use of the pneumococcal vaccine. The highest resistance rates were seen in *S. pneumoniae* isolated from the youngest children aged two years or less. Faropenem medoxomil was the most active oral b-lactam based on in vitro susceptibility test results suggesting that further studies are warranted to determine clinical efficacy against pediatric respiratory tract infections. In light of the continued prevalence of antibiotic-resistance among U.S. pediatric respiratory tract isolates of *S. pneumoniae,* these data suggest that there is an unmet need for new and safe oral agents that are active against both penicillin-resistant and multi-drug-resistant strains.

Poster D-238, titled An Evaluation of Dried MIC Susceptibility Plate Compared to the CLSI (M7) Reference Broth Microdilution Method with the New Antimicrobial Agent, Faropenem.
The aim of the study was to show that a Sensititre® 18-24 hour dried susceptibility plate containing faropenem medoxomil was an accurate and reproducible method for testing bacterial isolates when compared with the CLSI (M7) reference broth microdilution method. Dried MIC panels provide a more convenient method for clinical laboratories to test faropenem medoxomil since they have a longer shelf life, are easier to transport to sites participating in clinical trials and can be used to test many different types of bacteria regardless of their growth medium requirements. Also, if clinical isolates are tested with a dried panel in clinical trials it is a regulatory requirement for a sponsor to demonstrate equivalency to the CLSI (M7) reference broth microdilution method.

Poster C2-214, titled Comparative Affinity of Faropenem to Penicillin Binding Proteins (PBPs) of Pneumococci with Varying Beta-Lactam Susceptibilities.
The objective of the study was to compare the affinities of faropenem medoxomil and other b-lactam agents (penicillin G, amoxicillin, cefuroxime and imipenem) for the PBPs of clinical isolates of *S. pneumoniae* with varying resistance profile (strains that were penicillin-susceptible, penicillin-intermediate, penicillin-resistant, macrolide-resistant and fluoroquinolone-resistant). Faropenem medoxomil exhibited the highest affinities for most of the PBPs (except PBP2X) from the different resistant strains when compared with the other b-lactam antibiotics. b-Lactam antibiotics with high affinity for selected PBPs are generally more rapidly bactericidal which generally means they can kill the bacterial cell more quickly. The potent antibacterial activity of faropenem medoxomil and

high-affinity for all PBPs (except PBP2X) suggests that faropenem medoxomil will retain important killing properties (bactericidal activity) against strains of *S. pneumoniae* that are both susceptible and resistant to currently marketed antibacterial agents.

The Company will present the following Faropenem posters on Monday, September 17, 2007 at 1:00 PM, Hall D:

Poster L-480, titled A Double-Blind, Randomized, Dose Ranging Study to Evaluate the Safety of Faropenem Medoxomil (FM) at 300 or 600 mg BID for Seven Days in Healthy Volunteers.

The primary objective of this trial was to evaluate the safety and tolerability of two doses of faropenem medoxomil, 300 mg BID and 600 mg BID. A secondary objective was to evaluate oral faropenem medoxomil pharmacokinetics. The results suggest that both faropenem medoxomil 300 mg and faropenem medoxomil 600 mg are safe and well tolerated. Faropenem medoxomil is active against the major pathogens responsible for community-acquired respiratory tract infections. These safety and pharmacokinetics data in healthy volunteers suggest that faropenem at a dose of 600 mg BID would be an appropriate candidate for further clinical development in adult patients.

Poster L-481, titled A Phase II Double-Blind, Randomized Trial Comparing Faropenem Medoxomil at 300 mg BID for Seven Days and 600 mg BID for Five Days in Subjects with Acute Maxillary Sinusitis Diagnosed by Antral Tap.

The focus of the tolerability assessment was on gastrointestinal adverse events of faropenem medoxomil 300 mg BID and faropenem medoxomil 600 mg BID. Clinical efficacy was a secondary endpoint. Gastrointestinal adverse events were similar in the two groups, 300 mg and 600 mg (14.9% and 14.7%, respectively). No unexpected adverse events were identified with the higher faropenem medoxomil dose. Clinical cure rates achieved with the faropenem medoxomil 600 mg dose were comparable to those achieved with the faropenem medoxomil 300 mg dose; however, the study was not powered for efficacy comparison. In this population of subjects with acute bacterial sinusitis (ABS), the two dosing regimens had similar safety and tolerability profiles. Combined with the Phase I comparison of the two dosing regimens (poster L-480), the higher 600 mg dosing regimen appears similar to the 300 mg dosing regimen. The higher dose will be used in future faropenem medoxomil Phase III clinical trials.

The Company will present the following Faropenem posters on Tuesday, September 18, 2007 at 11:15 AM, Hall D:

Poster G-980, titled Monitoring Changes in Susceptibility of Middle Ear Fluid (MEF), Nasopharyngeal (NP) and Oropharyngeal (OP) Pathogens to Faropenem in a Phase II Acute Otitis Media (AOM) Study.

The objective of the study was to monitor changes in the susceptibility of bacteria collected at visit 1 by comparing them with susceptibility results obtained on isolates collected at visit 2 and other subsequent visits to faropenem medoxomil. No differences in the susceptibility of middle ear fluid, nasopharyngeal or oropharyngeal isolates to faropenem medoxomil was detected in organisms persisting after days 4-6 in any subjects treated with any of the four doses. These data suggest faropenem medoxomil therapy did not appear to lead to any resistance development pressure on nasopharyngeal/oropharyngeal flora that may relocate to the middle ear causing recurrent Acute Otitis Media (AOM) with resistant organisms.

Poster G-983, titled Use of Parent-reported Outcome Measure in Acute Otitis Media Clinical Trials.

The objective of this study was to compare the rate of symptom resolution in children in two studies (one with tympanocentesis and one without) to examine the association between the AOM-Severity of Symptom scale and clinician assessment. A total of 328 subjects were included in the randomized study and 70 in the observational study. In the first 12 hours, there was reduction in the average score from 8.5 to 4.9 in the randomized trial and 6.4 to 4.8 in the observational study. The large early reduction in clinical score in the randomized study coincided with tympanocentesis. Differences in scores between clinical failures and clinical cures diagnosed by physician assessment appeared later and were smaller in the randomized study than the observational study. This study indicates that tympanocentesis has an immediate effect on AOM symptoms and alters the natural history of AOM. The utility of a PRO as a primary outcome in a study with tympanocentesis is limited.

Poster G-987, titled Dose-effect of Faropenem Medoxomil (FM) in the Treatment of Acute Otitis Media.

A total of 328 subjects were randomized to four treatments (7.5 mg/kg, 15, 30, 40) of faropenem medoxomil. The bacteriological response rates ranged from 55% in patients treated with 7.5 mg/kg to 94% in patients treated with 40 mg/kg. Differences in bacteriological eradication were most evident with *H. influenzae* infections. Eradication was 0 of 9 in subjects treated with 7.5 mg/kg, and 16 of 19 (84%) in subjects treated with 40 mg/kg. This study demonstrates the bacteriological and clinical effectiveness of faropenem medoxomil in the treatment of AOM. The study will provide critical data for dose selection in Phase III.

The Company will present the following Faropenem poster on Wednesday, September 19, 2007 at 11:15 AM, Hall D:

Poster A-1435, titled Pharmacokinetic-Pharmacodynamic (PK-PD) Assessment of Faropenem (FAR) in a Lethal Murine-Bacillus anthracis (BA) Inhalation Post-Exposure Prophylaxis Model.

Faropenem medoxomil has shown activity against anthrax disease development in the mouse model. In addition, a strong relationship was observed between dose and dose schedule and corresponding plasma concentrations of faropenem medoxomil with efficacy. This study demonstrates that faropenem medoxomil, currently being developed for community respiratory infections in adult and pediatric subjects, may be useful for prevention of anthrax disease development in the event of a bioterrorist attack. In addition, the relationship established between faropenem medoxomil plasma concentrations and efficacy provides an estimate for dose selection.

REP8839 Presentation

The Company will present the following REP8839 poster on Thursday, September 20, 2007 at 10:00 AM, Room E253D:

Poster F1-2116, titled *In vitro* Activity of REP8839 against Pasteurella species and Other Fastidious Bacteria Isolated from Infected Animal Bites in Humans.

The aim of the study was to further define the spectrum of activity of REP8839 against a collection of 101 fastidious Gram-negative organisms and *Streptococcus* species plus 117 anaerobic isolated from dog and cat bite wounds. REP8839 was active against some of the Gram-positive organisms such as the anaerobic peptostreptococci. Among the Gram-negative bacteria, *Bacteroides ureolyticus* and *Fusobacterium* species were quite susceptible. These results suggest that REP8839 may provide some additional coverage against some but not all pathogens isolated from animal bites in humans.

In accordance with General Instruction B.2. of Form 8-K, the information presented under this Item 7.01 shall not be deemed filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

Safe Harbor

The presentations discussed herein contain plans, intentions, objectives, estimates and expectations that constitute forward-looking statements about Replidyne, Inc. that involve significant risks and uncertainties. Actual results could differ materially from those discussed due to a number of factors including, the success and timing of pre-clinical studies and clinical trials; the Company s ability to obtain and maintain regulatory approval of product candidates and the labeling under any approval that may be obtained; plans to develop and commercialize product candidates; the loss of key scientific or management personnel; the size and growth of the potential markets for the Company s product candidates and the Company s ability to serve those markets; regulatory developments in the U.S. and foreign countries; the rate and degree of market acceptance of any future products; the accuracy of Company estimates regarding expenses, future revenues and capital requirements; the Company s ability to obtain and

maintain intellectual property protection for our product candidates; the successful development of the Company s sales and marketing capabilities; the success of competing drugs that are or become available; and the performance of third party manufacturers. These and additional risks and uncertainties are described more fully in the Company s Form S-1 and most recent periodic report filed with the SEC under the Securities Exchange Act of 1934. Copies of filings made with the SEC are available through the SEC s electronic data gather analysis and retrieval system (EDGAR) at www.sec.gov. All forward-looking statements made in the presentations discussed herein are made as of the date hereof and the Company assumes no obligation to update the forward-looking statements in the document.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REPLIDYNE, INC.

Dated: September 17, 2007

By: /s/ Mark L. Smith
Mark L. Smith
Chief Financial Officer
Principal Accounting Officer