March 31, 2014
Afternoon Testimony Before the FDA Anti-Infective Drugs Advisory Committee by Dr. Nida Degesys
NDA 021-883
AMSA and NPA

Good afternoon, I'm Nida Degesys, and I come before you today as a physician and representing over 40,000 physicians in training as the National President of the American Medical Student Association, and as a member of the National Physicians Alliance FDA Taskforce. I have no conflicts of interest to declare.

When I see a patient with a skin infection, whether it is cellulitis or an abscess, my primary sources of information are the patient and accurate culture results- which identify the pathogen and advise which if any antibiotics should be used based on the results of clinical trials in the types of patients I treat. For a clinician, accurate scientifically-valid reports of effectiveness are critical.

The approval that Durata Therapeutics is seeking for Dalbavancin are based solely on non-inferiority trials. Recent history points to the dangers of inappropriate clinical trials standards: even the FDA has acknowledged that improperly designed and conducted noninferiority trials cannot reliably distinguish effective drugs from placebo and some of these drugs have been linked to serious, sometimes fatal adverse events. Safety and effectiveness are only demonstrated with robust, reproducible evidence from adequate and well controlled clinical trials. Doctors and patients are not willing to accept more uncertainty in situations where other therapies exist, which is the setting in which non-inferiority trials are conducted.

While Durata Therapeutics will argue that they are providing a medication for an unmet need: a need for antibiotics against "resistant pathogens", they in fact do not address the issues of disease due to "resistant pathogens" at all, since dalbavancin was not studied to show superiority in disease due to resistant pathogens. Since there are already numerous medications available to treat MRSA skin infections, why are we considering the approval of another drug, one related to an older drug vancomycin, one that has NOT been shown to be better than what we currently have?

The company also makes claims that dalbavancin is better for patients because it can be given once a week, but this is a minor benefit for patients, since data shows that skin infections (including cellulitis) can be treated for as few as 5 days. A complete course of dalbavancin is two injections, requiring patients to return for an additional injection at Day 8, which is longer therapy than with currently available medications, and longer than the duration of therapy we saw this morning with tedizolid. This "improved convenience" is not clinically relevant since we don't have to treat skin infections for two weeks. Prolonged therapy will actually PROMOTE antibiotic resistance by giving drugs that are not necessary.

As was stated this morning, it is well documented that there is no benefit of antibiotics vs placebo in the treatment of skin abscesses when patients have incision and drainage of the abscess, even for MRSA suspected infections. 25% of patients in this trial had cutaneous abscesses, and the study compared dalbavancin to an ineffective control, vancomycin.

Dalbavancin, and this morning's drug tedizolid, received priority reviews and post-marketing exclusivity based on the GAIN Act yet the studies do not at all address the issues of providing better treatments for those with disease due to resistant pathogens. Why should the public pay more for longer for drugs whose added benefits are unclear? Why should FDA divert resource for priority reviews for drugs whose added benefit over available therapies is unclear? GAIN is providing incentives for drugs that do not address antibiotic resistance even though that was the reason for needing GAIN in the first place.

In summary, what we have here is a new drug that a) does not fill a new niche in terms of clinical need or even convenience; b) has only been studied in non-inferiority trials showing it is "not worse," but is not necessarily better or even as good as drugs we already have; and that c) could potentially have more side effects than our current standard drugs for same indications. If approved, dalbavancin will undoubtedly be marketed to me and my fellow physicians as a "novel approach" to treating resistant skin infections, including abscesses, which are better treated with simple I&D rather than antibiotics. And we physicians, seeing those words "FDA-approved" will believe we are offering our patients the latest and the greatest. I implore you as members of this panel to go back to your original

mission and ask, is it worth risking yet-unknown side effects of dalbavancin to give it market approval, when it has not been shown to be superior to our current antibiotic regimens? Or might expanding our antibiotic repertoire in this manner - without demanding adequate clinical trials - actually end up harming patients and even advancing the development of antibiotic resistance? We must insist that new drugs be studied in adequate controlled clinical trials in the clinically relevant populations and under the condition in which we need to use the new drugs. Thank you for listening.