Midway Pharmaceuticals, Inc.

Polymer Therapeutic Protects Gut from Radiation Damage, Infection after Cancer Treatment

- **High molecular weight PEG 15-20 Prevents Fusion of Cell Membrane "Lipid Rafts", Blocking Cell Death, Preventing Bacterial Sepsis, and Promoting Healing**
- **Midway Pharmaceuticals Plans Clinical Trials of PEG 15-20 Compound in 2010**

SPRING HOUSE, PA (December 3, 2009): A non-absorbed, oral co-polymer therapy under development by Midway Pharmaceuticals demonstrated the ability to protect against damage to healthy gastrointestinal tissues and to prevent lethal bacterial infections in animal models of radiation damage. The results suggest the compound, a high molecular weight co-polymer of polyethylene glycol (PEG), may provide a new way to prevent serious GI side effects of radiation in patients receiving fractionated radiotherapy for abdominal cancers or in accidental exposures to harmful radiation.

The new results are published online and in the December issue of the *American Journal of Physiology* by John Alverdy, MD, Director, Center for Surgical Infection Research, University of Chicago, Pritzker School of Medicine and colleagues at the University of Chicago, and University of Arkansas for Medical Sciences and Surgical Service. Dr. Alverdy is a founder of Midway Pharmaceuticals, an emerging specialty pharmaceutical company that is developing the polymer commercially for GI diseases, cancer supportive care and other indications.

"Radiation therapy for abdominal and pelvic cancers causes epithelial cell damage and inflammation to healthy intestinal cells, and by disrupting the epithelial barrier, can permit gut bacteria to invade the body and cause GI symptoms and lethal sepsis," said Dr. Alverdy. "We previously reported that a non-absorbed, high molecular weight PEG co-polymer (PEG 15-20) can prevent the adherence and possible invasion of *Pseudomonas aeruginosa* to the intestinal wall, preserve intestinal barrier function and prevent mortality in a mouse model of lethal sepsis caused by bacteria often found in the gut of seriously ill patients.

"This new study demonstrates that orally delivered PEG 15-20 can prevent intestinal injury following fractionated irradiation and lethal gut-derived sepsis in the case of high-doses of radiation. We found that PEG 15-20 achieved its protective effects in part by associating with lipid rafts in the epithelial cell membrane and preventing their coalescence and fusion, thus interfering with cell signaling pathways and limiting cell death by apoptosis, as well as promoting healing. Moreover, PEG 15-20 also attenuated *P. aeruginosa* virulence in response to secreted products from cultured intestinal epithelial cells exposed to radiation, and also physically distanced the bacterium away from the epithelial cell surface. At the same time, toxicity studies with PEG 15-20 have shown that the polymer is not systemically absorbed, and does not trigger diarrhea or any untoward effects on the health and growth of animals ingesting large doses for

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up to a month. Taken together, these findings provide compelling evidence that oral PEG 15-20 has the potential to be an effective agent against the complications of abdominal radiation."

He noted that animals receiving daily doses of water containing the PEG 15-20 demonstrated significantly lower radiation injury scores compared to controls. Moreover, treated mice challenged with *Pseudomonas aeruginosa* showed a 40% decrease in mortality compared to controls.

"Seventy percent of all cancer patients receive radiation therapy and it plays a critical role in 25% of cancer cures, " said co-author Martin Hauer-Jensen, MD, PhD, FACS Professor of Pharmaceutical Sciences, Surgery, and Pathology, and Director, Division of Radiation Health at the University of Arkansas for Medical Sciences. "Nonetheless, normal tissue toxicity remains the single most important obstacle to achieving an uncomplicated cancer cure, as radiation-induced injury to the GI tract is a critical dose-limiting factor during treatment of abdominal and pelvic tumors. PEG 15-20 appears highly protective against intestinal radiation injury in animal models, which provides a solid basis for future clinical studies in patients undergoing radiation therapy. These results also suggest that PEG 15-20 may be useful as a medical countermeasure after accidental radiation exposure or in the setting of radiologic terrorism."

"Preventing GI injury during cancer radiotherapy is a highly unsatisfied need and represents a potential $2.2 billion market opportunity," said Rifat Pamukcu, MD, President and Chief Executive Officer of Midway Pharmaceuticals. "We expect to begin clinical trials of MDY-1001, a proprietary form of PEG 15-20, as a potential radioprotectant in humans in 2010. Based on its effects on lipid raft fusion, we also believe this compound, and others in this new class of polymeric drugs, may have utility in a variety of additional clinical indications. These include infectious diarrheas, such as that associated with cholera, C. difficle and E. coli; treatment of other gastrointestinal conditions such as inflammatory bowel disease and irritable bowel syndrome; and prevention of life-threatening systemic infections by resident gut pathogens in immunocompromised patients, such as those undergoing chemotherapy, and the critically ill."

About Midway Pharmaceuticals
Midway Pharmaceuticals is an emerging pharmaceutical company focused on developing proprietary drugs for the treatment of gastrointestinal diseases. The company's platform technology capitalizes on the finding that certain high molecular weight polymers, taken orally but not systemically absorbed, can inhibit the pathogenic behavior of bacteria in the G.I. tract, enhance gut barrier function and promote intestinal healing. The company expects to be in Phase 1 trials in 2010 with its first drug candidate, MDY-1001, for the prevention of radiation enteritis, a dose-limiting side effect of cancer radiation therapy. For more information, please visit our website at http://www.midwaypharma.com.

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