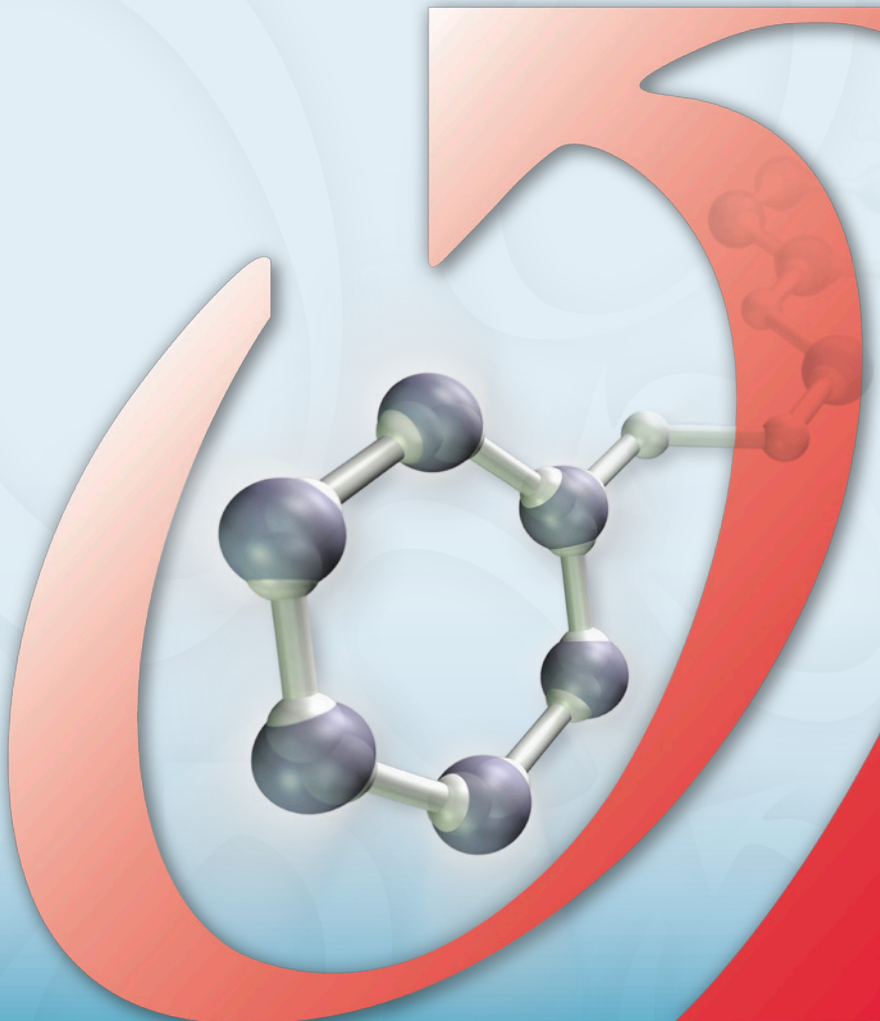
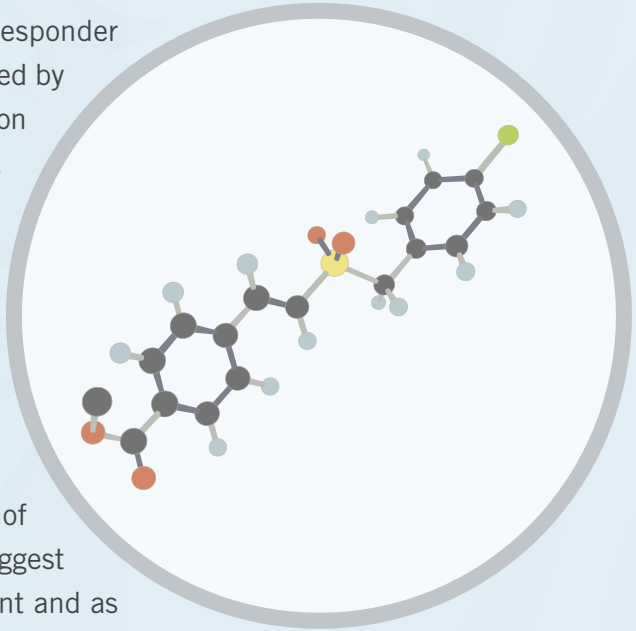
ONCONOVA

TARGETING CANCER | PROTECTING HEALTHY CELLS



Ex-RAD® (ON 01210.Na)

Ex-RAD provides protection from lethal ionizing radiation in animal models and has been associated with minimal observed adverse events in Phase I studies to date, positioning *Ex-RAD* for use in military or first responder personnel as these individuals cannot afford to be affected by performance-limiting adverse events. Unlike most radiation protectors, *Ex-RAD* is not a free-radical scavenger, chelator, or cell cycle arrestor. *Ex-RAD* employs a novel mode of action, involving the enhancement of internal DNA repair pathways, which significantly reduces levels of p53, p21, bax, c-abl and p73 proteins; key players in the DNA damage cascade induced upon exposure to harmful radiation. These effects likely cause a halt in cell death pathways and lead to increased recovery and survival of irradiated cells. The novel mechanisms of action with minimal side effects at effective dosage suggest that *Ex-RAD* could be useful both as a prophylactic agent and as an agent for mitigation. *Ex-RAD* is formulated for injection, and an oral formulation for broader use is currently being developed.



Radioactive contamination and injury from ionizing radiation can arise from accidents involving nuclear reactors and industrial or medical sources. Recent events have highlighted the potential for non-accidental radiation injury as a result of malicious, criminal, or terrorist actions. Pharmaceutical agents that prevent and repair cellular radiation damage can help in mitigating radiation injury. *Ex-RAD* development is initially focused on military applications and supported through a funded collaboration with the U.S. Department of Defense (DoD).

Ex-RAD is being developed under the FDA Animal Rule, wherein marketing approval for new countermeasures, for which human efficacy studies are not feasible or ethical, can be based on animal efficacy studies and safety data in healthy volunteers. Under this approval pathway, the FDA requires adequate, well-controlled efficacy studies in animal models that establish the drug product as reasonably likely to produce clinical benefit in humans. In multiple cell-based and whole animal models, *Ex-RAD* has demonstrated protection from radiation injury when administered either before or after radiation exposure, by subcutaneous or oral administration.

Onconova has completed four Phase I clinical studies with *Ex-RAD* in healthy volunteer subjects, three with *Ex-RAD* by injection and one using the oral formulation. Following subcutaneous administration, the drug was well-absorbed, reaching maximal blood levels in ~2 hours, with good local tolerance and no evidence of systemic side effects. *Ex-RAD* is currently suitable for subcutaneous injection or oral administration. Orally administered *Ex-RAD* is highly bioavailable and well tolerated.

Oral administration of a radiation protectant would provide increased patient compliance, ease-of-use and portability for at-risk population in the event of nuclear radiation incidents and emergencies. It could also serve as a therapeutic agent in radiotherapy by protecting healthy cells from the harmful effects of radiation when given to patients and healthcare providers exposed to scatter radiation as an occupational hazard.

For more information on
Onconova-sponsored clinical trials,
please visit **www.clinicaltrials.gov**
or **www.onconovatrials.com**

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