



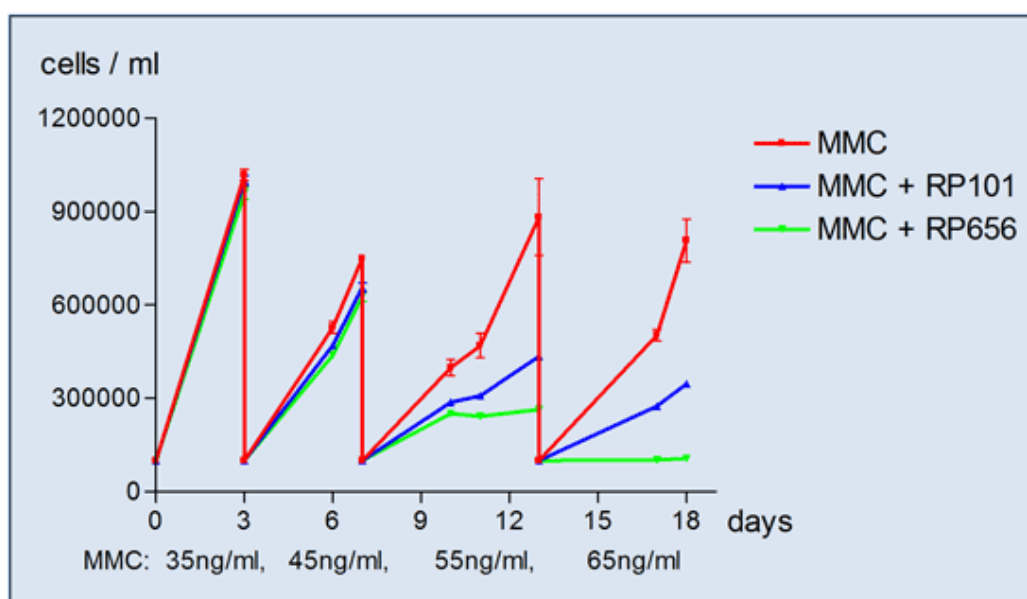
## 2nd Generation Product Candidates

Our goal in the development of follow-on compounds was to generate second generation derivatives of RP101 with significantly increased potency.

Over the past six years, new derivatives of RP101 have been identified and chosen for further evaluation. Like RP101, all are nucleosides, but the new candidates have been shown to be much more potent than RP101 in standard screening systems.

Three of the substances are **RP525**, **RP656**, and **RP7101** which were up to ten times more effective than RP101.

### Screening: effect in vitro



The figure shows the treatment of AH13 rat tumor cells with rising doses of the cytotoxic drug MMC (Mitomycin C) alone or in combination with RP101 or RP656.

The lead substance (E)-5-(2-bromovinyl)-deoxyuridine (RP101) is a 2'-deoxyuridine derivative, which is a thymidine analogue. All substances of the second generation are derivatives of RP101. They were stepwise designed for enhancing the resistance preventing effect in comparison to RP101 in our standard screening



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system. The target is the same as that of RP101, heat shock protein Hsp27.