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Anti-tumor activity of C-raf antisense—correction

To the editor—In March of 1998, our partner, Novartis Pharmaceuticals, informed us of several cases of data manipulation by a single individual scientist in the Novartis Research Department in Basel, Switzerland. This individual confessed to data manipulation that affected tumor xenograft results obtained with some of our antisense inhibitors, including part of the work presented in our report (*Nature Med.* **2**, 668–675; 1996) describing anti-tumor activity of a phosphorothioate antisense oligodeoxynucleotide targeted against C-*raf* kinase. The results presented in Figs. 5 and 7 of this article were generated under the supervision of this individual and, as such, may have affected the validity of some of the results described therein. Since the discovery of this incident, Novartis and Isis have jointly and aggressively worked to determine which experiments were affected and to repeat the key experiments as necessary. We can now report the results of that investigation.

Our report described a phosphorothioate oligodeoxynucleotide that in a highly specific manner inhibited expression of C-*raf* kinase in cell culture and in tumor xenograft models. We reported antiproliferative activity in cell culture and anti-tumor activity in animals against three tumor xenograft models (A549, T24 and MDA.MB231) at doses below 6 mg/kg per day. We can now confirm that all the *in vitro*, as well as the *in vivo* mRNA expression data, is accurate but that the data showing inhibition of tumor growth following administration of the C-*raf* antisense in tumor xenograft models is not (Figs. 5 and 7). That is, we are unable to confirm any *in vivo* anti-tumor activity of the C-*raf* antisense molecule under the conditions reported.

We have observed substantial anti-tumor activity against a range of tumor types in xenograft models after administration of the C-*raf* antisense. However, the doses required to achieve anti-tumor activity in these models are generally higher than that described in the earlier report (10–20 mg/kg compared with 0.6 mg/kg).

We deeply regret any confusion that this may have caused the scientific community and are eager to address any issues or problems stemming from our earlier report.

BRETT P. MONIA
Director, Molecular Pharmacology
Isis Pharmaceuticals, 2292 Faraday Ave.
Carlsbad, CA 92008, Email bmonia@isisph.com

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