We are publishing the following draft correction and clarification to Proc Natl Acad Sci U S A. 2007 Sep 4;104(36):14283-8. We are now working directly with the PNAS Editor to have this correction published by the journal as well.

The authors note that the text on page 14284, right column, in Results, line 6 from the bottom of the page, “An \( \approx 25 \)-fold increase in target expression levels at 5 mM theophylline, relative to those in the absence of effector, was observed in L2bulge1 (Fig. 2C and SI Fig. 8). In contrast, an \( \approx 18 \)-fold reduction in expression levels at 5 mM theophylline, relative to those in the absence of effector, was observed in L2bulgeOff1 (Fig. 2D and SI Fig. 8).” is incorrect. The corrected text should state the dynamic ranges of the L2bulge1 and L2bulgeOff1 switches as 25 and 18 “in fold”, respectively, with “in fold” as defined in the SI text (Materials and Methods).

Throughout the paper the expression levels from mRNA encoding each engineered riboswitch are reported relative to the level produced from an mRNA encoding the fully active ribozyme control, sTRSV, which defines a base expression level of 1 (SI Figs. 7, 13, SI text). Dynamic ranges are then reported as absolute changes in expression levels, which are calculated as the difference between the ‘on’ and ‘off’ expression levels from each ribozyme switch.

The magnitude of the absolute dynamic range for each switch is reported using the unit “in fold.” While this particular wording is consistent throughout the paper the authors regret that the usage of “in fold” in reference to an absolute change is atypical, and can lead to unnecessary confusion in interpreting the presented results.

The fold-change in riboswitch regulated expression levels, if defined using a direct numerical ratio of the ‘on’ and the ‘off’ levels as is often favored by the RNA biochemistry and other research communities, can be determined from the data presented in Figure 13 of the Supplementary Information. Most engineered constructs produce between a 1.4- to 2.4-fold-change in expression levels. The L2Bulge8- and L2cmd-based switches produce a 3-fold change in expression levels.

The authors believe that, for engineering purposes, the absolute change in expression levels can be a more effective measure for evaluating and comparing the dynamic ranges of riboswitches that exhibit different baseline expression levels because relative measures can be skewed by lower baseline expression levels. Along these lines, the authors believe that the most informative description of the performance of a riboswitch, which supports comparison to other riboswitches, is one in which activity is reported relative to the full potential dynamic range for that given construct. For riboswitches this would represent the gene expression levels in the absence of the reporter construct and from the reporter construct in the absence of the riboswitch (in this work, sTRSV and sTRSV Contl, respectively), thereby representing the full transcriptional range of the promoter system (see SI Fig. 13).

Overall, this important correction and further clarification should enhance the understanding of the work presented and does not impact the primary results or conclusions.