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## POTENTIAL NON-GROWTH USES OF rhIGF-I

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### INTRODUCTION

Recombinant human insulin-like growth factor (rhIGF)-I, singly or in combination with its binding protein (recombinant human IGF binding protein [rhIGFBP]-3), was recently approved by the U.S. Food and Drug Administration for the treatment of severe short stature (height <-3 standard deviations) caused by primary IGF-I deficiency. In addition to its role as the principal mediator of somatic growth in humans (together with growth hormone [GH]), IGF-I exerts multiple metabolic and organ-specific effects. IGF-I acts by binding the type 1 IGF receptor (IGF1R), an  $\alpha_2\beta_2$  transmembrane tyrosine kinase

receptor, leading to phosphorylation cascades involving the mitogen-activated protein (MAP) kinase pathway and the phosphoinositide 3 (PI3) kinase/Akt pathway and, through the latter, the mammalian target of rapamycin (mTOR) pathway. Growing appreciation for the pleiotropic actions of IGF-I has expanded its potential therapeutic usefulness beyond height enhancement. The ongoing trials to assess the role and efficacy of this agent and the current state of investigation regarding IGF-I in experimental models are shown in the Table. We herein review the highlights of some pertinent trials of the potential non-growth uses of rhIGF-I.

### ENHANCING INSULIN SIGNALING

The effects of rhIGF-I and rhIGF-I/rhIGFBP-3 have been studied in patients with type 1 diabetes (T1DM)<sup>1-5</sup> and type 2 diabetes (T2DM).<sup>6-9</sup> The rationale for the use of these agents in diabetes is based on the

### From The Editor's Desk

Dear Colleague:

In the first issue of 2007, volume 23 number 1, the lead article by Drs. Kim and Grimberg deals with a clinical experimental area of interest—namely, the non-growth uses of IGF-I currently under investigation. Most of the ongoing research trials in this field are at the pre-clinical stage. These protocols should be of academic interest to the readers of GGH; perhaps in the future, some of them may be of potential clinical application if proven safe and efficacious. I also want to bring to your attention a most interesting ethical dilemma posed by the paper "Growth Attenuation in Developmental Disabilities." This paper has been widely discussed in the media and lay press (ie, "A Convenient Truth" by Peter Singer, *The New York Times*, January 26, 2007) and in several blogs on the Internet. The lucid editorial comments by Dr. Sandberg bring forth the ethical considerations in a succinct manner. Please let me know if you have encountered similar situations and/or treated such patients.

The printed version of the journal includes 7 additional reviews and the online version includes 10 additional reviews of importance in the field. In addition, please note the the book review written by Dr. Robert Blizzard in the e-section of the journal. The book is titled *Size Matters: How Height Affects the Health, Happiness, and Success of Boys – and the Men They Become* by Stephen Hall (Houghton Mifflin, 2006). This book should be a great resource for you and your patients with short stature. There are few books like this one, although another that I have enjoyed and have recommended to my patients was written several years ago, *The Height of Your Life* by Ralph Keys (Warner Books, 1982).

Sincerely,  
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