Long Acting Growth Hormone

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Disclosures

• Past consultant for LG Life Sciences and Biopartners

• Advisor Ascendis Pharma
Growth Hormone Market

- Currently hGH is administered as daily injections, and the global market for daily hGH replacement products exceeds $3 billion.

- The daily hGH market is fragmented and undifferentiated: Novo Nordisk, Pfizer, Eli Lilly, Sandoz, Merck KGaA and Roche account for approximately 95% of volume market share.

- Pediatric indications comprise up to 90% of the market:
  - Growth Hormone Deficiency (GHD)
  - Turner Syndrome (TS)
  - Idiopathic short stature (ISS)
  - Prader-Willi Syndrome (PWS)
  - Small for Gestational Age (SGA)

[Chart showing distribution of pediatric indications: GHD: 51%, TS: 18%, ISS: 19%, PWS: 7%, SGA: 2%, Other Indications: 3%]
Concerns regarding long acting GH

- Is long acting GH physiologic?
- GH is secreted throughout the day in 6 to 8 discrete peaks
- Concerns about long acting GH?
- Does it lead to unphysiologically high GH and/or IGF-1 levels.
- Does it affect bone maturation, carbohydrate tolerance, antibody formation?
- Is the growth velocity as good as with daily GH?
Is Daily rhGH “Natural”?  
Current Replacement Therapy in Pediatric GHD

24 Hour Serum GH Profiles

- GHD Mean
- Normal
- 0.043 mg/kg

Slide courtesy of Dr. Paul Fielder
Compliance and Persistence

• A major cause of failure of growth hormone (GH) therapy can be patient noncompliance and non-persistence with the prescribed regimen.

• Steady decline in persistence rates within first 11 months of GH treatment, to 67% in pediatric patients and 54% in adults. (unpublished data Caremark, Inc. Birmingham, Al, January to December 2005)

• Only 44% of pediatric patients, initiated in 1997, remained on therapy after 4 years
  – Declining to 20% for 4-year persistence rate for those that began GH therapy at the same age in 2001
  (unpublished data, NCGS, Genentech, Inc., South San Francisco, CA, Jan 1, 2006)

Rosenfeld R., Bakker B.; Compliance and persistence in pediatric and adult patients receiving growth hormone therapy; Endocrine Practice Vol 14 No 2 March 2008.
Adherence to Medication

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

Adherence to Medication

Lars Osterberg, M.D., and Terrence Blaschke, M.D.

Drugs don't work in patients who don't take them.

— C. Everett Koop, M.D.

Adherence to (or compliance with) a medication regimen is generally defined as the extent to which patients take medications as prescribed by their healthcare providers. The word “adherence” is preferred by many healthcare providers, because “compliance” suggests that the patient is passively following the doctor’s orders and that the treatment plan is not based on a therapeutic alliance or contract established between the patient and the physician. Both terms are imperfect and uninformative descriptions of medication-taking behavior. Unfortunately, applying these terms to patients who do not consume every pill at the desired time can stigmatize these patients in their future relationships with healthcare providers. The language used to describe how patients take their medications needs to be reassessed, but these terms are still commonly used. Regardless of which word is preferred, it is clear that the full benefit of the many effective medications that are avail-

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Adherence to Medication

**Development rationale for a sustained release product:**
- Better patient compliance through less frequent dosing
- Comparable efficacy and safety profile to daily hGH products

**Ideal target:**
- Once-a-week subcutaneous injection

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**Table 3. Strategies for Improving Adherence to a Medication Regimen.**

<table>
<thead>
<tr>
<th>Identify poor adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Look for markers of nonadherence: missed appointments (“no-shows”), lack of response to medication, missed refills</td>
</tr>
<tr>
<td>Ask about barriers to adherence without being confrontational</td>
</tr>
<tr>
<td>Emphasize the value of the regimen and the effect of adherence</td>
</tr>
<tr>
<td>Elicit patient’s feelings about his or her ability to follow the regimen, and if necessary, design supports to promote adherence</td>
</tr>
<tr>
<td>Provide simple, clear instructions and simplify the regimen as much as possible</td>
</tr>
<tr>
<td>Encourage the use of a medication-taking system</td>
</tr>
<tr>
<td>Listen to the patient, and customize the regimen in accordance with the patient’s wishes</td>
</tr>
<tr>
<td>Obtain the help from family members, friends, and community services when needed</td>
</tr>
<tr>
<td>Reinforce desirable behavior and results when appropriate</td>
</tr>
<tr>
<td>Consider more “forgiving” medications when adherence appears unlikely†</td>
</tr>
<tr>
<td>Medications with long half-lives</td>
</tr>
<tr>
<td>Depot (extended-release) medications</td>
</tr>
<tr>
<td>Transdermal medications</td>
</tr>
</tbody>
</table>

Poor compliance reduces treatment outcomes

- Poor compliance with daily growth hormone therapy is associated with reduced height velocity and impaired quality of life\(^1\)
  - Two out of three of the patients miss more than one injection on average per week

- Once-weekly TransCon Growth Hormone may improve compliance and overall treatment outcomes

\(^1\) PLoS ONE 2011, 6(1), e16223
Adherence to Medication

• Maintaining full compliance with daily injections has been difficult for many patients and dose omissions occur frequently
• In children lack of compliance with daily GH has been associated with significantly diminished growth velocities
• A long acting GH may reduce dosing frequency, improve compliance and improve overall treatment outcomes.

Cutfield WS et al. PLoS One 2011, 6 (1), 6223
Low Treatment Adherence in Pubertal Children Treated with Thyroxin or Growth Hormone

Nina Lass  Thomas Reinehr

Department of Pediatric Endocrinology, Diabetes and Nutrition Medicine, Vestische Hospital for Children and Adolescents Datteln, University of Witten/Herdecke, Datteln, Germany
**Results:** The correlation between recorded TA and calculated TA based on prescription refill rates was very good ($p < 0.001$, $r = 0.83$). TA was lower ($p < 0.01$) in pubertal children compared to prepubertal children and in children self-administering their medication compared to those whose drug was administered by their parents, both in GH- and thyroxin-treated children. Overall, 67% of the pubertal children treated with GH and 58% of the pubertal children treated with thyroxin missed at least 1 dose per week. TA was higher ($p < 0.001$) in children with thyroxin treatment compared to children treated with recombinant human GH (8 vs. 26% missed >3 doses/week).
Long Acting Growth Hormone

• As early as 1979 Lippe et al studied the use of gelatin for the creation of a somatotropin gel to be used as a depot formulation. The preparation failed to achieve satisfactory systemic GH concentrations

• Lippe B, Frasier SD, Kaplan SA Use of a GH - gel Arch Dis Child 1979, 54: 609-13
Encapsulation of peptides

• Encapsulation of peptides in biodegradable microcapsules or microspheres is done using poly lactic glycolic acid (PLGA) and use of zinc ions as stabilizers to enhance monomeric release of GH from the microspheres

Long Acting GH

• Improved sustained release GH preparations will need further study of their long term efficacy, but if successful, they will be highly attractive in terms of patient compliance and convenience.

Jostel A, Shalit SM. Trends Endocrinol 2006, 6: 139-45
<table>
<thead>
<tr>
<th>Table 1</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Long-acting growth hormone formulations.</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Product</strong></td>
<td><strong>Current status</strong></td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Depot formulations</strong></td>
<td></td>
</tr>
<tr>
<td>Nutropin Depot</td>
<td>No longer available</td>
</tr>
<tr>
<td>LB03002</td>
<td>Approved in Europe</td>
</tr>
<tr>
<td>PEG-GH PHA-794428</td>
<td>No longer in development</td>
</tr>
<tr>
<td>NN4126-0083</td>
<td>No longer in development</td>
</tr>
<tr>
<td>ARX201</td>
<td>No longer in development</td>
</tr>
<tr>
<td>Jintrolong</td>
<td>Marketed in China for childhood GHD</td>
</tr>
<tr>
<td>BBT-031</td>
<td>Preclinical studies only</td>
</tr>
<tr>
<td>CP-016</td>
<td>Preclinical studies only</td>
</tr>
<tr>
<td><strong>Pegylated formulations</strong></td>
<td></td>
</tr>
<tr>
<td>ACP-001/TransCon</td>
<td>Phase 2 in children, Phase 2 in adults</td>
</tr>
<tr>
<td>NNC0195-0092</td>
<td>Phase 2 in children, Phase 3 in adults</td>
</tr>
<tr>
<td><strong>Prodrug formulations</strong></td>
<td></td>
</tr>
<tr>
<td>TV-1106</td>
<td>Phase 2 and 3 in adults</td>
</tr>
<tr>
<td>MOD-4023</td>
<td>Phase 2 in children, phase 3 in adults</td>
</tr>
<tr>
<td>LAPSrhGH/HM</td>
<td>Phase 2 in adults</td>
</tr>
<tr>
<td>10560A</td>
<td>Phase 2 in children, Phase 3 in adults</td>
</tr>
<tr>
<td>VRS-317</td>
<td>Phase 2 in children, Phase 3 in adults</td>
</tr>
<tr>
<td>GX-H9</td>
<td>Phase 2 in adults</td>
</tr>
<tr>
<td>ALTU-238</td>
<td>No longer in development</td>
</tr>
<tr>
<td><strong>GH fusion protein technology</strong></td>
<td></td>
</tr>
<tr>
<td>Profuse GH</td>
<td>Preclinical studies only</td>
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</tbody>
</table>
Growth Hormone Research Society perspective on the development of long-acting growth hormone preparations

Jens Sandahl Christiansen¹*, Philippe F Backeljauw², Martin Bidlingmaier³,⁴, Beverly M K Biller⁵, Margaret C S Boguszewski⁶, Felipe F Casanueva⁷, Philippe Chanson⁸, Pierre Chatelain⁹, Catherine S Choong⁴, David R Clemons¹⁰, Laurie E Cohen¹¹, Pinchas Cohen¹², Jan Frystyk¹, Adda Grimberg¹³, Yukihiro Hasegawa¹⁴, Morey W Raymond¹⁵, Ken Ho¹⁶, Andrew R Hoffman¹⁷,⁸, Jeff M P Holly¹⁸, Reiko Horikawa¹⁹, Charlotte Höybye²⁰, Jens Otto L Jorgensen¹, Gudmundur Johannsson²¹, Anders Juul²², Laurence Katznelson²³, John J Kopchick²⁴, K O Lee²⁵, Kuk-Wha Lee²⁶, Xiaoping Luo²⁷, Shlomo Melmed²⁸, Bradley S Miller²⁹, Madhusmita Misra³⁰, Vera Popovic³⁰, Ron G Rosenfeld³¹, Judith Ross³², Richard J Ross³³, Paul Saenger³⁴, Christian J Strasburger³⁵, Michael O Thorner³⁶, Haim Werner³⁷ and Kevin Yuen³⁸

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Correspondence should be addressed to A R Hoffman

Email
Pharmacokinetics of Nutropin Depot™ in Pediatric GHD

Tmax ~ 0.5-0.6 days
Cmin ~ ? days

0.75 mg/kg subcutaneous injection (n=12)
1.5 mg/kg subcutaneous injection (n=8)

Mean±SD

Initial Release Phase (Days 0-2)
Sustained Release Phase

Slide kindly provided by Dr. Paul Fielder
EO Reiter et al. JCEM 2001

**Nutropin Depot** in prepubertal children

1.5 mg/kg once monthly (n=36)
0.75 mg/kg twice monthly (n=38)

n=69 (93%) completed 6 months
n=61 elected to continue
n=56 completed 12 months

<table>
<thead>
<tr>
<th>Pretreatment growth rate (n=69)</th>
<th>4.5+/−2.3 cm/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months annualized growth rate (n=69)</td>
<td>8.4+/−2.1 cm/yr</td>
</tr>
<tr>
<td>12 months growth rate (n=56)</td>
<td>7.8 cm/yr</td>
</tr>
</tbody>
</table>
Nutropin Depot (Genentech)

Nutropin Depot is no longer available. Genentech cited significant resources required for its manufacture as the reason for the discontinuation of the drug.

Genentech 2004 press release July 7 2004, online
LB03002 – A Once-Weekly Formulation of rhGH
Co-developed by LG Life Sciences and Biopartners GmbH

- **Biohydrix**: *LGLS’ proprietary extended release platform technology*
  - Biocompatible hyaluronic acid matrix
  - Naturally biodegradable, safe, high degree of bioavailability

- **Composition of LB03002**
  - Solid microparticles: hGH, HA (sodium hyaluronate) and lecithin
  - Injection vehicle: medium-chain triglycerides (MCT)
PKPD / Dose-finding study

Pharmacokinetics

PKPD / Dose-finding study

Pharmacodynamics

LB03002: Pharmacokinetics in Children

• No accumulation of hGH with LB03002 given once-a-week over the dose range studied
• Dose proportionality across the three LB03002 doses (AUC)

Source: Saenger et al, Horm Res 2009; 72 (suppl 3) FC10-002
LB03002: IGF-1 in PGHD 24 months

Source: Saenger et al, Horm Res 2011; 76 (suppl 2) P1-d3-291
## LB03002: Efficacy in PGHD - 12 and 24 months

<table>
<thead>
<tr>
<th></th>
<th>First year treatment</th>
<th>Weekly treatment</th>
<th>Daily treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=87)</td>
<td>(N=80)</td>
<td></td>
</tr>
<tr>
<td><strong>HV (cm/yr)</strong></td>
<td>Baseline</td>
<td>2.64 ± 1.11</td>
<td>2.87 ± 1.04</td>
</tr>
<tr>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; year</td>
<td>11.72 ± 2.58</td>
<td>12.16 ± 3.09</td>
</tr>
<tr>
<td></td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; year</td>
<td>8.33 ± 1.92</td>
<td>7.28 ± 2.34</td>
</tr>
<tr>
<td><strong>HVSIDS</strong></td>
<td>Baseline</td>
<td>-3.23 ± 1.52</td>
<td>-3.09 ± 1.52</td>
</tr>
<tr>
<td></td>
<td>Month 12</td>
<td>5.74 ± 3.35</td>
<td>6.26 ± 3.66</td>
</tr>
<tr>
<td></td>
<td>Month 24</td>
<td>2.21 ± 1.89</td>
<td>1.47 ± 1.92</td>
</tr>
<tr>
<td><strong>Δ HTSIDS</strong></td>
<td>Baseline - Month 12</td>
<td>1.39 ± 0.66</td>
<td>1.44 ± 0.73</td>
</tr>
<tr>
<td></td>
<td>Baseline - Month 24</td>
<td>1.95 ± 0.92</td>
<td>1.92 ± 0.95</td>
</tr>
<tr>
<td><strong>Bone maturation (BA/CA)</strong></td>
<td>Month 12</td>
<td>0.69 ± 0.16</td>
<td>0.68 ± 0.19</td>
</tr>
<tr>
<td></td>
<td>Month 24</td>
<td>0.78 ± 0.18</td>
<td>0.77 ± 0.18</td>
</tr>
</tbody>
</table>

* p-value (two-sample t-test) for group comparison

Source: Saenger et al, Horm Res 2011; 76 (suppl 2) P1-d3-291
## Comparison to KIGS Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LB03002</th>
<th>KIGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>7.82 ± 2.5</td>
<td>7.10 ± 3.3</td>
</tr>
<tr>
<td>Bone age (years)</td>
<td>4.35 ± 2.2</td>
<td>5.1 ± 3.0</td>
</tr>
<tr>
<td><strong>Height velocity (cm/year)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2.69 ± 1.1</td>
<td>4.9 ± 2.0</td>
</tr>
<tr>
<td>Month 12</td>
<td>11.63 ± 2.6</td>
<td>9.1 ± 2.7</td>
</tr>
<tr>
<td><strong>Height SDS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>- 4.34 ± 1.8</td>
<td>-3.5 ± 1.1</td>
</tr>
<tr>
<td>Month 12</td>
<td>- 3.06 ± 1.5</td>
<td>-2.6 ± 1.1</td>
</tr>
</tbody>
</table>

Conclusions

• LB03002 achieved comparable height velocity with daily rhGH at doses of 0.5 and 0.7 mg/kg/week

• 0.5 mg/kg/week was selected for phase III

• Dose proportionality across the three LB03002 doses (AUC)

• No accumulation of hGH or IGF-1 with LB03002 given once-weekly over the dose range studied
Phase III / Safety and Efficacy

- Glucose and Fat metabolism
- HbA1c within normal range in all patients at all visits
- Fasting glucose and insulin showed no significant difference in changes between treatment groups
- Total cholesterol and triglycerides showed no significant difference in changes between treatment groups
VRS-317: Construct

Designed to improve PK, reduce clearance

110 hr half-life in monkeys

hGH = 22 kDa
VRS-317 = 119 kDa
The graph shows the mean annualized height velocity for different treatment regimens. The regimens are:

- 5.0 mg/kg monthly (n = 23)
- 2.5 mg/kg semimonthly (n = 19)
- 1.15 mg/kg weekly (n = 21)

The height velocities are as follows:

- 5.0 mg/kg monthly: 8.15 cm/yr
- 2.5 mg/kg semimonthly: 8.28 cm/yr
- 1.15 mg/kg weekly: 9.21 cm/yr
- 7.83 cm/yr (Age-Matched Historical Control)
Opko/Pfizer

• GH is modified at the C terminus peptide (CTP)

CTP of the beta chain of hCG was shown to account for the long half life of hCG compared to LH which has a similar sequence but lacks the CTP moiety. CTP was created during evolution to provide hCG with the longevity required to maintain pregnancy

Prolor is hGH protein fused to one copy of CTP at the N terminus and two copies at the C terminus
### Annualized Height Velocity Results

**6m Annualized Height Velocity – All Patients Completing 6m Treatment (35)**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose</th>
<th>hGH Content</th>
<th>N</th>
<th>Mean (cm/year)</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td>0.25 mg/kg/w MOD-4023</td>
<td>0.18 mg/kg/week</td>
<td>9</td>
<td>13.48</td>
<td>2.71</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>0.48 mg/kg/w MOD-4023</td>
<td>0.35 mg/kg/week</td>
<td>9</td>
<td>12.25</td>
<td>2.64</td>
</tr>
<tr>
<td>Cohort 3</td>
<td>0.66 mg/kg/w MOD-4023</td>
<td>0.48 mg/kg/week</td>
<td>10</td>
<td>14.37</td>
<td>5.26</td>
</tr>
<tr>
<td>Cohort 4</td>
<td>0.034 mg/kg/d Genotropin</td>
<td>0.21 mg/kg/week</td>
<td>7</td>
<td>15.46</td>
<td>2.68</td>
</tr>
</tbody>
</table>
Annualized 1\textsuperscript{st} Year HV – MOD-4023
Excellent Catch Up Growth Compared to Historical Data

\begin{itemize}
  \item Cohort 1
  \item Cohort 2
  \item Cohort 3
\end{itemize}
Phase 2 Preliminary Results – Summary & Perspectives

• All doses provided excellent catch-up growth response compared to control group and historical controls
• Promising safety profile to date (36 patients completing 6m and 16 patients completing 12m)
• Preliminary statistical analysis indicates that there are no statistically significant differences between the cohorts
• MOD-4023 mean annualized HV at 6m ranged from 12.25 -14.37cm, compared to annual HV of ~10 cm as published by Bakker (2008) and Ranke (2010) for the same GHD patient population (peak GH, age).

Based on the PK, PD and efficacy results - MOD-4023 supports once-weekly administration to pediatric GHD patients.
TRANSCON LINKER DESIGN

- TransCon linkers consist of three elements:
  - Transient covalent bond to the parent drug
  - Activation group
  - Permanent covalent bond to the carrier

- TransCon linkers release an active unmodified parent drug based only on conditions of pH and temperature

- The activation group controls initiation and rate of linker hydrolysis

- After active parent drug release, the linker remains permanently attached to the carrier and is primarily eliminated by renal excretion
ONCE-WEEKLY TRANSCON GROWTH HORMONE

- The daily growth hormone market is a $3+ billion specialty market

- Current therapies require daily injections, which results in poor compliance and suboptimal treatment response\(^1\)

- TransCon growth hormone is a long-acting prodrug designed to be inactive at the injection site and release unmodified growth hormone in the bloodstream
  - Maintains the same mode-of-action as endogenous and daily hGH
  - Efficacy, safety, tolerability and immunogenic profile comparable to daily hGH

- Phase 2 study in adults with growth hormone deficiency: Comparable dose response and tolerability to daily growth hormone therapy

- Phase 2 study in children with growth hormone deficiency ongoing
  - Interim results October 2014, top-line results H1 2015
PHASE 2 IN GHD CHILDREN ONGOING

- Six month Phase 2 study in GHD children of ACP-001 vs. daily hGH
  - Multicenter, randomized, open label, active-controlled, parallel-group study investigating the safety, tolerability and efficacy in pre-pubertal children with GHD (n=52)
  - Primary efficacy endpoint: 6 month mean height velocity
  - Enrolling children that meet internationally recognized guidelines, similar enrollment criteria will be used in Phase 3 design
  - Doses of 0.14 mg, 0.21 mg and 0.30 mg hGH/kg/week administered once-weekly versus daily hGH equivalent to 0.21 mg hGH/kg/week

- Study being conducted across Europe and North Africa

- Interim analysis in October 2014: Annualized height velocity based on 3 month data on 50% of patients

- Top-line data expected in H1 2015
Excellent dose response for IGF-I

IGF-I SDS (Mean) – Week 1 and week 13

- TransCon hGH (0.14 mg/kg/wk)
- TransCon hGH (0.21 mg/kg/wk)
- TransCon hGH (0.30 mg/kg/wk)
Mean Annualized Height Velocity at 13 weeks

0.14 mg rhGH/kg/week
TransCon Growth Hormone

0.21 mg rhGH/kg/week
TransCon Growth Hormone

0.30 mg rhGH/kg/week
TransCon Growth Hormone

0.21 mg rhGH/kg/week
Genotropin®
Change in HV SDS from Screening to 13 weeks

![Bar chart showing the mean change in HV SDS from screening to 13 weeks for different doses of rhGH/kg/week. The chart includes bars for 0.14 mg rhGH/kg/week TransCon Growth Hormone, 0.21 mg rhGH/kg/week TransCon Growth Hormone, 0.30 mg rhGH/kg/week TransCon Growth Hormone, and 0.21 mg rhGH/kg/week Genotropin®. ]
What are requirements for a successful long acting growth hormone?

• Same growth rate as with daily GH
• Small needle, preferably 31 g
• Small injection volume
• Suitable for use with a pen device
• Side effects not any more than daily GH
• IGF -1 levels similar as with daily GH
• Same price as daily GH
On 30 May 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Somatropin Biopartners, 2 mg, 4 mg, 7 mg, 10 mg and 20 mg, powder and solvent for prolonged-release suspension for injection intended for long-term treatment of growth failure in children and adolescents due to insufficient secretion of endogenous growth hormone, and as replacement therapy of endogenous growth hormone in adults with growth-hormone deficiency (GHD). The applicant for this medicinal product is BioPartners GmbH. It may request a re-examination of the CHMP opinion, provided it notifies the European Medicines Agency in writing of its intention within 15 days of receipt of the opinion.
Long acting GH for replacement therapy

- Currently available data suggest that long acting GH is even further away from the normal pulsatile secretory pattern than daily GH is efficacious and safe.

- Future data on metabolism and safety will further support its place in the management of GH replacement in adults and treatment of GH deficient children because patient preference is high for these products.

Johannsson G. Editorial, JCEM June 2011 96 : 1668-70
Goal of therapy: Restore therapeutic hGH levels

- The goal of growth hormone therapy is to restore growth hormone levels to therapeutic levels without inducing supraphysiological levels of either hGH or IGF-I
  - Daily hGH therapy has been optimized to provide maximum plasma levels of 15-20 ng/mL in pediatric GHD and ~2 ng/mL for AGHD
A Growth Hormone Research Society Perspective on Long-Acting Growth Hormone Development

• **Conclusions.** LAGH compounds may represent an advance over daily GH injections because of increased convenience, providing the potential for improved adherence and outcomes. Better methods to assess adherence must be developed and validated. Long-term surveillance registries that include assessment of efficacy, cost-benefit, disease burden, QoL, and safety are essential for understanding the impact of chronic exposure to all preparations of LAGH.
Thank you