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BAXTER HEALTHCARE SA  BAXTER INTERNATIONAL  BECTON DICKINSON
BEIJING JINGJING MEDICAL  BIOGEN IDEC  BIOTEST
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DYAX  GRIFOLS  GW IP
HAEMONETICS  HANMI SCIENCE  ISIS PHARMACEUTICALS
KAMADA  KEDRION  NOVOZYMES BIOPHARMA
OCTAPHARMA  OCTAPHARMA USA  PPTA
Sangamo BioSciences  SANQUIN  SHANGHAI RAAS BLOOD PRODUCTS
SunCoast Blood Bank  TONROL BIO-PHARMACEUTICAL
BUSINESS BRIEFS

* For the first half of its fiscal year 2015 ended December 31, 2014, CSL reported that sales of its CSL BEHRING division increased 8% from $2.357 billion to $2.492 billion, driven by 16% growth in albumin sales at constant currency (CC) from $313 million to $358 million and 13% growth in sales of specialty plasma products at CC (e.g. Kcentra, Berinert P) from $403 million to $443 million. The jump in albumin sales was attributable primarily to strong demand growth in China.

Immunoglobulin (Ig) sales rose by 5%, from $1.085 billion to $1.122 billion; this result reflected 11% growth in Ig unit sales offset by changes in the geographic mix that adversely affected average sales price. In particular, the company reported strong growth in Europe following approval of an indication for chronic inflammatory demyelinating polyneuropathy (CIDP) in 2013.

Intravenous immunoglobulin (IVIG) accounted for 27% of total revenue, followed by albumin (12%), plasma-derived coagulation products (9%), recombinant factor VIII (9%), subcutaneous immunoglobulin (SCIG) (9%), specialty perioperative products (7%), other specialty products (9%) and hyperimmune globulins (4%). Pharmaceuticals, vaccines and other products made up the balance of 12% of revenues.

CSL reported initiation of a Phase III clinical study of Beriplex, its four-factor prothrombin complex concentrate, in Japan, and the commencement of a Phase IIb clinical study to evaluate the safety and tolerability of “CSL112,” an investigational reconstituted high-density lipoprotein, in 1200 acute myocardial infarction patients; data from a recently completed Phase IIa study supports the proposed mechanism of action and further development, according to the company.

* KAMADA has posted full-year 2014 revenues of $71.9 million, up slightly from $70.6 million in 2013. Gross profit for the Israeli manufacturer of human alpha1-proteinase inhibitor (AAT) products declined to $15.6 million from $26.4 million in 2013, with gross margin dropping to 22% from 37%. Excluding a $4.5 million milestone payment in 2013 and an extraordinary $3.0 million inventory write-off in 2014, gross profit for 2014 decreased to $18.6 million from $21.9 million in the prior year.

An operating loss of $10.0 million in 2014 contrasts with operating income of $3.7 million in 2013. A net loss of $12.6 million compares with a net income in 2013. Cash and short-term investments stood at $51.9 million as of December 31, 2014, compared with $74.2 million at year-end 2013. The company used $9.9 mil-lion to fund operations, $3.1 million for capital expenditures and $7.7 million for re-payment of convertible debt.

Kamada has recently reported “positive data” from its ongoing open-label Phase 1/2 clinical trial extension study of its intravenous AAT to treat pediatric patients with recently diagnosed type 1 diabetes; interim data were also presented from a Phase 1/2 clinical study of its AAT for the treatment of graft versus host disease (GVHD) at the American Society of Hematology annual meeting last December.
* In Brazil, the Federal Ministry of Health awarded the following contracts under a December 2014 tender for 2015 delivery:

<table>
<thead>
<tr>
<th>Product, presentation (supplier)</th>
<th>Quantity</th>
<th>Price (R$)</th>
<th>Price ($)</th>
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<tr>
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<td>100,000</td>
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<tr>
<td>Intravenous immunoglobulin, 5g (Octapharma)</td>
<td>160,000</td>
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<tr>
<td>Intravenous immunoglobulin, 5g (Sanquin)</td>
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<td>Factor VIII, per IU (Grifols)</td>
<td>120,000,000</td>
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<td>$0.096</td>
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<tr>
<td>Factor VIII, per IU (CSL Behring)</td>
<td>60,000,000</td>
<td>0.275</td>
<td>$0.096</td>
</tr>
</tbody>
</table>

* SHANGHAI RAAS BLOOD PRODUCTS announced that its full year 2014 net profit jumped 255% to 510.9 million Chinese Yuan Renminbi (CNY) ($82 million) over the previous year, reflecting both organic growth and profit contributions of a number of recent acquisitions, including BANGHE PHARMACEUTICALS and TONROL BIO-PHARMACEUTICAL. Several of these strategic acquisitions were related to the plasma industry, while others involved companies unrelated to the biopharmaceutical industry. Total company turnover in 2014 was CNY 1,319,735,230 ($211.4 million).

As a result of its recent acquisitions, Shanghai RAAS now owns and operates 28 plasma collection centers – 16 more than two years ago – and has increased its plasma collection capacity from 400 to 900 metric tons annually. Altogether, approximately 5,000 metric tons (about five million liters) of human plasma were collected in China in 2013, as well as 4,000 tons of whole blood.

The company’s plasma products portfolio has expanded from seven to eleven human therapeutics over that same period. According to Shanghai RAAS’ 2014 annual report, the company plans to increase its plasma products footprint both domestically and internationally over the next five years, with the intent to capitalize on the fact that the Chinese government has not licensed any new plasma fractionation facility since 2001.

* BIOTEST announced that full-year 2014 revenues increased by 16.2% to €582.0 million ($652 million) compared to €500.8 million ($561 million) for the previous year. The company attributed this revenue growth in part to success in gaining market shares, particularly in Middle Eastern and Far Eastern countries.

As a result of higher research and development costs, additional expenses relating to a planned production capacity expansion at the headquarters location in Dreieich, and overall lower profit margins notably attributable to “crisis regions,” Biotest’s earnings before interest and tax (EBIT) came in at €53.4 million ($59.8 million), matching the EBIT result (€53.8 million) for 2013. Complete financial results and the company’s annual report will be released on March 24.
* OCTAPHARMA USA has announced a new financial support program for U.S. patients who are currently receiving Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]), or have a prescription to begin Wilate therapy. The new “Octapharma Co-Pay Assistance Program” offers eligible patients a maximum of $6,000 annually for co-payment, co-insurance and deductible expenses associated with their treatment without regard for their ability to pay. Patients must have third-party commercial insurance to participate in the program.

“We realize that patient out-of-pocket expenses associated with healthcare can sometimes be daunting, therefore, Octapharma has committed to support a program specifically designed to supplement these costs,” a senior Octapharma official said in a prepared statement.

* Less than three weeks after U.S. marketing approvals of its INTERCEPT Blood System for platelets and plasma, CERUS has announced the pricing of an underwritten public offering of 12,727,273 shares of its common stock, offered at $5.50 per share for expected gross proceeds of $70.0 million (€64.4 million). The net proceeds to Cerus from this offering are expected to be approximately $65.5 million, after deducting the underwriting discount and estimated offering expenses payable by Cerus.

The offering is expected to close on or about January 12, subject to customary closing conditions. In addition, Cerus has granted the underwriters a 30-day option to purchase up to an additional 1,909,090 shares of its common stock to cover over-allotments, if any. The company plans to use the net proceeds from the offering for continued development activities related to the INTERCEPT Blood System, and to fund commercialization efforts for the INTERCEPT Blood System in the U.S. and elsewhere, and for other general corporate purposes, including regulatory activity, selling, general and administrative expenses and working capital.

* Separately, CERUS announced that Delaware-based BLOOD BANK OF DELMARVA (BBD) and SunCoast Blood Bank in Sarasota, Florida have signed three-year purchase agreements to acquire Cerus’ INTERCEPT Blood System for platelets and plasma. BBD supplies approximately 13,000 platelet and 21,000 plasma units per year to hospitals in Delaware, Maryland and Virginia. Sun-Coast supplies about 6,000 units of platelets and 5,500 plasma units to 12 hospitals in its catchment area.

“The implementation of the INTERCEPT system aligns with our mission of providing safe, effective blood products that best serve our hospital and patient community,” a senior BBD official said. “We are excited to be one of the first centers to adopt pathogen reduction as a proactive measure to mitigate the risk of transfusion-transmitted infections in our blood supply.”

A senior BBD medical officer further noted that “the majority of platelet transfusions occur in cancer patients, some of which will receive multiple units over the course of their therapy. It’s exciting and rewarding to...favorably impact the treatment of these patients by providing platelet products that substantially reduce the risk of transmitting viruses and bacteria, and limit the risk of transfusion mediated graft versus host disease.”
* BAXTER INTERNATIONAL has announced that BAXALTA, the biopharmaceutical spinoff company that is expected to separate from Baxter in mid-2015, will be headquartered in the city of Bannockburn, in northern Illinois. The company has entered into a long-term lease agreement – extending for more than 10 years – for the approximately 260,000 square foot facility. Following the separation, Baxalta will have approximately $6 billion (£5.36 billion) in global revenues, which mainly comprise sales of plasma-based therapeutics and recombinant therapies for bleeding disorders.

The decision to locate its new headquarters in Bannockburn reaffirms our commitment to Northern Illinois and our strong employee base here,” a senior Baxter official said.

* Below are the final awards under the 2014 Jordanian Procurement Department tender for selected human plasma derivatives, for deliveries in 2015:

<table>
<thead>
<tr>
<th>Product, presentation (supplier)</th>
<th>Quantity</th>
<th>Price ($)</th>
</tr>
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<tbody>
<tr>
<td>Intravenous immunoglobulin, 1g (Octapharma)</td>
<td>600</td>
<td>$77.50</td>
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<td>Intravenous immunoglobulin, 2.5g (CSL Behring)</td>
<td>1,800</td>
<td>$125.00</td>
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<td>Intravenous immunoglobulin, 5g (CSL Behring)</td>
<td>6,000</td>
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<td>Intravenous immunoglobulin, 10g (CSL Behring)</td>
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<td>$499.00</td>
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<td>Anti-D immunoglobulin, 200-300 mcg (CSL Behring)</td>
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<td>$56.00</td>
</tr>
<tr>
<td>Tetanus immunoglobulin, 250 IU (CSL Behring)</td>
<td>6,000</td>
<td>$17.60</td>
</tr>
<tr>
<td>Rabies immunoglobulin, 2 mL (CSL Behring)</td>
<td>4,000</td>
<td>$79.00</td>
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<tr>
<td>Rabies immunoglobulin, 4 mL (CSL Behring)</td>
<td>4,000</td>
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<tr>
<td>Albumin 20%, 50 mL (CSL Behring)</td>
<td>45,500</td>
<td>$28.00</td>
</tr>
<tr>
<td>Factor VIII, 250 IU (Octapharma)</td>
<td>5,500</td>
<td>$0.265/IU</td>
</tr>
<tr>
<td>Factor VIII, 500 IU (Octapharma)</td>
<td>2,500</td>
<td>$0.259/IU</td>
</tr>
<tr>
<td>Factor IX, 500 IU (Octapharma)</td>
<td>2,600</td>
<td>$0.062/IU</td>
</tr>
<tr>
<td>Recombinant Factor VIII, 250, 500, 1000 IU (Pfizer)</td>
<td>1090/1360/545</td>
<td>$0.51/IU</td>
</tr>
</tbody>
</table>

* BIOGEN IDEC announced that ALPROLIX’ revenues in the fourth quarter of 2014 were $40 million and $76 million since its launch in May. ELOCTATE’s revenue in the same period was $37 million and $58 million since its launch in July.
**BIOGEN IDEC’S longer-acting recombinant factor IX product, Alprolix, is being used by just under 25% of the hemophilia B prophylaxis, according to The Marketing Research Bureau’s newly released “Survey on Hemophilia Care & Price Monitoring in the United States – Wave #22” report. This survey of 27 U.S. hemophilia treatment centers (HTCs) also documented significant patient conversion to Biogen Idec’s recently launched longer-acting recombinant factor VIII product, Eloctate, even as BAXTER INTERNATIONAL’S ADVATE plasma/albumin-free recombinant factor VIII reinforced its dominance by capturing incremental share of the factor VIII patient market over the past year. This survey found that average weekly dosing was more significantly reduced in patients on Alprolix in relation to conventional factor IX products than it was in patients on Eloctate in relation to conventional factor VIII products.**

While CSL BEHRING’S Humate-P continued to dominate the von Willebrand disease (vWD) market, its market share declined largely as a result of patient switching to OCTAPHARMA’S Wilate product. Pricing trends were mixed, with prices for some products or product classes significantly increasing, while others declined over the past year. A total of 3,277 patients with hemophilia A, 1,164 patients with hemophilia B, 3,119 patients with von Willebrand disease (vWD) and 558 patients with rare coagulation disorders were registered at the HTCs interviewed for this research report.

**The U.S. FDA has approved labeling changes that expand the administration options for CSL BEHRING’S Hizentra 20% subcutaneous immunoglobulin product to include the ability to individualize therapy with flexible dosing. Treatment may now be specified at regular intervals from daily to once every two weeks (biweekly) for persons with primary immunodeficiency disorders. FDA approval of flexible dosing was based on pharmacometrics (modeling and simulation); clinical trials using these alternative dosing regimens were not conducted.**

**BLOOD & BIOTECHNOLOGY**

**The U.S. FDA has accepted for review CSL BEHRING’S Biologics License Application (BLA) for marketing authorization of its long-acting fusion protein linking recombinant coagulation factor IX with recombinant albumin (rIX-FP). Upon marketing approval, rIX-FP will provide hemophilia B patients with a long-acting treatment option with dosing intervals up to 14 days, according to the company. In 2012, the FDA granted rFIX-FP Orphan Drug designation, which qualifies CSL Behring for certain tax credits, elimination of FDA license application fees and certain marketing incentives.**

The rFIX-FP BLA was based on results from a Phase II/III study in previously treated hemophilia B patients aged 12 to 61 years, under the “PROLONG-9FP” program. This pivotal multicenter, open-label safety, pharmacokinetics and efficacy study was designed to compare the change in frequency of spontaneous bleeding events between on-demand treatment and a weekly prophylaxis regimen in patients previously receiving only on-demand treatment. The study evaluated multiple prophylaxis regimens, including seven- and 14-day intervals. A sub-study evaluated the prevention and control of bleeding in patients with hemophilia B undergoing a surgical procedure.
A team of U.S. and UK investigators has reported that gene therapy mediated by a single intravenous infusion of a self-complementary adeno-associates virus serotype 8 (AAV8) vector has resulted in long-term therapeutic factor IX expression associated with clinical improvement in 10 patients with severe hemophilia B. Peripheral vein infusion of a scAAV2/8-LP1-hFICco vector resulted in a dose-dependent increase in circulating factor IX to a level that was 1% to 6% of the normal value over a median period of 3.2 years, with observation of all patients ongoing.

In the high-dose group, a consistent increase in the factor IX level to a mean of 5.1 ± 1.7% was observed in all six patients, which resulted in a reduction of more than 90% in both bleeding episodes and the use of prophylactic factor IX concentrate. A transient increase in the mean alanine aminotransferase level to 86 IU per liter (range, 36 to 202) occurred between week 7 and week 10 in four of the six patients in the high-dose group, but resolved over a median of five days (range, 2 to 35) after prednisone treatment.

At a follow-up period of up to three years, no late toxic effects from the therapy were reported by any participating study site. Complete findings are published in the November 20 issue of The New England Journal of Medicine.

Administration of a novel second-generation single-stranded 2-methoxyethyl antisense oligonucleotide that targets and reduces circulating levels of factor XI was associated with a significant reduction in venous thromboembolism (VTE) risk among patients undergoing knee replacement surgery, according to Dutch investigators at the University of Amsterdam. Developed by ISIS PHARMACEUTICALS and dubbed “FXI-ASO,” this investigational product was administered at a 200 mg dose in 134 patients and at a 300 mg dose in 71 patients. Sixty-nine other knee surgery patients were treated with 40 mg of enoxaparin, a low molecular weight heparin product.

The rate of VTE in the enoxaparin group was 30.4%, 26.9% in the FXI-ASO 200 mg group and 4.2% in the FXI-ASO 300 mg group. “Only three clots were present in the 300 mg group,” the study’s lead investigator noted. “This rate, 4.2%, has never been seen in the setting of knee surgery, where the best evidence is around 10% or 15%.”

Major bleeding rates were 8.3% in the enoxaparin group, 2.8% in the FXI-ASO 200 mg group and 2.6% in the FXI-ASO 300 mg group. “This is the first evidence that factor XI plays an important role in postoperative VTE,” he added. “Reducing factor XI is a very effective method of preventing VTE. Our findings support the concept that thromboembolism and hemostasis can be separated.”

The U.S. FDA has given bluebird bio’s Lentiglobin BB305 lentiviral vector and human β-globin gene a “breakthrough therapy” designation, which will accelerate its development for the treatment of transfusion-dependent beta-thalassemia. This designation is based on initial trial data and is granted to investigational therapies with the potential to improve treatment of serious diseases in relation to existing therapies.

The Lentiglobin BB305 technology is currently in early-stage clinical testing (see the December/January 2015 issue of International Blood/Plasma News). Beta-thalassemia, which results in diminished circulating blood hemoglobin levels, is caused by mutations in the human β-globin gene.
Announcement:

The Marketing Research Bureau is pleased to announce the completion of its latest U.S. hemophilia care market report:

HEMOPHILIA CARE & PRICE MONITORING

WA VE #22 – 2015 (United States)

This study, based on thirty in-depth telephone interviews with hemophilia treatment centers and other hemophilia stakeholders, updates the hemophilia care market situation in the United States, with particular focus on:

• Adoption rate of the long-acting recombinant factors VIII and IX;
• Market shares of coagulation factor products;
• Analysis of brand switching;
• Acquisition and reimbursement prices;
• Acceptance of immune tolerance and prophylaxis;
• Awareness of new products and gene therapy in development;
• Role of home care companies, impact of the 340B program and
• Patients’ issues.

To obtain more information, please contact The Marketing Research Bureau at:

(203) 799-0298 email: mrb_ibpn@earthlink.net

*BAXTER INTERNATIONAL reported that a total of six adult patients with hemophilia B have been treated in an ongoing Phase I/II open-label trial with “BAX 335,” the company’s investigational gene therapy product. In the two highest dose cohorts, factor IX activity levels of about 10% or higher have been observed in two patients, who also experienced no bleeding events since receiving a recombinant adenovirus (rAAV) vector carrying the gene that encodes a special high-activity version (the Padua variant) of factor IX. One of those two patients exhibited elevated liver enzyme levels, indicative of an immune response; it is being treated with oral corticosteroids per the study protocol. No patients have developed factor IX inhibitors to date.

“We continue to make steady progress in advancing our hemophilia B [gene therapy] program with this technology and look forward to better understanding the applicability of this technology platform in hemophilia A patients as well,” a senior Baxter R & D official said. Baxter acquired “BAX 335” through its purchase of CHATHAM THERAPEUTICS, an affiliate of Asklepios BioPharmaceutical (AskBio), in April 2014. Two years earlier, Baxter entered into an agreement to evaluate Chatham’s “Biological Nano Particle” advanced rAAV technology in conjunction with the Padua factor IX variant in a Phase I/II trial in up to 16 hemophilia B patients (see the April 2014 issue of International Blood/Plasma News).
Hemophilia A patients receiving twice-weekly prophylaxis with BAXTER INTERNATIONAL’S investigational extended half-life recombinant factor VIII (rFVIII) treatment, “BAX 855,” experienced a 95% reduction in median annualized bleed rate (ABR) as compared to those in the on-demand arm (1.9 vs. 41.5, respectively), according to efficacy and safety data from a Phase III pivotal study presented at the 8th Annual Congress of the European Association for Haemophilia and Allied Disorders (EAHAD) in Helsinki. These study findings supported Baxter’s submission of a Biologics License Application (BLA) to the U.S. FDA for approval of “BAX 855” last December. Baxter expects to file for marketing authorization with the European Medicines Agency in 2016.

This prospective, global, multicenter, open-label, two-arm study evaluated “BAX 855” in 137 previously treated hemophilia A patients (PTPs) aged 12 years and older. Patients were assigned either to twice-weekly prophylaxis (40-50 IU/kg, n=120) or on-demand treatment (10-50 IU/kg, n=17). In addition to a reduced ABR, “BAX 855” was effective in treating bleeding episodes, 96% of which were controlled with one or two infusions at a median dose of 29.0 IU/kg per infusion. Treatment was rated either “excellent” or “good” for 96.2% of episodes. In the prophylaxis group (n=101), 40% of patients experienced no bleeding events. Pharmacokinetic analysis showed that “BAX 855” had a 1.4- 1.5-fold extended half-life compared to ADVATE recombinant factor VIII with a median infusion interval of 3.6 days.

The U.S. FDA has accepted Sangamo BioSciences’ investigational new drug (IND) application for its “SB-BCLmR-HSPC” genome editing technology, designed to provide a long-lasting therapeutic option for transfusion-dependent beta-thalassemia. The company plans to initiate a Phase I/II clinical of this novel gene therapy, which will evaluate its safety, tolerability and several measures of efficacy.

Also called “ZFP Therapeutic,” “SB-BCLmR-HSPC” is being developed by Sangamo in collaboration with BIOGEN IDEC, contends that it has the potential to provide a lasting therapeutic solution with “significant safety advantages over existing transplant therapies that involve hematopoietic stem progenitor cells (HSPCs) from a matched related donor.” “We are using our genome editing technology to target a key genetic switch in a patient’s own HSPCs to enable continued production of fetal hemoglobin in the red blood cells of adults,” a senior Sangamo R & D official said.

ALNYLAM PHARMA has announced updated results from its ongoing Phase I study of “ALN-AT3,” an investigational RNAi therapeutic targeting anti-thrombin (AT) for the treatment of hemophilia and rare bleeding disorders. New results from this study provide ‘initial evidence that ‘ALN-AT3’ may potentially correct the hemophilia phenotype associated with administration and AT knockdown. Specifically, subcutaneously administered “ALN-AT3” resulted in an increase in thrombin generation of up to 334% and a marked improvement in whole blood clotting. The most advanced severe hemophilia A subject in the cohort remained bleed-free for 47 days without replacement factor prophylaxis, according to the company.
RESEARCH AND DEVELOPMENT

* Based on positive efficacy and safety data from a pivotal multi-center Phase III clinical trial in 59 subjects with primary immunodeficiency disorders, ADMA BIOLOGICS announced that it is now preparing to apply for U.S. marketing approval of “RI-002,” its investigational intravenous immunoglobulin (IVIG) derived from plasma donors selected for their high titers of neutralizing antibodies to respiratory syncytial virus (RSV). These findings were presented at the American Academy of Allergy, Asthma and Immunology (AAAI) annual meeting in Houston.

Over the course of 55.9 evaluated patient years and 793 intravenous infusions of “RI-002” in subjects ranging from three to 73 years of age, there were no serious bacterial infections, a single serious adverse event (SAE) due to infection, and a single five-day hospitalization for infection (0.018 hospitalizations per subject per year). In addition there were 3.44 non-serious infections per patient/year.

There was a marked increase in all measured anti-pathogen antibodies in 31 subjects in whom pharmacokinetic data were captured, including the largest increase – 5.3-fold – in the level of neutralizing antibody titers to RSV. In subjects infused at both three- and four-week intervals, IgG trough levels remained above those required by the FDA for IVIG. The safety profile of “RI-002” was similar to that of other immunoglobulins, according to an ADMA statement.”

“In addition to meeting the primary endpoint, this pivotal trial achieved secondary endpoints that compare favorably to historical clinical trial results of other comparably run IVIG trials,” a senior ADMA scientific officer said. **A pediatric immunologist not affiliated with the trial commented that “the recently completed clinical trial for ‘RI-002’ suggests that its unique antibody profile may provide certain improved outcomes for a subset of the primary immunodeficiency patient population.”**

* After reviewing an interim analysis completed on the first 205 previously untreated patients (PUPs) or minimally treated patients (MTPTs) in the “Survey on Inhibitors in Plasma Product-Exposed Toddlers” (SIPPET) Study, the Data Safety Monitoring Board determined that (1) the SIPPET Study is safe to continue, (2) there is no futility issue to stop the study from continuing, and (3) going forward it is critical to maintain the data in confidence to preserve the integrity of the study. The objective of this investigator-initiated, prospective, controlled, randomized and open-label study is to definitively answer whether use of plasma-derived factor VIII (FVIII) concentrates that include von Willebrand factor in PUPs are less immunogenic than recombinant FVIII products and therefore associated with as much as a two-fold lower incidence of inhibitors in the at-risk PUP and MTPT population.

Other non-randomized studies to date have yielded contradictory findings, according to SIPPET collaborators.

“The absence of futility means that the original hypothesis of SIPPET of an at least two-fold lower incidence of FVIII inhibitors with plasma-derived, VWF-containing products is still viable and valid,” according to an independent investigator at the Leiden University Medical Center. **SIPPET is being conducted at numerous treatment sites in 14 countries in Europe, Asia, the U.S. and Africa with 300 PUPs and MTPTs.**
Administration of plasma, platelets and red blood cells in a 1:1:1 ratio resulted in a higher likelihood of achieving hemostasis and a reduced risk of death due to exsanguination in the first 24 hours following major trauma-induced bleeding than a 1:1:2 blood component ratio, according to findings from a Phase 3 randomized clinical trial of 680 severely injured patients admitted to 12 Level I trauma centers in U.S. and Canada. Blood products in 1:1:1 and 1:1:2 ratios were transfused during active resuscitation in addition to all local standard-of-care interventions. Primary outcomes were 24-hour and 30-day all-cause mortality.

No significant differences were detected in mortality at 24 hours (12.7% in the 1:1:1 group vs. 17.0% in the 1:1:2 group; difference, -4.2% [95% confidence interval, -9.6% to 1.1%]; P = 0.12) or at 30 days (22.4% vs. 26.1%, respectively; difference, -3.7% [95% CI, -10.2% to 2.7%]; P = 0.26). But exsanguination, which was the predominant cause of death in the first 24 hours, was significantly reduced in the 1:1:1 transfusion group (9.2% vs. 14.6% in the 1:1:2 transfusion group; difference, -5.4% [95% CI, -10.4% to -0.5%; P = 0.03).

Additionally, more patients in the former achieved hemostasis than in the latter group (86% vs. 78%, respectively; P = 0.006). Despite the fact that the 1:1:1 group received more plasma (median 7 units vs. 5 units, P < 0.001) and platelets (12 units vs. 6 units, P < 0.001) over the first 24 hours, no differences were observed between the groups for 23 prespecified complications, including acute respiratory distress syndrome, multiple organ failure, sepsis and transfusion-related complications. Complete findings from this study are published in the February 3 issue of JAMA.

PLASMA FRACTIONATION NOTES

The PLASMA PROTEIN THERAPEUTICS ASSOCIATION (PPTA) has launched the “Cross Donation Check System” (CDCS), a new electronic database designed to assist plasma centers in checking donors more efficiently and effectively. Effective February 2, more than 400 plasma collection centers across the U.S. began using the CDCS, which is designed to help streamline the donation process. This new system “reinforces the International Quality Plasma Program (IQPP) Cross Donation Management Standard that was implemented in 2010,” according to PPTA.

“Our IPOQ-certified plasma centers are committed to donor health and safety, because without healthy donors, we would not have plasma that is needed to make plasma-derived therapies,” the chair of the PPTA Source board of directors said. “Launching the nationwide Cross Donation Check System takes the industry one step further in its mission to elevate its standards in ensuring the safety of our valuable donors.”

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PRODUCT SAFETY UPDATE

* Donor plasma spiked with dengue virus and subjected to amotosalen and UVA light (CERUS’ INTERCEPT System for plasma) was rendered non-infectious when inoculated in cell culture, according to a study by French Polynesian researchers at the Centre de Transfusion Sanguine de la Polynésie Française. The mean dengue virus titer in plasma before inactivation was 5.61 log 50% tissue culture infectious dose (TCID<sub>50</sub>/mL and the mean viral RNA load was 10.21 log copies/mL. In inactivated plasma, the mean dengue RNA load was 9.37 log copies/mL, but did not produce any replicative virus nor detectable viral RNA.

The study investigators, whose findings appear in the November 2014 issue of the journal Transfusion, concluded that amotosalen combined with UVA light inactivated 5.61 logs of dengue virus in fresh frozen plasma, and therefore is “an efficient method to prevent plasma transfusion-transmitted infections.”

PEOPLE

* BIOTEST’S Supervisory Board has appointed Dr. Bernhard Ehmer to replace Prof. Dr. Gregor Schulz as CEO, effective January 1. Dr. Ehmer, who was additionally appointed as a member of the Executive Board late last year, previously served as president and CEO of Imclone Systems, where he focused on the clinical development and marketing planning for new biopharmaceuticals, and successfully integrated most of the key functions of Imclone into the organization of Eli Lilly, its parent company. After earning a PhD in Medicine, he successively worked for Boehringer Mannheim, Merck KG&A and as CEO of Fresenius Biotech before joining Imclone.

In addition to Dr. Ehmer, Dr. Michael Ramroth, CFO and Dr. Georg Floss, COO will continue to serve as members of the company’s Executive Board.

* Susan Rossmann, MD, PhD will transition next month from president-elect to president of AMERICA’S BLOOD CENTERS, as Dave Green ends his two-year term. Dr. Rossmann, who is the chief medical officer at Gulf Coast Regional Blood Center in Houston, has served as chair of ABC’s Scientific, Medical, and Technical (SMT) Committee, and is currently a member of the ABC Working Group for Donor Education and Communication.
RECENT U.S. PATENTS

* Method of Inactivating Virus in Circular Blood and Its Applications in Treating Viral Diseases. #8,808,977. Assigned to Beijing Jingjing Medical Equipment Co., Ltd. (Beijing, China). A method for reducing the virus load from a whole blood sample, involving mixing the photosensitizer methylene blue with a separated plasma fraction of whole blood removed from a patient, by means of a peristaltic pump to enable an interaction between the methylene blue and the at least one virus present in the separated plasma fraction; illuminating the photosensitizer methylene blue-plasma mixture with a 600-700 nm wavelength LED for 60 seconds; and filtering the photosensitizer methylene blue and virus from the plasma mixture by passing the mixture through a filter comprising attapulgite, thereby providing a light-treated plasma; mixing the light-treated plasma with the separated red blood cell-containing fraction to form a reconstituted whole blood; and transfusing the reconstituted whole blood into the patient, or a blood bag or blood storage device, wherein the sequence of steps prior to the transfusing step are performed once or multiple times.


* Protein Purification Method. #8,809,509. Assigned to Chugai Seiyaku Kabushiki Kaisha (Tokyo, Japan). A method for manufacturing a medical protein formulation suspected of containing DNA contaminants, which are removed by applying the composition to a protein-A or protein-G affinity column, which binds the medical protein, washing the column to elute non-bound components or the composition, eluting the bound medical protein with an aqueous solution of pH of 2.0 to 3.9 and an ionic concentration of 50 mM or less, and following several additional steps specified in the patent.

* Method for Purification of Complement Factor H. #8,809,510. Assigned to Octapharma AG (Lachen, Switzerland). A method for purification of complement Factor H from a complement Factor H containing source, which is a caprylate precipitate obtained by the addition of caprylate ions to fractions of blood or blood plasma, comprising the steps of (a) reconstituting the caprylate precipitate to provide a complement Factor H containing solution; (b) performing a cation exchange chromatography; (c) performing an anion exchange chromatography; (d) performing a hydroxyl apatite chromatography; and (e) followed by ultra/diafiltration to obtain a complement Factor H concentrate.

* Aglycosylated Immunoglobulin Mutants. #8,815,237. Assigned to Massachusetts Institute of Technology (Cambridge, MA) and The Rockefeller University (New York, NY). An IgG antibody comprising a first mutation in the C’E loop of the CH2 domain of the Fc region that eliminates antibody glycosylation in the CH2 domain and a second mutation in the F/G loop of the CH2 domain, wherein the antibody exhibits at least 50% binding activity to activating receptor FcγRIIA or FcγRIIIA, relative to the corresponding wild type antibody, wherein the mutation in the F/G loop of the CH2 domain comprises K326I.
* **Clotting Factor-Fc Chimeric Proteins to Treat Hemophilia. #8,815,250.** Assigned to Biogen Idec Hemophilia Inc. (Waltham, MA). A method of treating a hemostatic disorder in a subject in need thereof, comprising administering a therapeutically effective amount of a chimeric protein comprising a first and a second polypeptide, wherein the first polypeptide comprises (i) a clotting factor, which is factor VI or factor VIIa, and (ii) at least a portion of an immunoglobulin constant region fused to the clotting factor, which is a FcRn binding partner, and the second polypeptide comprises at least a portion of an immunoglobulin constant region, which is a FcRn binding partner, without the clotting factor of said first polypeptide and without an immunoglobulin variable domain, and wherein said first and second polypeptides are linked.

* **Compositions and Methods for Enhancing Coagulation Factor VIII Function. #8,816,054.** Assigned to The Children’s Hospital of Philadelphia (Philadelphia, PA). A factor VIII (FVIII) variant, consisting essentially of a modified PACE/furin cleavage site and a B domain deletion (BDD) for modulating hemostasis, said PACE/furin cleavage site consisting of amino acids RHQR, said FVIII variant being a human FVIII variant selected from a group of five variants specified in the patent, said variants exhibiting increased specific activity and stability relative to human FVIII-BDD lacking said substitution and deletions.

* **Plasma Kallikrein Binding Proteins. #8,816,055.** Assigned to Dyax Corp. (Burlington, MA). An isolated antibody that binds to the active form of human plasma kallikrein.

* **Lyophilized Platelet Rich Plasma for the Use in Wound Healing (Chronic or Acute) and Bone or Tissue Grafts or Repair. #8,821,858.** Assigned to GW IP, LLC (Shreveport, LA). A process for preparing platelet rich plasma to obtain growth factors for use in wound healing.

* **Fibrin Sealant. #8,821,861.** Assigned to The Board of Trustees of the University of Illinois (Urbana, IL). A fibrin sealant composition, comprising (a) a first container containing a first composition comprising isolated or recombinant thrombin, and (b) a second container containing a second composition comprising purified or recombinant fibrinogen, polyphosphate (polyPn), wherein n is at least 25, and calcium.

* **Device and Method for Concentrating and Detecting Pathogenic microbes from Blood Products and/or Their Derivatives. #8,822,211.** Assigned to Becton Dickinson Infusion Therapy Systems Inc. (Franklin Lakes, NJ). A device for concentrating contaminating microbes possibly present in a blood product.

* **Albumin Variants. #8,822,417.** Assigned to Novozymes Biopharma DIC A/S (Bagsvaerd, Denmark). A polypeptide which is a variant of albumin, comprising one or more alterations at one or more positions corresponding to 104, 106, 108, 109, 110 and 120 in SEQ ID NO: 2 with one or more of A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, Y.
**Procoagulant Peptides.** 

#8,822,638. Assigned to Baxter International Inc. (Deerfield, IL) and Baxter Healthcare SA (Glattpark, Switzerland). A peptide or peptide derivative whose amino acid sequence, or variant amino acid sequence, is specified in the patent, wherein said peptide or peptide derivative has procoagulant activity.

**Process for the Preparation of a Virus-Inactivated FV Concentrate Starting from Human Plasma, Scalable to Industrial Level.** 

#8,822,643. Assigned to Kedrion S.p.A. (Castelvecchio Pascoli, Italy). Process for the purification of FV starting from human plasma or an FV-enriched intermediate fraction, wherein the protein is intact; said process comprising two chromatography steps on weak anion exchangers, wherein the first step is conducted in FV “non-binding” mode while the second step is in FV “capture” mode; wherein the two chromatography steps are separated by at least one viral inactivation step performed by solvent-detergent treatment; wherein after the second chromatography step, the FV containing solution is subjected to a viral removal step by nanofiltration, wherein cryosupernatant is used as starting material; wherein cryosupernatant is diluted with WFI to obtain a conductivity value comprised between 3 and 10 mS/Cm and supplemented with protease inhibitor aprotinin and contacted with the first weak anion exchanger resin in a ratio that may vary from 0.15 to 2.0 g of dry resin per liter of diluted cryosupernatant.

**Method for the Mass Production of Immunoglobulin Constant Region.** 

#8,822,650. Assigned to Hanmi Science Co., Ltd. (Hwaseong-si, South Korea). A method of producing an immunoglobulin constant region, by means of transforming an E. coli cell with a recombinant expression vector; culturing a resulting E. coli transformant in a medium; and isolating the immunoglobulin constant region expressed by the transformant.

**Plasma Kallikrein Binding Proteins.** 

#8,822,653. Assigned to Dyax Corp. (Burlington, MA). An isolated monoclonal antibody that binds to the active form of human plasma kallikrein and does not bind human prekallikrein.

**Mutated Antithrombins, a Process for Preparing the Same and Their Use as Drugs.** 

#8,822,654. Assigned to Universite Paris – Sud XI (Orsay, France); Assistance Publique-Hopitaux de Paris (Paris, France); and Universite Paris Descartes (Paris, France). A composition comprising a mutated antithrombin having an anticoagulant activity of the non-mutated antithrombin, or having substantially no anticoagulant activity, whose structural and functional properties are specified in the patent.

**Manufacture of Factor H (FH) and FH-Derivatives from Plasma.** 

#8,822,656. Assigned to Baxter International Inc. (Deerfield, IL) and Baxter Healthcare SA (Glattpark, Switzerland). A method for preparing an enriched factor H composition from plasma, comprising the steps of (a) precipitating proteins from a cryo-poor plasma fraction, in a first precipitation step, with between about 6% and about 10% alcohol at a pH of between about 7.0 and about 7.5 to obtain a first precipitate and a first supernatant; and (b) extracting factor H from the precipitate with a factor H extraction buffer, thereby preparing an enriched factor H composition.
MEETINGS

June 16-17, 2015
PPTA Plasma Protein Forum
JW Marriott
Washington, D.C.
Phone: 202-789-3100
Email: info@pptaglobal.org
Website: www.pptaglobal.org

September 1-3, 2015
4th Annual Bioplasma World Asia 2015 IMAPAC
Shanghai, China
Phone: +65 6493 2093
Fax: +65 6270 2792
Email: info@imapac.com
Website: www.imapac.com

June 20-25, 2015
XXVth Congress of the International Society on Thrombosis and Hemostasis
Metro Toronto Convention Centre
Toronto, Canada
Phone: 919-929-3807
Email: info@isth.org
Website: www.isth.org

October 22-23, 2015
WFH Global Forum
Montreal, Quebec
Phone: 514-875-7944
Email: dander@wfh.org
Website: www.wfh.org

June 27-July 1, 2015
25th Regional Congress of the ISBT
ExCel Exhibition and Convention Centre
London, United Kingdom
Phone: +31 20 7601 760
Email: office@isbtweb.org
Website: www/isbtweb.org

November 5-6, 2015
IPIC2015
International Primary Immunodeficiencies Congress
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Budapest, Hungary
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GRIFOLS DISCUSES:
Join us for a live presentation on Wednesday 22nd April 2015
Location: Interphex at Javits Center NY, meeting room number 2D01.
Novel Technologies for Human Blood Plasma Fractionation
FROM 1.30 PM TO 2.30 PM  SPEAKER: DR. DIETER FASSNACHT
Grifols Engineering presents its:
Grifols Sterile Filling GSF® Biopharmaceutical Process machinery
FROM 3.30 PM TO 4.30 PM  SPEAKER: JORDI BOIRA DIRECTOR OF APPLIED ENGINEERING
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