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BUSINESS BRIEFS

* **SHIRE announced that it has completed its $32 billion merger with BAXALTA, creating a combined company with over 22,000 employees across 100 countries, focused on development and commercialization of therapeutics for patients with rare diseases and other highly specialized conditions** (see the January 2016 issue of *International Blood/Plasma News*). Through this combination, which makes Baxalta a wholly-owned subsidiary, Dublin-based Shire anticipates double-digit compound annual top-line growth, with over $20 billion in annual projected revenue by 2020, of which approximately 65% will be generated by its rare disease products.

The operating structure of the combined company is expected to yield annual operating savings of at least $500 million within the first three years post-closing, according to Shire. It expects to generate additional revenue synergies and a combined non-GAAP effective tax rate of 16% to 17% by 2017. Baxalta shareholders have received a combination of $18 in cash and 0.1482 Shire American Depository Shares (ADS's) for each Baxalta share (or 0.4446 of a Shire ordinary share if the Baxalta shareholder validly elected to receive ordinary shares).

"Upon the completion of our combination with Baxalta, Shire is now the global leader in rare diseases, with the number one rare diseases platform based on both revenue and pipeline programs," said Shire CEO Flemming Ornskov, MD, MPH.

* **Sales of plasma-derived and recombinant therapeutics, which accounted for €404.1 million (80.4%) of LFB's turnover of €502.4 million ($553 million) in 2015, were virtually unchanged from 2014 (-0.3%)**, according to the company's 2015 annual report. Production difficulties in the third quarter and a reduction in the national approved reimbursement rate for medicines in the "Rare Diseases/Hemostasis" category accounted for a modest €11.6 million decline in **French** sales from 2014, offset by sales outside of France that were up by €12.1 million (+8.7%).

Boosted by 52% growth in sales of immunoglobulins outside of France, overall turnover from the sales of LFB's products in the "Immunology" category increased by 3.6% from 2014 to €147.2 million ($162 million). Notable upturns in immunoglobulin sales were recorded in **Brazil** and **Mexico**.

At €139.7 million ($154 million), sales in the "Rare-Diseases/Hemostasis" category were down 6.6% from 2014. The drop in sales was explained by volatility in markets subject for tender procedures and instability in certain countries. Countering this trend were "buoyant" **French** and international sales of LFB's *WILFACTIN* von Willebrand factor concentrate, also sold under the trademark *WILLFACT* in northern **Europe**.

Products in the company's "Perinatal and Intensive Care" category declined 6.1% to €117.3 million ($129 million), of which €93.8 million was sold domestically. Partly accounted for by a suspension of sale of LFB's recombinant antithrombin, *ATryn*, in the **U.S.** following a delay in the accreditation of LFB USA's subcontractor, this downturn in the "Perinatal and Intensive Care" category was mitigated by continued growth of LFB's *CLOTTAFACT* human fibrinogen concentrate.

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* **BONFILS BLOOD CENTER, which serves approximately 100 health care organizations in the state of Colorado, announced plans to merge with BLOOD SYSTEMS (BSI), effective January 1, 2017**. Bonfils will retain its name and will continue to provide the same services, but will cease to exist as a legal entity. In 2014, it became an affiliate of BSI, which comprises eight regional blood organizations serving about 700 hospitals in 24 states. These include Blood Centers of the Northwest, BloodSource, Community Blood Services, Inland Northwest Blood Center, Lifeblood, LifeShare and United Blood Services.

* **CSL BEHRING has been awarded the collective contract to fractionate plasma generated by the blood establishments of the following Italian "NAIP" regions: Abruzzo, Basilicata, Friuli-Venezia Giulia, Liguria, Umbria, Aosta Valley, and Veneto, as well as the autonomous provinces of Trento and Bolzano**. Under this contract, which went into effect in February 2016, hospitals in these regions will have the option of receiving all or some of the following products in exchange of their plasma: albumin, IVIG, factor VIII and fibrinogen. Information relating to this toll fractionation agreement was posted by the Health Services Region of Veneto at www.regione.veneto.it/web/sanita/cras-servizio-di-plasma-derivazione.

This contract stipulates that the fractionator will be responsible for the transfer of the plasma [from the blood establishments to the fractionation plant], processing [into finished plasma derivatives], and their storage and delivery [to health facilities]. The contract comprises a five-year fractionation commitment valued at €87,505,000 ($96.3 million), with a possible biennial renewal option amounting to €35,002,000 ($38.5 million), excluding taxes. Other contenders for this fractionation contract included **GRIFOLS** and **KEDRION**.

According to the National Blood Center report *ISTISAN* published last month, in 2014 the NAIP Regions (which included Emilia-Romagna and Tuscany) shipped 338,809 kilograms for fractionation and the "LPS" region, which includes Lombardy-Piedmont-Sardinia, shipped 231,239 kilograms of plasma for fractionation. Together, these two groups of regions shipped 73.3% of **Italy's** total of 777,942 kilograms in 2014. The remaining regions do not have collective fractionation contracts.

* **Below are current 2016 blood component prices in Hungary**:

Product	Forints	$ (U.S.)
Whole blood (unit)	7,319	25.24
Red cell concentrate (unit)	7,319	25.24
Fresh frozen plasma (unit)	11,000	37.93
Fresh frozen plasma, filtered (~250 mL)	12,500	43.10
Platelet unit (from whole blood)	6,400	22.07
Platelet dose (from four whole blood units)	25,600	88.28
Platelet dose (from single apheresis donor)	65,000	224.14
Anti-D immunoglobulin (300 mcg)	12,129	41.82
Human albumin (20 grams)	16,200	55.86

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* **The Italian National Blood Centre (NBC) recently published a report, titled *Analysis of the Demand of the Main Plasma Derivatives in Italy 2011-2014* (ISTISAN 16/7), which analyzes the country's self-sufficiency in blood components and plasma-derived and recombinant medicinal products at regional and national levels, and assesses the country's self-sufficiency for toll-fractionation plasma products at the regional and national levels**. The report also analyzes costs sustained by the Italian National Health Service for the provision of these products. NBC is the technical body of the Italian Ministry of Health (MoH), operating under the name "Istituto Superiore de Sanita."

Selected findings from this report are summarized below:

- Italy's albumin consumption declined from 2011 and 2012, and again in 2013, but went back up in 2014 to reach a volume close to 2011. A preliminary NBC estimate of the 2015 demand suggests a 1% to 3% decline from 2014. The country's 2014 standardized demand was 597.5 kilograms per million inhabitants.

Albumin Consumption in Italy from 2011 to 2014

	2011	2012	2013	2014
Kilograms	36,443	35,949	35,379	36,320

Wide regional variations in albumin consumption have been reported, ranging from 254.7 kg/million inhabitants in Trento, 282.0 kg/million in Bolzano, 288.1 kg/million in Friuli-Venezia Giulia, 1,015.7 kg/million in Sardinia, and 1,036.8 kg/million in Campania.

- Italy's consumption of polyvalent immune globulin (IgG), both intravenous and subcutaneous, increased from 2011 to 2014 to 4.4 metric tons, or 73.1 kg/million inhabitants. Regional variations in IgG consumption are also apparent, ranging from 43.6 kg/million in Calabria to 148.0 kg/million in Tuscany. The National Blood Center estimates that total 2015 demand for IgG was 4.6 tons.

- 546.5 million VIII international units (IUs), equivalent to 9 units per capita, were used in 2014; this represented a 39% increase from 2011. Recombinant products accounted for 73.1% of the total. The regions of Aosta Valley and Umbria respectively posted 4.3 and 5.1 IUs per capita, while Calabria and Lazio respectively recorded 12.9 and 13.3 IUs per capita, the higher latter figures are attributed to the comparatively high number of treatment centers in Rome, the region's capital. Further, 58.6 million of factor IX units were used in 2014, or 1.0 IU per capita. Recombinant products comprised 81% of supplied factor IX units.

- With among the world's highest rates of consumption of antithrombin III, demand for the product in Italy has fluctuated year-over-year but remained essentially unchanged between 2011 and 2014. In 2014, 124.3 million IUs were used, or 2.0 IUs per capita (compared to 0.8 IUs in Germany and 0.2 IUs in Sweden in 2014). Considered an important factor of the hemostatic equilibrium, it is used to counter the anticoagulant action of heparin.

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- Between 2012 and 2014, Italy's albumin self-sufficiency level rose modestly from 63% to 66%, while self-sufficiency in IgG products declined from 84% to 78%.

  The self-sufficiency levels for these two products were the highest in the Aosta Valley, Friuli-Venezia Giulia and Trento regions, and the lowest in the Apulia, Campania and Sardinia regions.

* **In 2015, the three blood centers operating in Lithuania (Vilnius, Kaunas and Santariskiu) produced the following blood components from 100,512 units of collected whole blood** (Lithuania's population is just under 3 million, resulting in a ratio of 34 donations per thousand inhabitants):

Leukocyte-poor erythrocytes	49,685 units
Leukocyte and platelet-poor erythrocytes	19,989 units
Pooled platelets from whole blood	1,971 doses
Single donor apheresis platelets	999 doses
Fresh frozen plasma	60,236 units
Fresh frozen plasma used for transfusion	14,858 units
Poor-poor fresh frozen plasma	1,999 units
Cryoprecipitate	1,999 units

The following blood component prices, issued by the country's Ministry of Health, have been in effect in **Lithuania** since October 2015:

Blood Component	Euros	$ (U.S.)
Leukocyte-poor erythrocytes (250 ml ± 50 ml)	89.20	98.31
Leukocyte and platelet-poor erythrocytes (250 ml ± 50 ml)	84.38	92.99
Washed erythrocytes (280 ml ± 60 ml)	109.01	120.14
Fresh frozen plasma (220 ml ± 50 ml)	8.52	9.39
Pooled platelets from whole blood (2 x 10^{11})	110.53	121.81
Single donor apheresis platelets dose (2 x 10^{11})	150.61	165.99
Cryoprecipitate (30 – 40 ml)	13.03	14.36

* **ExThera Medical announced that it has closed a Series B financing round with an equity investment led by new investor FRESENIUS MEDICAL CARE VENTURES GmbH, to support ongoing development of its proprietary *Seraph Microbind Affinity Blood Filter* technology designed to remove pathogens from whole blood.** The financing round, which included existing investors and the coversion of the company's convertible note, generated a total of $15.3 million.

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Proceeds from the financing will be used to support **European** and **U.S.** clinical trials and regulatory submissions, and to scale manufacturing of the Martinez, California-based company's therapeutic blood filter, which incorporates microspheres coated with molecular receptor sites that mimic the receptors on human cells that pathogens use when they invade the body.

Intended to reduce mortality and complications from bloodstream infections and blood-borne infections in high-risk patients, the *Seraph* blood filter is currently being evaluated in **Europe** in dialysis patients infected with *Staphylococcus aureus* and methicillin-resistant *S. aureus*. The company claims that it is the "only device of its kind capable of capturing and removing a broad range of sepsis-causing bacteria, viruses, toxins ad pro-inflammatory cytokines from whole blood.

Announcement

The Marketing Research Bureau is pleased to announce the following research report:

THE PLASMA PROTEINS MARKET IN THE UNITED STATES - 2015

This report is a comprehensive market analysis of the therapeutic plasma and recombinant proteins sold in the U.S. in 2015. It provides sales data and historical trends, in units, dollars and market shares by company. Regulatory, economic and health care issues impacting the market are also discussed. The following topics are covered in the report:

- Plasma Collections and Fractionation
- Overview of the Plasma-derived and Recombinant Proteins Market
- Intravenous, Subcutaneous & Intramuscular Immune Globulins (polyvalent and specific)
- Albumin
- Factor VIII and Factor IX (Plasma-derived and Recombinant, including extended half-life products
- Activated Prothrombin Complex and Recombinant Factor VIIa and other Specialized Coagulation Factors
- Other Plasma-derived Therapeutic Proteins:
  - Alpha-1 Antitrypsin
  - Antithrombin III
  - Fibrinogen
  - C-1 Esterase Inhibitor
  - Protein C
  - Factor XIII
  - Fibrin Sealant
  - Thrombin
- Product Distribution Channels
- Profiles of the Major U.S. Fractionators

To order or to receive more information:

Phone: (203) 799-0298 Fax: (203) 799-3871 Email: mrb_ibpn@earthlink.net

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* **SHIRE and KAMADA announced that the U.S. FDA has approved a expanded label for *GLASSIA* (Alpha-1 Proteinase Inhibitor [Human]), making it the first treatment for adult patients with alpha-1 antitrypsin (AAT) deficiency-related emphysema that can be self-infused at home after appropriate training**. *GLASSIA* is a liquid ready-to-use augmentation product approved for treatment of clinically evident emphysema due to severe AAT deficiency. Kamada and **BAXALTA** (formerly the BioScience division of **BAXTER INTERNATIONAL** and now part of Shire) entered into an exclusive strategic cooperation agreement for the distribution and license of *GLASSIA* in 2010; it was approved for **U.S.** marketing later that year.

"Self-infusion, after proper training, can be a convenient way for Alphas to receive their augmentation therapy, said Henry Moehring, **ALPHA-1 FOUNDATION** president and CEO. *GLASSIA* and other alpha-1 proteinase inhibitor products are generally administered once weekly.

BLOOD & BIOTECHNOLOGY

* **CMC BIOLOGICS announced that it will supply bulk drug intermediate for *AFSTYLA* (Antihemophilic Factor [Recombinant], Single Chain), CSL BEHRING'S newly FDA-approved long-lasting recombinant factor VIII therapy for treatment of adults and children with hemophilia A** (see the May 2016 issue of *International Blood/Plasma News*). Under an agreement with CSL Behring, CMC Biologics will manufacture the first intermediate of the recombinant factor single-chain product at its Copenhagen facility, which was inspected by the FDA as part of the approval for commercial manufacture of *AFSTYLA*.

CMC Biologics is a contract development and manufacturing organization (CDMO) with marketed products manufactured in both its Seattle, Washington and Copenhagen facilities. With a total of three facilities in the **U.S.** and **Europe** and extensive experience in scale-up and cGMP manufacture of protein-based therapeutics for pre-clinical, clinical and commercial production, the company provides "fully integrated biopharmaceutical development and manufacturing solutions to clients globally."

* **Pennsylvania-based INOVIO PHARMACEUTICALS and Korean DNA vaccine developer and manufacturer GeneOne Life Science announced that they have received approval from the U.S. FDA to initiate a 40-subject Phase I human trial to evaluate Inovio's Zika DNA vaccine (GLS-5700) intended to prevent infection from this virus**. Zika virus infection has become epidemic, with mosquito-borne transmission has been reported in 58 countries and territories.

In preclinical testing, this synthetic vaccine induced robust antibody and T cell responses in small and large animal models, demonstrating its potential to prevent infection in humans. The Phase I study will evaluate the vaccine's safety, tolerability and immunogenicity; interim results are expected later this year.

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* **BAXALTA (now part of SHIRE) reported positive results from a Phase 1 open-label, dose escalation study assessing the safety and pharmacokinetic profile of BAX 930, a recombinant ADAMTS13 (rADAMTS13) intended to treat patients with severe hereditary thrombotic thrombocytopenic purpura (hTTP)**. ADAMTS13 is an enzyme that cleaves the VWF protein. hTTP (also known as Upshaw Schulman syndrome) is a rare, life-threatening microvascular disease characterized by extensive formation of platelet-rich microthrombi due to ADAMTS13 deficiency.

At nine study sites in the **U.S.**, **Europe** and **Japan**, 15 subjects, age 12 to 65 years, with severe hereditary ADAMTS13 deficiency received a single infusion of rADAMTS13 at doses of 5 (n=3), 20 (n = 3) and 40 (n = 9) U/kg. The median half-life was 57.9 hours and C_{max} values obtained from the three dosing cohorts demonstrated a linear dose response that suggests dose proportionality.

No serious adverse events were reported following administration of BAX 930. Im-munogenicity tests performed at screening, pre-dose and upon study completion did not detect binding or inhibitory anti-ADAMTS13 antibodies in any subject. The investigators concluded that rADAMTS13 infusion was safe and well tolerated in these hTTP patients. Current ADAMTS13 replacement therapy requires large volumes of fresh frozen plasma that contain variable quantities of ADAMTS13, and typically requires hours to infuse. In contrast, BAX 930 can be quickly reconstituted, and thus may be suitable for treatment in the patient's home, according to the company. Baxalta has been granted Orphan Drug Designation for BAX 930 by the U.S. FDA and by the European Medicines Agency (EMA).

* **Both an investigational recombinant human prothrombin (MEDI8111) and a plasma-derived human factor II (pdhFII) dose-dependently decreased blood loss and bleeding time in hemophilia A mice**, according to **Swedish** investigators at **AstraZeneca's CVMD iMED unit in Mölndal**. Doses required to achieve a 50% reduction in blood loss and bleeding time were 37 and 87, and 100 and 155 mg/L, respectively. Plasma concentrations of both thrombin generation and thrombin-antithrombin complex (TAT) increased dose-dependently as well with administration of MEDI8111 and pdhFII. Similar results were observed in hemophilia B mice.

The investigators concluded that MEDI8111 dose-dependently decreased bleeding in hemophilia A and B mice, which supports a current hypothesis that factor II is one of the major components responsible for the efficacy of prothrombin complex concentrate (PCC) and activated prothrombin complex concentrate (aPCC) in hemophilia patients. The authors also concluded that "data suggest that MEDI8111 may be useful for preventing bleeding in patients with hemophilia A and B."

Complete findings from this study, titled "Recombinant human prothrombin (MEDI8111) prevents bleeding in haemophilia A and B mice," are published in the May 2016 issue of the journal Haemophilia.

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RESEARCH AND DEVELOPMENT

* **More than five years after suspending guidelines on the use of human albumin in the wake of exposed research fraud by a prolific German colloids investigator named Joachim Boldt, the Executive Committee of the German Medical Association has re-issued newly updated human albumin usage guidelines**. They appear as a document titled "Cross-Sectional Guidelines for Therapy with Blood Components and Plasma Derivatives: Chapter 5 Human Albumin – Revised," published online last month in the journal *Transfusion Medicine and Hemotherapy*.

Specific recommendations are made with respect to the appropriateness or lack of appropriateness of albumin administration for:

- Acute volume replacement during the perioperative phase
- Acute volume replacement in intensive-care patients with and without sepsis
- Acute volume replacement in specific surgical (e.g. cardiac surgery, hepatic surgery and non-surgical settings (e.g. burns, pregnant patients, neonates)
- Therapy of hypoalbuminemia in intensive-care patients, liver cirrhosis, malnutrition and enteropathy/malabsorption syndrome
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome and nephrotic syndrome
- Special indications (e.g. post-paracentesis, ovarian hyperstimulation syndrome, hemodilution in neonates with polycythemia)

The guidelines recommend to prescribe albumin when robust evidence exists. For example, they recommend to use albumin in cirrhosis with spontaneous bacterial peritonitis, hepatorenal syndrome, large volume paracentesis, cardiac surgery for hypo-volemia and hemodynamic stabilization and in plasmapheresis. On the other hand, albumin is not recommended for hemodynamic stability in perioperative surgery, traumatic injury or intensive-care, except when alternatives such as crystalloids have been exhausted.

Overall, the guidelines limit the use of albumin to specific situations and conditions, possibly resulting in a modest growth in its use in the future. The German Medical Association's guideline affirmed that albumin is generally well tolerated, citing an investigation of the safety of approximately 112 million units administered worldwide showing that "adverse reactions directly associated with albumin were an extremely rare event." The complete guideline can be accessed at https://www.karger.com/Article/Pdf/446043.

* **ProMetic Life Sciences reported that the U.S. FDA has granted a Fast Track designation for its investigational human plasma-derived plasminogen product, which is currently in a Phase 2/3 clinical trial in patients with congenital plasminogen deficiency**. The product has been also granted Orphan Drug Designation by the U.S. FDA and the European Commission.

"To date, our plasminogen therapy has been well tolerated and initial compassionate use treatments have shown a rapid response in lesion resolution and have helped avoid the need for surgery," said Mr. Pierre Laurin, ProMetic's CEO.

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* **GRIFOLS reported that 39 U.S. and Spanish clinical study sites participating in its AMBAR trial of plasma exchange, low volume plasma exchange (LVPE) and intravenous immunoglobulin (IVIG) therapy in persons with mild to moderate Alzheimer's disease have recruited 345 of a planned 364 subjects as of April 2016**, according to a presentation at the American Society for Apheresis (ASFA) meeting last month in Palm Springs, California. Interim data were presented on 186 subjects recruited as of June 2015, who were between 55 and 85 years of age, had a MMSE score between 18 and 26, and had a recent CAT or MRI scan documenting absence of cerebrovascular disease.

  Treatment appeared to be feasible with an acceptable adverse event profile. Three treatment arms received six full plasma exchange procedures with 5% albumin replacement, followed by LVPE and low periodic dosages of IVIG or no IVIG. A fourth arm received sham treatments. Of 138 subjects who passed all screening and were enrolled, 129 were randomized and 115 received treatments (20 complete, 78 ongoing and 17 withdrawn from study). At the interim analysis, 1,367 procedures had been performed; about 2,500 had been performed at the time of the presentation.

  While the randomization code has not been broken, combined improvement or worsening results for all study subjects were reported for several standard cognitive or functional testing scales, including ADAS-Cog, MMSE and ADCS-ADL.

PLASMA FRACTIONATION NOTES

* **KEDRION BIOPHARMA and NACIMBIO (National Immunobiological Company, RosTECH group) have signed a joint venture agreement under which the two companies will collaborate to relaunch a Russian plasma fractionation plant in Kirov**. The facility, which will produce human plasma-based therapeutics for the **Russian** market, is scheduled to be operational in 2019, after plant renovation, installation of new equipment for production and all activities included in the transfer of experience, expertise and technologies from Kedrion to Nacimbio have been completed.

  "Currently, Russia depends on imports for 90% of its blood-derived product requirements. In 2019, however, once the Kirov plant is completed, it will be capable of processing 600 tons of plasma per year," said Nacimbio CEO Nikolay Semenov. "We plan to invest about four billion Rubles ($78 million) in the Kirov plant," he added. With this manufacturing facility operating at full capacity, Mr. Semenov projected that the Russian Federation will be able to meet domestic demand for albumin, immunoglobulin and factor IX in full, while meeting up to 15% of factor VIII demand.

* Separately, **KEDPLASMA USA, a KEDRION BIOPHARMA company, has opened its 13th plasma collection center in Gastonia, North Carolina**. The 13,000 square foot facility has the capacity to house 60 collection beds and machines and will employ over 35 individuals in its inaugural year, according to the company.

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* **Chinese investigators have concluded, after a sample testing study, that use of recovered plasma (RP) in the manufacture of plasma derivatives, if coupled with a two-year inventory hold, will not increase infectious disease risk relative to use of apheresis plasma (AP)**. Supplementary testing was conducted and the residual risk (RR) of human immunodeficiency virus (HIV) hepatitis B virus (HBV) and hepatitis C virus (HCV) in the two types of blood donors was calculated through the incidence-prevalence period model. Prevalence of the markers for hepatitis E virus, hepatitis A virus, severe fever with thrombocytopenia syndrome bunyavirus, cytomegalovirus, parvovirus B19 and West Nile virus were calculated as well.

No significant difference in RR for HIV, HBV or HCV was found on initial screening of the two types of blood donors. However, after the 90-day quarantine period that is standard in **China**, the RR of HCV and HIV associated with AP plasma was significantly lower than that for RP. A quarantine period of two years for RP resulted in an infectious risk for the two pathogens that was not significantly different than for AP.

Currently, plasma recovered from whole blood is not permitted for manufacture into plasma derivatives in **China**. Because of a lack of source plasma collected by apheresis and the country's surplus of RP, the Chinese government is considering allowing RP as an equivalent source for the production of plasma derivatives. The authors of this study, affiliated with the Institute of Blood Transfusion in the Chinese Academy of Medical Sciences in Chengdu, concluded that "**transferring RP for manufacturing will not increase the risk of plasma derivatives with a 2-year inventory period for RP or nucleic acid testing (NAT) for whole blood donors."** Complete findings from this study appear in the May 2016 issue of the journal *Transfusion*.

* At the **PLASMA PROTEIN THERAPEUTICS ASSOCIATION'S** Plasma Protein Forum 2016 held earlier this month, Mr. Shinji Wada, President of Grifols Plasma Operations and Chair of PPTA Source Board of Directors, presented the following data relating to construction of new **U.S.** plasma collection centers over the past five years:

Year	Number of Plasma Collection Centers*	Additional New Centers Over the Previous Year
2010	403	
2011	404	1
2012	411	3
2013	427	16
2014	478	51
2015	530	52

*All plasma centers, whether IQPP-certified or not, FDA-licensed and/or in the process of being FDA-licensed

Mr. Wada also noted that growth in plasma collections between 2014 and 2015, estimated to be slightly below 10%, was mainly driven by new centers, while collections at existing centers increased only by 3% over that period.

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PRODUCT SAFETY UPDATE

* **CERUS announced an agreement with the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response, to support clinical and other development activities related to its** *INTERCEPT Blood System* for **pathogen reduction of red blood cell (RBC) components**. This funding support may extend to studies necessary to support an FDA submission and accelerated commercial scale-up to facilitate potential adoption by **U.S.** blood centers.

Cerus reported positive results from a European Phase III clinical trial of the *INTERCEPT* Red Blood Cell System in January 2015, and also from a **U.S.** Phase II clinical trial in December 2014. The company plans to submit an application for CE Mark registration of *INTERCEPT* RBCs in the second half of 2016.

Cerus will receive initial funding of up to $30,750,939 to support activities related to a clinical trial to assess the safety and efficacy of *INTERCEPT* RBCs compared to conventional RBCs in **Puerto Rico**, a region impacted by the current Zika virus epidemic. This funding will also support activities related to *in vitro* studies to facilitate pivotal Phase III clinical trials in the continental **U.S. If exercised by BARDA and completed, subsequent project activity options would bring the total non-dilutive funding opportunity to up to $180,509,914 over the five-year contract period**. These subsequent options would fund activities related to broader implementation in areas of Zika virus risk, clinical and regulatory development programs in support of licensure, and development, manufacturing and scale-up activities.

Related to manufacturing, Cerus and its partners will be responsible for co-investment in the amount of $14.5 million. Additionally, the BARDA contract includes the possibility of funding the deployment of previously licensed *INTERCEPT*-treated platelet and plasma components for use in Hawaii to support self-sufficiency of that region in the event of an active Zika outbreak.

"This contract offers the potential to fund activities related to anticipated Phase III clinical studies for the *INTERCEPT* Red Blood Cell System in the **U.S.** and the required manufacturing and development activities needed to pursue a potential U.S. commercial launch," said Dr. Laurence Corash, Cerus' chief scientific officer. **"We believe that T-cell inactivation levels with *INTERCEPT* provide the opportunity for future replacement of gamma irradiation, which would also align with the Department of Homeland Security's initiative to eliminate nuclear source irradiators in the U.S. through the introduction of non-nuclear technologies."**

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RECENT U. S. PATENTS

* **Fibronectin-Based Binding Molecules and Uses Thereof. #9,296,810.** Assigned to **Novartis AG** (Basel, Switzerland). A Fn3-based binding molecule comprising SEQ ID NO: 120.

* **Oxygen Depletion Devices and Methods for Removing Oxygen from Red Blood Cells. #9,296,990.** Assigned to **New Health Sciences, Inc.** (Bethesda, MD). A method for adding oxygen to red blood cells, comprising passing red blood cells through an oxygen addition device, wherein said device comprises (1) a receptacle of a solid material having an inlet and an outlet receiving and expelling a gas; and (2) a plurality of hollow fibers extending within said receptacle from an entrance to an exit thereof, wherein said plurality of hollow fibers receive and convey said red blood cells, wherein said red blood cells are passaged within said hollow fibers.

* **Recombinant Protein Expression Using a Hybrid Chef1 Promoter. #9,297,024.** Assigned to **CMC ICOS Biologics, Inc.** (Bothell, WA). An expression vector comprising Chinese Hamster Elongation Factor-1α (CHEF1) transcriptional regulatory DNA and a cytomegalovirus promoter and/or an adenovirus tripartite leader (AdTPL) sequence, wherein the CHEF1 transcriptional regulatory DNA comprises Sequence ID NO: 1.

* **Recombinant Production of Mixtures of Antibodies. #9,303,081.** Assigned to **Merus B.V.** (Utrecht, Netherlands). A composition comprising a mixture of two or three non-identical antibodies and a suitable carrier, wherein two different heavy chains and a common immunoglobulin light chain able to pair with the two different heavy chains are present in the mixture of the two or three non-identical antibodies, and wherein the mixture of two or three non-identical antibodies comprises a bispecific antibody and at least one monospecific antibody.

* **Methods of Treating Anaemia. #9,303,089.** Assigned to **Kymab Limited** (Cambridge, UK). A method of treating or reducing the risk of anaemia in a human, the method comprising administering an anti-target-of-interest (TOI) trap, antibody or antibody fragment to the human, wherein the TOI is selected from eight moieties specified in the patent, wherein the trap, antibody or antibody fragment specifically binds a human transferrin encoded by a transferrin nucleotide sequence comprising a SNP rs3811647; and wherein the trap, antibody or antibody fragment comprises a human gamma-1 heavy chain constant region characterized in the patent.

* **Solid Phase for Mixed-Mode Chromatographic Purification of Proteins. #9,309,282.** Assigned to **Bio-Rad Laboratories, Inc.** (Hercules, CA). A method for purifying monomeric antibodies from a source solution comprising monomeric antibodies and antibody fragments, involving contacting said source solution with a mixed-mode chromatography medium comprising a specified ligand coupled to a solid support.

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* **Anti-Bacterial Polypeptides and Pathogen Specific Synthetic Antibodies. #9,309,298.** Assigned to Arizona Board of Regents, a Body Corporate of the State of Arizona, Acting for and on Behalf of Arizona State University (Scottsdale, AZ). A composition, comprising an isolated polypeptide linked to a targeting moiety, wherein the targeting moiety is a polypeptide with an amino acid sequence comprising DRIFHKMQHKPYKIKKR (SEQ ID NO: 2).

* **Complexation of Fatty Acid-Conjugated Molecules With Albumin.** #9,309,303. Assigned to The University of the Sciences in Philadelphia (Philadelphia, PA). A method of delivering a first molecule to a target within the body of a human, the method comprising (1) contacting a first composition and a second composition outside the body of the human, wherein the first composition comprises a conjugate of the first molecule and a fatty acid, wherein the second composition comprises a human serum albumin, and wherein the first and second compositions are contacted for a time and under conditions sufficient for the conjugate to bind with the albumin to for a complex; and (2) thereafter administering the complex to a tissue from which the target is accessible, whereby the first molecule is delivered to the target.

* **Method for Expansion of Stem Cells and the Use of Such Cells. #9,309,496.** Assigned to The Research Foundation for The State University of New York (Albany, NY). A method for expanding a hematopoietic stem cell population, the method comprising providing to the stem cell population a Sal-like 4 (SALL4) polypeptide attached to a transport moiety capable of crossing a cell membrane, in an amount effective to expand the stem cell population.

* **Composition Exhibiting a von Willebrand Factor (vWF) Protease Activity Comprising a Polypeptide Chain With the Amino Acid Sequence AAGGILHLELLV. #9,309,506.** Assigned to **Baxalta Inc.** (Bannockburn, IL) and **Baxalta GmbH** (Opfikon, Switzerland). A method of treating a disease in which a patient has a supranormal vWF content or an increased level of high-molecular weight vWF, wherein the method comprises administering an effective dose of an isolated polypeptide that has vWF protease activity and comprises a peptide chain with a 180 kD to about 120 kD molecular weight as determined by SDS-PAGE under reducing conditions and comprises the amino acid sequence AAGGILHLELLV (SEQ ID NO: 1), and wherein the polypeptide is purified from human plasma or is encoded by a nucleic acid present in a human cDNA library.

* **Conjugated Blood Coagulation Factor VIIa. #9,309,507.** Assigned to **Polytherics Limited** (Cambridge, UK). A factor VIIa-polyethylene glycol conjugate, wherein one or more polyethylene glycol groups are conjugated to FVIIa by a linker group bridging the Sulphur atoms of two cysteine residues that formed a disulphide bond in FVIIa, wherein R^1 is a substituent which is a direct bond, an alkylene group or an optionally-substituted aryl or heteroaryl group.

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* **Purification of VWF for Increased Removal of Non-Lipid Enveloped Viruses. #9,315,560.** Assigned to **Baxalta Inc.** (Bannockburn, IL) and **Baxalta GmbH** (Opfikon, Switzerland). A method for removing a non-lipid enveloped virus from a protein-containing solution comprising (1) applying the protein-containing solution to a cation exchange resin at a pH of 1.6 pH units or more above the isoelectric point of a protein in the protein-containing solution; and (2) washing the cation exchange resin with a wash buffer to form an eluate, said wash buffer having a pH that is lower than the pH of the protein-containing solution applied to the cation exchange resin, wherein the protein has a molecular mass of at least about 150 kilodaltons, and whereby the non-lipid enveloped virus is removed from the protein-containing solution.

* **Methods and Materials for Prolonging Useful Storage of Red Blood Cell Preparations and Platelet Preparations. #9,315,775.** Assigned to Mayo Foundation for Medical Education and Research (Rochester, MN) and **Dynasil Biomedical Corporation** (Watertown, MA). A method for treating a platelet concentrate, comprising exposing a platelet concentrate to CO_2 gas under conditions wherein the pCO_2 level of said platelet concentrate is about 150 mmHg of pCO2 to about 600 mmHG of pCO_2.

* **Milk Fat Globule Epidermal Growth Factor—Factor VIII and Sepsis. #9,321,822.** Assigned to The Feinstein Institute for Medical Research (Manhasset, NY). A method of reducing thymocyte apoptosis in sepsis in a human, the method comprising administering at least 20 μg/kg body weight (BW) an amount of a milk fat globule epidermal growth factor-factor VIII (MFG-E8), wherein the MFG-E8 has an amino acid sequence at least 99% identical to SEQ ID NO: 1, and wherein the MFG-E8 is administered by intravenous administration.

* **Compositions and Methods for Modulating Thrombin Generation. #9,321,826.** Assigned to The Children's Hospital of Philadelphia (Philadelphia, PA). A method for inhibiting clot formation in a subject in need thereof, said method comprising administering to said subject at least one composition comprising at least one peptide having at least 80% homology with SEQ ID NO: 1, 2, 3 or 4 and at least one pharmaceutically acceptable carrier, wherein said peptide has a length of about 20 to about 80 amino acids.

* **Factor VIII Variants Having a Decreased Cellular Uptake. #9,321,827.** Assigned to **Novo Nordisk A/S** (Bagsvaerd, Denmark) and **Sanquin Blood Supply Foundation** (Amsterdam, Netherlands). A recombinant factor VIII (FVIII) variant consisting of the amino acid sequence of SEQ ID NO: 9.

* **Anti-RSV G Protein Antibodies. #9,321,830.** Assigned to **Trellis RSV Holdings, Inc.** (South San Francisco, CA). An isolated monoclonal antibody (mAb) which is 3D3 or 2B11 wherein the light chain variable region (VL) has the amino acid sequence SEQ ID NO: 45 and the heavy chain variable region (VH) has the amino acid sequence SEQ ID NO: 31 (3D#) or the VL has the amino acid sequence SEQ ID NO: 47, and the VH has the amino acid sequence SEQ ID NO: 33 (2B11) each VH coupled to human kappa or lambda constant region and each VH coupled to human IgG1 constant region, or an immunoreactive fragment thereof which is a single chain form.

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MEETINGS

September 3-8, 2016
34th International Congress of the ISBT
Dubai, United Arab Emirates
Dubai World Trade Centre
Phone: +31 20 570 9600
Email: Dubai@isbtweb.org
Website: www.isbtweb.org

September 19-21, 2016
5th Annual Bioplasma World Asia 2016
Hong Kong
Phone: + 65 3109 0123
Website: www.imapac.com

September 21-24, 2016
17th Biennial Meeting of the European Society for Immunodeficiencies
CCIB - Centre Convencions Internacional de Barcelona
Barcelona, Spain
Phone: +34 932 301 000
Website: http://www.ccib.es/

September 28-30, 2016
ECTH 2016
European Congress on Thrombosis and Haemostasis
World Forum
The Hague, Netherlands
Phone: +31 20 67 93411
Website: www.ecth2016.org

October 22-25, 2016
AABB Annual Meeting and CTTXPO
Orange County Convention Center
Orlando, FL
Phone: 301-907-6977
Website: www.aabb.org

December 3-6, 2016
American Society of Hematology
San Diego Convention Center
San Diego, CA
Phone: 202-776-0544
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