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<110> BAXALTA INCORPORATED
BAXALTA GMBH

<120> Viral Vectors Encoding Recombinant FVIII Variants with Increased
Expression for Gene Therapy of Hemophilia A

<130> 008073-5191-WO

<140> PCT/US2020/013722

<141> 2020-01-15

<150> US 62/793058

<151> 2019-01-16

<160> 57

<170> PatentIn version 3.5

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Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Lys Ser His Thr
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Pro Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
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His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
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Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
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850 855 860

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Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
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Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
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Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
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Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
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755 760 765

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Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys
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Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser
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915 920 925

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Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp
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Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His
1505 1510 1515

Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser
1520 1525 1530

Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr
1535 1540 1545

Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val
1550 1555 1560

Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser
1565 1570 1575

Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln
1580 1585 1590

Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys
1595 1600 1605

Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys
1610 1615 1620

Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys
1625 1630 1635

Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg
1640 1645 1650

Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu
1655 1660 1665

Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr
1670 1675 1680

Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile
1685 1690 1695

Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys
1700 1705 1710

Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr
1715 1720 1725

Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser
1730 1735 1740

Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr
1745 1750 1755

Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu
1760 1765 1770

His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp
1775 1780 1785

Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser
1790 1795 1800

Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly
1805 1810 1815

Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr
1820 1825 1830

Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu
1835 1840 1845

Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu
1850 1855 1860

Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His
1865 1870 1875

Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln
1880 1885 1890

Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp
1895 1900 1905

Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn
1910 1915 1920

Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His
1925 1930 1935

Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met
1940 1945 1950

Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser
1955 1960 1965

Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr
1970 1975 1980

Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr
1985 1990 1995

Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly
2000 2005 2010

Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly
2015 2020 2025

Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro
2030 2035 2040

Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala
2045 2050 2055

Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His
2060 2065 2070

Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser
2075 2080 2085

Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile
2090 2095 2100

Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser
2105 2110 2115

Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr
2120 2125 2130

Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn
2135 2140 2145

Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile
2150 2155 2160

Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg
2165 2170 2175

Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys
2180 2185 2190

Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln
2195 2200 2205

Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser
2210 2215 2220

Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp
2225 2230 2235

Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe
2240 2245 2250

Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys
2255 2260 2265

Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser
2270 2275 2280

Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys
2285 2290 2295

Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val
2300 2305 2310

Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His
2315 2320 2325

Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu
2330 2335 2340

Gly Cys Glu Ala Gln Asp Leu Tyr
2345 2350

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 <212> DNA
 <213> Artificial Sequence

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 ccacctgtcc tgaaacgcca ccagagg 87

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 aaacgccacc agagg 75

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 agg 63

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 <212> DNA
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 <213> Artificial Sequence

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 <400> 51
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 cgccaccaga gg 72

<210> 52
<211> 72
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 52
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cgccaccaga gg 72

<210> 53
<211> 93
<212> DNA
<213> Artificial Sequence

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 <212> DNA
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<400> 56	
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 <211> 7865
 <212> DNA
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<220>

<223> Synthetic

<400> 57

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