

РљРѕРј РћРґРґРҒ L01E X03.

***PαP°CḡPjP°PePsP»PsPiC-C#PSC- PIP»P°CfC,PëPIPsCfC,C-.***

*PαP°CḡPjP°PePsPrPëPSP°PjC-PeP°.*

P'PsC,CḡC-C" PSC,<sup>PÿPḡ</sup> C" P·P°Cf'PsP±PsPj PrP»Cḡ PīPμCḡPsCḡP°P»CHḡPSPsPiPs  
P·P°Cf'C,PsCf'CrPIP°PSPSCḡ, PīPsC,Cf'PḡPSPëPj P±P°PiP°C,PsPjC-CḡPμPSPμPIPëPj  
C-PSPiC-P±C-C,PsCḡPsPj C,PëCḡPsP·PëPSPeC-PSP°P·Pë (P†PÿPḡ) CḡPμC†PμPīC,PsCḡC-PI  
C,,P°PeC,PsCḡP° CḡPsCf'C,Cf' PμPSPPrPsC,PμP»C-Cḡ Cf'CrPrPëPS [Vascular Endothelial Growth  
Factor Receptors, VEGFR]-1, -2 C- -3, CḡPμC†PμPīC,PsCḡC-PI C,CḡPsPjP±PsC†PëC,P°CḡPSPsPiPs  
C,,P°PeC,PsCḡP° CḡPsCf'C,Cf' [Platelet-Derived Growth Factor Receptors, PDGFR]-α C- β C,P°  
CḡPμC†PμPīC,PsCḡP° C,,P°PeC,PsCḡP° Cf'C,PsPIP±Cf'CḡPsPIPëC... PeP»C-C,PëPS (c-KIT),  
PrP»Cḡ CḡPePëC... IC<sub>50</sub> PīCḡPμPīP°CḡP°C,Cf' Cf'C,P°PSPsPIPëC,CH 10, 30, 47, 71, 84 C,P°  
74 PSPjPsP»CHḡ/PjP» PIC-PrPīPsPIC-PrPSPs. PμC-Pr C#P°Cf' PrPsPeP»C-PSC-C#PSPëC...  
PμPeCf'PīPμCḡPëPjPμPSC,P°P»CHḡPSPëC... PrPsCf'P»C-PrPḡPμPSCḡ PīP°P·PsPīP°PSC-P±  
PrPsP·PsP·P°P»PμPḡPSPs C-PSPiC-P±Cf'PIP°PI P»C-PiP°PSPr-C-PSPrCf'PePsPIP°PSPμ  
P°Cf'C,PsC,,PsCf'C,,PsCḡPëP»CḡPIP°PSPSCḡ CḡPμC†PμPīC,PsCḡC-PI VEGFR-2, c-Kit C,P° PDGFR-  
β Cf' PeP»C-C,PëPSP°C.... PμC-Pr C#P°Cf' PrPsCf'P»C-PrPḡPμPSCḡ  
*in vivo* PīP°P·PsPīP°PSC-P± C-PSPiC-P±Cf'PIP°PI VEGF-C-PSPrCf'PePsPIP°PSPμ VEGFR-2  
C,,PsCf'C,,PsCḡPëP»CḡPIP°PSPSCḡ PI P»PμPiPμPSCḡC... C,PIP°CḡPëPS, P°PSPiC-PsPiPμPSPμP·  
Cf' C,PIP°CḡPëPS Cf' CḡC-P·PSPëC... PμPeCf'PīPμCḡPëPjPμPSC,P°P»CHḡPSPëC...  
PjPsPrPμP»CḡC... C,P° CḡC-Cf'C, PjPSPsPḡPëPSPSPëC...  
PeCf'PμPSPsC,CḡP°PSCf'PīP»P°PSC,P°C,C-PI PīCf'C...P»PëPSPë P»CḡPrPëPSPë Cf' C,PIP°CḡPëPS.

*PαP°CḡPjP°PePsPiPμPSPsPjC-PeP°*

PJ C,,P°CḡPjP°PePsPiPμPSPμC,PëC#PSPsPjCf' PjPμC,P°P°PSP°P»C-P·C- PrP°PSPëC... 31  
PeP»C-PSC-C#PSPsPiPs PrPsCf'P»C-PrPḡPμPSPSCḡ PīP°P·PsPīP°PSC-P±Cf', CḡPePëPḡ  
PīCḡPëP·PSP°C#PëP»Pë CḡPe PjPsPSPsC,PμCḡP°PīC-Cḡ P°P±Ps Cf'CrPjC-Cf'PSPs P·  
C-PSCḡPëPjPë PīCḡPμPīP°CḡP°C,P°PjPë, Cf' 19 % PīP°C†C-C" PSC,C-PI P· HLA-B\*57:01  
P°P»PμP»PμPj C,P° Cf' 10 % PīP°C†C-C" PSC,C-PI P±PμP· PSCḡPsPiPs  
Cf'PīPsCf'C,PμCḡC-PiP°P»Pë CḡC-PIPμPSCḡ  
P°P»P°PSC-PSP°PjC-PSPsC,CḡP°PSCf'C,,PμCḡP°P·Pë (PḡP·Pÿ), Cf'  
5 CḡP°P·C-PI PIPëC%PëPḡ P·P° PIPμCḡC...PSCḡ PjPμPḡCf' PSPsCḡPjPë (P'PḡPḡ) (3  
Cf'C,Cf'PīC-PSCḡ), 133 P· 2235 PīP°C†C-C" PSC,C-PI PIPeP°P·P°PSPëC... PIPëC%Pμ  
PeP»C-PSC-C#PSPëC... PrPsCf'P»C-PrPḡPμPSCḡ PjP°P»Pë HLA-B\*57:01 P°P»PμP»CHḡ (PrPëPI.  
CḡPsP·PrC-P» B«PḡCf'PsP±P»PëPIPsCf'C,C- P·P°Cf'C,PsCf'CrPIP°PSPSCḡB»).B B B B B **B**

*PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°.*

*PḡP±Cf'PsCḡP±C†C-Cḡ*

PμC-Cf'P»Cḡ PīPμCḡPsCḡP°P»CHḡPSPsPiPs PīCḡPëPḡPsPjCf' CḡP°P·PsPIPsC— PrPsP·Pë  
PīP°P·PsPīP°PSC-P±Cf' 800 PjPi PīP°C†C-C" PSC,P°PjPë P· Cf'PsP»C-PrPSPëPjPë  
PīCf'C...P»PëPSP°PjPë C<sub>max</sub> PīCḡPëP±P»PëP·PSPs 19 B± 13 PjPePi/PjP» PI PīP»P°P·PjC-  
PeCḡPsPIC- PrPsCf'CḡPīP°C"C,CHḡCf'Cḡ PI Cf'PμCḡPμPrPSCḡPsPjCf' C#PμCḡPμP·  
3,5 PiPsPrPëPSPë (PrC-P°PīP°P·PsPs: 1,0-11,9 PiPsPrPëPS), P°B P·PSP°C#PμPSPSCḡ AUC<sub>(0-∞)</sub>  
Cf'C,P°PSPsPIPëC,CHḡ PīCḡPëP±P»PëP·PSPs 650 B± 500 PjPePi×PiPsPr/PjP». P©PsPrPμPSPSPëPḡ  
PīCḡPëPḡPsPj PīCḡPμPīP°CḡP°C,Cf' P·Cf'PjPsPIP»CḡC" P·CḡPsCf'C,P°PSPSCḡ AUC<sub>(0-T)</sub> PI 1,23-4  
CḡP°P·Pë. PμCḡPë P·P±C-P»CHḡCḡPμPSPSC- PrPsP·Pë P'PsC,CḡC-C" PSC,Cf'<sup>PÿPḡ</sup> PīPsPSP°Pr 800  
PjPi PIC-PrPīPsPIC-PrPSPμ P·CḡPsCf'C,P°PSPSCḡ AUC C,P° C<sub>max</sub> PIC-PrCf'CrC,PSC".

$P\ddot{Y}P\acute{e}C\acute{I}C, P_{\mu}P_jPSP_{\mu} PIC\acute{I}P_jPsPeC, C\acute{r}PIP^{\circ}PSPSC\dot{I} P\ddot{I}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm C\acute{r} P\cdot C\dot{H}PsC\acute{I}C, P^{\circ}C'',$   
 $C\dot{I}PeC\%_{\circ}Ps PIC-PS P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}P_jP^{\circ}C''C, CHC\acute{I}C\dot{I} C\dot{H}P^{\circ}P\cdot PsP_j P\cdot C-P\parallel P_{\mu}C\dot{H}.$   
 $P-P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\dot{I} P'PsC, C\dot{H}C-C''PSC, C\acute{r}^{P\ddot{Y}P^{\#}} C\dot{H}P^{\circ}P\cdot PsP_j C-P\cdot C-P\parallel P_{\mu}C\dot{H} P\cdot$   
 $PIP\acute{e}C\acute{I}PsPeP\acute{e}P_j P^{\circ}P\pm Ps PSP\acute{e}P\cdot CHPeP\acute{e}P_j PIP_jC-C\acute{I}C, PsP_j P\parallel P\acute{e}C\dot{H}C-PI P\cdot C\acute{r}P_jPsPIP\rangle C\dot{H}C''$   
 $P\cdot P\pm C-P\rangle CHC\acute{e}P_{\mu}PSPSC\dot{I} PN\acute{e}PsPiPs AUC C, P^{\circ} C_{max} P\ddot{I}C\dot{H}P\acute{e}P\pm P\rangle P\acute{e}P\cdot PSPs PI 2 C\dot{H}P^{\circ}P\cdot P\acute{e}. P\ddot{Y}PsP_jC\acute{r}$   
 $P'PsC, C\dot{H}C-C''PSC, ^{P\ddot{Y}P^{\#}} P\ddot{I}PsPIP\acute{e}PSP_{\mu}PS P\ddot{I}C\dot{H}P\acute{e}P\cdot PSP^{\circ}C\ddagger P^{\circ}C, P\acute{e}C\acute{I}C\dot{I} P\ddot{I}C\dot{H}P\acute{e}PSP^{\circ}PN\acute{e}P_jPSC- P\cdot P^{\circ} 1$   
 $PiPsPrP\acute{e}PSC\acute{r} PrPs P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}PsP_jC\acute{r} C-P\parallel C- P^{\circ}P\pm Ps C\ddagger P_{\mu}C\dot{H}P_{\mu}P\cdot 2 PiPsPrP\acute{e}PSP\acute{e} P\ddot{I}C-C\acute{I}P\rangle C\dot{I}$   
 $PSCHPsPiPs (PrP\acute{e}PI. C\dot{H}PsP\cdot PrC-P\rangle B\langle P\ddot{Y}PiPsC\acute{I}C-P\pm P\cdot P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\dot{I} C, P^{\circ}$   
 $PrPsP\cdot P\acute{e}B\rangle).$

$P-P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\dot{I} PsPrPSC-C''C- P\ddot{I}PsPrC\dot{H}C-P\pm PSP_{\mu}PSPsC- C, P^{\circ}P\pm P\rangle P_{\mu}C, PeP\acute{e}$   
 $P\ddot{I}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm C\acute{r} 400 P_jPi P\cdot P\pm C-P\rangle CHC\acute{e}C\acute{r}PIP^{\circ}P\rangle Ps AUC_{(0-72)} PSP^{\circ} 46 \% C, P^{\circ} C_{max}$   
 $P\ddot{I}C\dot{H}P\acute{e}P\pm P\rangle P\acute{e}P\cdot PSPs PI 2 C\dot{H}P^{\circ}P\cdot P\acute{e} C- P\cdot P_jP_{\mu}PSC\acute{e}C\acute{r}PIP^{\circ}P\rangle Ps t_{max} P\ddot{I}C\dot{H}P\acute{e}P\pm P\rangle P\acute{e}P\cdot PSPs PSP^{\circ} 2$   
 $PiPsPrP\acute{e}PSP\acute{e} P\ddot{I}PsC\dot{H}C-PIPSC\dot{I}PSPs P\cdot P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}PsP_jPsP_j C\ddagger C-P\rangle PsC- C, P^{\circ}P\pm P\rangle P_{\mu}C, PeP\acute{e}$   
 $P\ddot{I}C\dot{H}P_{\mu}P\ddot{I}P^{\circ}C\dot{H}P^{\circ}C, C\acute{r}. P\dot{I}C- PrP^{\circ}PSC- C\acute{I}PIC-PrC\ddagger P^{\circ}C, CH P\ddot{I}C\dot{H}Ps C, P_{\mu}, C\%_{\circ}Ps$   
 $P\pm C-PsPrPsC\acute{I}C, C\acute{r}P\ddot{I}PSC-C\acute{I}C, CH P\ddot{I}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm C\acute{r} C, P^{\circ} C\dot{H}C-PIP_{\mu}PSC\dot{H} PN\acute{e}PsPiPs$   
 $P^{\circ}P\pm C\acute{I}PsC\dot{H}P\pm C\ddagger C-C- P\ddot{I}C\dot{H}P\acute{e} P\ddot{I}P_{\mu}C\dot{H}PsC\dot{H}P^{\circ}P\rangle CHPSPsP_jC\acute{r} P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}PsP_jC-$   
 $P\cdot C\dot{H}PsC\acute{I}C, P^{\circ}C\dot{H}C, CH P\ddot{I}C-C\acute{I}P\rangle C\dot{I} P\cdot P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\dot{I} P\ddot{I}PsPrC\dot{H}C-P\pm PSP_{\mu}PSPsC-$   
 $C, P^{\circ}P\pm P\rangle P_{\mu}C, PeP\acute{e} P\ddot{I}PsC\dot{H}C-PIPSC\dot{I}PSPs P\cdot P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}PsP_jPsP_j C\ddagger C-P\rangle PsC- C, P^{\circ}P\pm P\rangle P_{\mu}C, PeP\acute{e}$   
 $P\ddot{I}C\dot{H}P_{\mu}P\ddot{I}P^{\circ}C\dot{H}P^{\circ}C, C\acute{r}. P_j P\cdot P\ddot{I}P^{\#} C\dot{I}P\cdot PeC\acute{r} P\cdot C\ddagger P\acute{e}P_j, P\pm P_{\mu}C\dot{H}C\acute{r}C\ddagger P\acute{e} PrPs C\acute{r}PIP^{\circ}PiP\acute{e} C, P^{\circ}PeP_{\mu}$   
 $P_jPsP\parallel P\rangle P\acute{e}PIP_{\mu} P\cdot P\pm C-P\rangle CHC\acute{e}P_{\mu}PSPSC\dot{I} PIC\acute{I}P_jPsPeC, C\acute{r}PIP^{\circ}PSPSC\dot{I} P\ddot{I}C\dot{H}P_{\mu}P\ddot{I}P^{\circ}C\dot{H}P^{\circ}C, C\acute{r},$   
 $C, P^{\circ}P\pm P\rangle P_{\mu}C, PeP\acute{e} P'PsC, C\dot{H}C-C''PSC, C\acute{r}^{P\ddot{Y}P^{\#}} PSP_{\mu} P\ddot{I}PsC, C\dot{H}C-P\pm PSPs$   
 $P\ddot{I}PsPrC\dot{H}C-P\pm PSC\dot{H}PIP^{\circ}C, P\acute{e} (PrP\acute{e}PI. C\dot{H}PsP\cdot PrC-P\rangle B\langle P\ddot{Y}PiPsC\acute{I}C-P\pm$   
 $P\cdot P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\dot{I} C, P^{\circ} PrPsP\cdot P\acute{e}B\rangle).$

*P PsP·PiPsPrC-P»*

$P-P\ddot{I}P^{\#} C\dot{I}P\cdot C\acute{r}PIP^{\circ}PSPSC\dot{I} P\ddot{I}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm C\acute{r} P\cdot P\pm C-P\rangle PeP^{\circ}P_jP\acute{e} P\ddot{I}P\rangle P^{\circ}P\cdot P_jP\acute{e}$   
 $PeC\dot{H}PsPIC- C\acute{r} P\rangle CHPrP\acute{e}PSP\acute{e} in vivo C\acute{I}C, P^{\circ}PSPsPIP\acute{e}P\rangle Ps P\ddot{I}PsPSP^{\circ}Pr 99 \%$   
 $PSP_{\mu}P\cdot P^{\circ}P\rangle P_{\mu}P\parallel PSPs PIC-Pr PePsPSC\ddagger P_{\mu}PSC, C\dot{H}P^{\circ}C\ddagger C-C- P\ddot{I}C\dot{H}P_{\mu}P\ddot{I}P^{\circ}C\dot{H}P^{\circ}C, C\acute{r} PI PeC\dot{H}PsPIC-$   
 $PI P_jP_{\mu}P\parallel P^{\circ}C... PrC-P^{\circ}P\ddot{I}P^{\circ}P\cdot PsPSC\acute{r} PePsPSC\ddagger P_{\mu}PSC, C\dot{H}P^{\circ}C\ddagger C-PN\acute{e} 10-100 P_jPePi/P_jP\rangle.$   
 $P''PsC\acute{I}P\rangle C-PrP\parallel P_{\mu}PSPSC\dot{I} in vitro P\ddot{I}PsPeP^{\circ}P\cdot P^{\circ}P\rangle P\acute{e}, C\%_{\circ}Ps P\ddot{I}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm C''$   
 $C\acute{I}C\acute{r}P\pm C\acute{I}C, C\dot{H}P^{\circ}C, PsP_j PrP\rangle C\dot{I} PiP\rangle C-PePsP\ddot{I}C\dot{H}PsC, P_{\mu}C-PSC\acute{r} P (P-gp) C, P^{\circ}$   
 $P\pm C-P\rangle PeP^{\circ} C\dot{H}P_{\mu}P\cdot P\acute{e}C\acute{I}C, P_{\mu}PSC, PSPsC\acute{I}C, C- C\dot{H}P^{\circ}PeC\acute{r} P_jPsP\rangle PsC\ddagger PSPsC-$   
 $P\cdot P^{\circ}P\rangle PsP\cdot P\acute{e} [Breast Cancer Resistance Protein, BCRP].$

*P<sub>h</sub>P<sub>μ</sub>C, P<sup>o</sup>P<sub>±</sub>PsP<sub>»</sub>C-P·P<sub>j</sub>*

$P P_{\mu}P\cdot C\acute{r}P\rangle CHC, P^{\circ}C, P\acute{e} PrPsC\acute{I}P\rangle C-PrP\parallel P_{\mu}PSC\dot{H} in vitro P\ddot{I}C\dot{H}PsPrP_{\mu}P_jPsPSC\acute{I}C, C\dot{H}C\acute{r}PIP^{\circ}P\rangle P\acute{e},$   
 $C\%_{\circ}Ps P_jP_{\mu}C, P^{\circ}P\pm PsP\rangle C-P\cdot P_j P\ddot{I}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm C\acute{r} PsP\ddot{I}PsC\acute{I}P_{\mu}C\dot{H}P_{\mu}PrPePsPIP^{\circ}PSP\acute{e}PN\acute{e}$   
 $P\ddot{I}P_{\mu}C\dot{H}P_{\mu}PIP^{\circ}P\parallel PSPs CYP3A4 P\cdot P^{\circ} PSP_{\mu}P\cdot PSP^{\circ}C\ddagger PSPsC\dot{H} C\acute{r}C\ddagger P^{\circ}C\acute{I}C, CH CYP1A2 C, P^{\circ} CYP2C8.$

*P·P<sub>»</sub>C-P<sub>j</sub>C-PSP<sup>o</sup>C<sup>†</sup>C-C<sub>‡</sub>*

$P_{\mu}P^{\circ}P\cdot PsP\ddot{I}P^{\circ}PSC-P\pm PIP\acute{e}PIP_sPrP\acute{e}C, CHC\acute{I}C\dot{I} P\cdot PsC\dot{H}PiP^{\circ}PSC-P\cdot P_jC\acute{r} P\ddot{I}PsPIC-P\rangle CHPSPs, P\cdot$   
 $C\acute{I}P_{\mu}C\dot{H}P_{\mu}PrPSC-P_j P\ddot{I}P_{\mu}C\dot{H}C-PsPrPsP_j PSP^{\circ}P\ddot{I}C-PIPIP\acute{e}PIP_{\mu}PrP_{\mu}PSPSC\dot{I} 30,9 PiPsPrP\acute{e}PSP\acute{e}$   
 $P\ddot{I}C-C\acute{I}P\rangle C\dot{I} P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}PsP_jC\acute{r} C\dot{H}P_{\mu}PePsP_jP_{\mu}PSPPrPsPIP^{\circ}PSPsC- PrPsP\cdot P\acute{e} 800 P_jPi.$   
 $P\cdot P\rangle C-P_jC-PSP^{\circ}C\ddagger C-C\dot{I} P\ddot{I}C\dot{H}P_{\mu}P\ddot{I}P^{\circ}C\dot{H}P^{\circ}C, C\acute{r} PIC-PrP\pm C\acute{r}PIP^{\circ}C''C, CHC\acute{I}C\dot{I}$   
 $P\ddot{I}P_{\mu}C\dot{H}P_{\mu}PIP^{\circ}P\parallel PSPs P\cdot PeP^{\circ}P\rangle PsP_j, P\ddot{I}C\dot{H}P\acute{e} C\ddagger CHPsP_jC\acute{r} PIP\acute{e}PIP_{\mu}PrP_{\mu}PSPSC\dot{I}$   
 $P\ddot{I}C\dot{H}P_{\mu}P\ddot{I}P^{\circ}C\dot{H}P^{\circ}C, C\acute{r} PSP\acute{e}C\dot{H}PeP^{\circ}P_jP\acute{e} C\acute{I}C, P^{\circ}PSPsPIP\acute{e}C, CH < 4 \% PIC-Pr$   
 $P\ddot{I}C\dot{H}P\acute{e}PN\acute{e}PSC\dot{I}C, PsC- PrPsP\cdot P\acute{e}.$

$P' \cdot C\tilde{H}P_{\mu}P \cdot C\tilde{r}P \gg CHC, P^{\circ}C, C - PsPrPSPsC\ddagger P^{\circ}C\tilde{I}PSPsPiPs \cdot P \cdot P^{\circ}C\tilde{I}C, PsC\tilde{I}C\tilde{r}PIP^{\circ}PSPSC\ddagger$   
 $PiP^{\circ}P \cdot PsPiP^{\circ}PSC - P \pm C\tilde{r} \text{ (400 } PjPi \text{ 1 } C\tilde{H}P^{\circ}P \cdot PSP^{\circ} PrPsP \pm C\tilde{r}) \cdot P \cdot C\tilde{I}P\ddot{e}P \gg CH\ddot{P}SP\ddot{e}Pj \text{ CYP3A4 } C, P^{\circ} P\text{-gp}$   
 $C - PSPiC - P \pm C - C, PsC\tilde{H}PsPj \text{ PePu}C, PsPePsPSP^{\circ}P \cdot PsP \gg PsPj \text{ (400 } PjPi \text{ 1 } C\tilde{H}P^{\circ}P \cdot PSP^{\circ} PrPsP \pm C\tilde{r})$   
 $PiC\tilde{H}PsC, C\ddagger PiPsPj \text{ 5 } PrPSC - PI \text{ } PiPsC\tilde{I}PiC - P \gg CH\ddot{P} \cdot P \cdot P \pm C - P \gg CHC\epsilon C\tilde{r}C\tilde{H}C, CHC\tilde{I}C\ddagger$   
 $C\tilde{I}P_{\mu}C\tilde{H}P_{\mu}PrPSC - P \cdot PSP^{\circ}C\ddagger P_{\mu}PSPSC\ddagger AUC_{(0-24)} C, P^{\circ} P\ddot{Y}_{\max} PiP^{\circ}P \cdot PsPiP^{\circ}PSC - P \pm C\tilde{r} PSP^{\circ} 66 \% C, P^{\circ}$   
 $45 \% B \text{ } PIC - PrPiPsPIC - PrPSPs \text{ } C\tilde{r} \text{ } PiPsC\tilde{H}C - PIPSC\ddagger PSPSC - C \cdot P \cdot P \cdot P^{\circ}C\tilde{I}C, PsC\tilde{I}C\tilde{r}PIP^{\circ}PSPSC\ddagger Pj$   
 $PiP^{\circ}P \cdot PsPiP^{\circ}PSC - P \pm C\tilde{r} \text{ (400 } PjPi \text{ 1 } C\tilde{H}P^{\circ}P \cdot PSP^{\circ} PrPsP \pm C\tilde{r} \text{ } PiC\tilde{H}PsC, C\ddagger PiPsPj \text{ 7 } PrPSC - PI)$   
 $PsPeC\tilde{H}P_{\mu}PjPs. AUC \text{ } C, P^{\circ} P\ddot{Y}_{\max} PiP^{\circ}P \cdot PsPiP^{\circ}PSC - P \pm C\tilde{r} \cdot P \cdot P \pm C - P \gg CHC\epsilon C\tilde{r}C\tilde{H}C, CHC\tilde{I}C\ddagger$   
 $PjP_{\mu}PSC\epsilon PsC\tilde{H} \text{ } PjC - C\tilde{H}PsC\tilde{H} \text{ } PiC\tilde{H}PsPiPsC\tilde{H}C\ddagger C - PN_{\circ}PSPs \cdot P \cdot P \pm C - P \gg CHC\epsilon P_{\mu}PSPSC\tilde{H} \text{ } PrPsP \cdot P\ddot{e} \text{ } C\tilde{r}$   
 $PjP_{\mu}P \P P^{\circ}C... PIC - Pr \text{ 50 } PjPi \text{ } PrPs \text{ 2000 } PjPi. P\ddot{Y}PsPjC\tilde{r} \text{ } PI \text{ } C\tilde{H}P_{\mu}P \cdot C\tilde{r}P \gg CHC, P^{\circ}C, C -$   
 $P \cdot PjP_{\mu}PSC\epsilon P_{\mu}PSPSC\ddagger \text{ } PrPsP \cdot P\ddot{e} \text{ } PiP^{\circ}P \cdot PsPiP^{\circ}PSC - P \pm C\tilde{r} \text{ } PrPs \text{ 400 } PjPi \text{ 1 } C\tilde{H}P^{\circ}P \cdot PSP^{\circ} PrPsP \pm C\tilde{r} \text{ } C\tilde{r}$



PtPSPPrCrPeC,PsCtjPë CYP3A4, C,P°PeC- ClPe CtjPëC,,P°PjPiC-CtPëPS, PjPsP¶CrC,CH P·PSPëP¶CrPIP°C,Pë PePsPSCtPµPSC,CtjP°CtC-CH PïP°P·PsPiP°PSC-P±Cr PI PïP»P°P·PjC- PeCtjPsPIC-. PhPrPSPScP°CtPSPµ P·P°CtC,PsCtCrPIP°PSPSCl PïP°P·PsPiP°PSC-P±Cr P· PïPsC,CrP¶PSPëPjPë C-PSPrCrPeC,PsCtjP°PjPë P-gp P°P±Ps BCRP PjPsP¶Pµ P·PjC-PSPëC,Pë PµPeCtPïPsP·PëCtC-CH C,P° CtjPsP·PiPsPrC-P» PïP°P·PsPiP°PSC-P±Cr, PIPeP»CHCtP°CHCtPë CtjPsP·PiPsPrC-P» Cr PIC-PrPrC-P»P°C... CtPµPSC,CtjP°P»CHPSPSc— PSPµCtjPIPSPiPsC— CtPëCtC,PµPjPë. P PµPePsPjPµPSPrPsPIP°PSPs PiC-PrP±PëCtjP°C,Pë PrP»Cl CtCtPiCrC,PSCHPsC— C,PµCtjP°PiC-C— P°P»CHC,PµCtjPSP°C,PëPIPSC- P»C-PeP°CtjCtCHPeC- P·P°CtPSP±Pë Btj“ P· PIC-PrCtCrC,PSCHPsCH P°P±Ps PjC-PSC-PjP°P»CHPSPScH C-PSPrCrPeCtCHCtPsCH PrC-C”CH PSP° CtPµPNë C,,PµCtjPjPµPSC,,.

*P'PiP»PëPI P'PsC,CtjC-C”PSC,Ct<sup>PjPb</sup> PSP° C-PSC€C- P»C-PeP°CtjCtCHPeC- P·P°CtPSP±Pë*

P”PsCtP»C-PrP¶PµPSPSCl *in vitro* P· PiPµCtC-PSPePsPIPëPjPë PjC-PeCtjPsCtPSPjP°PjPë P»CHPrPëPSPë PïPsPeP°P·P°P»Pë, C%Ps PïP°P·PsPiP°PSC-P± C-PSPiC-P±CrC” CYP- C,,PµCtjPjPµPSC,Pë 1A2, 3A4, 2B6, 2C8, 2C9, 2C19 C,P° 2E1. PµC-Pr CtP°Ct PrPsCtP»C-PrP¶PµPSPSCl *in vitro* P· PeC-P»CHPeC-CtPSPëPj PIPëP·PSP°CtPµPSPSClPj PiCtjPµPiPSP°PS-PI-CtjPµCtPµPiC,PsCtjCr [Pregnane X Receptor, PXR] P»CHPrPëPSPë P±CrP»Ps PiCtjPsPrPµPjPsPSCtC,CtjPsPIP°PSPs PiPsC,PµPSCtC-PNëPSCr C-PSPrCrPeCtCHCtCr PrC-CH PiCtjPµPiP°CtjP°C,Cr PSP° CYP3A4 P»CHPrPëPSPë. PµP»C-PSC-CtPSC- C,,P°CtjPjP°PePsP»PsPiC-CtPSC- PrPsCtP»C-PrP¶PµPSPSCl, PI ClPePëC... P'PsC,CtjC-C”PSC, <sup>PjPb</sup> PiCtjPëP·PSP°CtP°PICtCl PïPs 800 PjPi 1 CtjP°P· PSP° PrPsP±Cr, PïPsPeP°P·P°P»Pë, C%Ps P'PsC,CtjC-C”PSC, <sup>PjPb</sup> PSPµ PjP°C” PeP»C-PSC-CtPSPs P·PSP°CtCrC%PsPiPs PIPiP»PëPICr PSP° C,,P°CtjPjP°PePsPeC-PSPµC,PëPeCr PePsC,,PµC—PSCr (PjP°CtjPePµCtjPSPëPNë CtCrP±CtC,CtjP°C, CYP1A2), PIP°CtjC,,P°CtjPëPSCr (PjP°CtjPePµCtjPSPëPNë CtCrP±CtC,CtjP°C, CYP2C9) P°P±Ps PsPjPµPiCtjP°P·PsP»Cr (PjP°CtjPePµCtjPSPëPNë CtCrP±CtC,CtjP°C, CYP2C19) PI PsPSPePsP»PsPiC-CtPSPëC... PïP°CtC-C”PSC,C-PI. P'PsC,CtjC-C”PSC, <sup>PjPb</sup> P·CrPjPsPIP»CHC” P·P±C-P»CHC€PµPSPSCl CtPµCtjPµPrPSCHPsC— AUC C,P° C<sub>max</sub> PjC-PrP°P·PsP»P°PjCr (PjP°CtjPePµCtjPSPëPNë CtCrP±CtC,CtjP°C, CYP3A4) PiCtjPëP±P»PëP·PSPs PSP° 30 %, P° C,P°PePsP¶ PiC-PrPIPëC%PµPSPSCl PSP° 33-64 % CtPiC-PIPIC-PrPSPSc€PµPSPSCl PePsPSCtPµPSC,CtjP°CtC-C— PrPµPeCtC,CtjPsPjPµC,PsCtjC,,P°PSCr PrPs PePsPSCtPµPSC,CtjP°CtC-C— PNëPsPiPs P°PeC,PëPIPSPsPiPs PjPµC,P°P±PsP»C-C,Cr PrPµPeCtC,CtjPsCtjC,,P°PSCr Cr CtPµCtC- PiC-CtP»Cl PïPµCtjPsCtjP°P»CHPSPsPiPs PiCtjPëPNëPsPjCr PrPµPeCtC,CtjPsPjPµC,PsCtjC,,P°PSCr (PjP°CtjPePµCtjPSPëPNë CtCrP±CtC,CtjP°C, CYP2D6). PµPsPjP±C-PSPsPIP°PSPµ P·P°CtC,PsCtCrPIP°PSPSCl P'PsC,CtjC-C”PSC,Cr<sup>PjPb</sup> PïPs 800 PjPi 1 CtjP°P· PSP° PrPsP±Cr C,P° PïP°PeP»C-C,P°PeCtPµP»Cr (CtCrP±CtC,CtjP°C, CYP3A4 C,P° CYP2C8) 80 PjPi/Pj<sup>2</sup> 1 CtjP°P· PSP° C,PëP¶PrPµPSCH PiCtjPëP·PIPPrPëC,CH PrPs PiC-PrPIPëC%PµPSPSCl AUC C,P° C<sub>max</sub> PïP°PeP»C-C,P°PeCtPµP»Cr PI CtPµCtjPµPrPSCHPsPjCr PSP° 26 % C,P° 31 % PIC-PrPïPsPIC-PrPSPs.

PµP°P·PsPiP°PSC-P± CtP»C-Pr P· PsP±PµCtjPµP¶PSC-CtC,CH P·P°CtC,PsCtPsPICrPIP°C,Pë PsPrPSPScP°CtPSPs P· C-PSC€PëPjPë PïPµCtjPsCtjP°P»CHPSPëPjPë CtCrP±CtC,CtjP°C,P°PjPë BCRP C,P° P-gp, PICtjP°C...PsPICrCHCtPë PNëPsPiPs C-PSPiC-P±C-C,PsCtjPSPëPNë PIPiP»PëPI PSP° CtC- P±C-P»PePë.

P”PsCtP»C-PrP¶PµPSPSCl *in vitro* C,P°PePsP¶ PiCtjPsPrPµPjPsPSCtC,CtjCrPIP°P»Pë, C%Ps PïP°P·PsPiP°PSC-P± C” PïPsC,PµPSCtC-PNëPSPëPj C-PSPiC-P±C-C,PsCtjPsPj C,CtjP°PSCtPïPsCtjC,PSPëC... P±C-P»PeC-PI UGT1A1 C,P° OATP1B1. PµP°P·PsPiP°PSC-P± PjPsP¶Pµ P·P±C-P»CHC€CrPIP°C,Pë PePsPSCtPµPSC,CtjP°CtC-CH P»C-PeP°CtjCtCHPePëC...

P·P°CÍPSP±C-PI, CÍPЕC- PμP»C-PjC-PSCrCЧC,ЧБCГCЦ PíPμCГPμPIP°P¶PSPs P·P°PIPrCÍPЕPё UGT1A1 C,P° OATP1B1.

*PŸCзPjC-CÍPSPμ P·P°CГC,PsCГCзPIP°PSPSCЦ P'PsC,ЧГC-C"PSC,Cз<sup>PŸPн</sup> C,P° CГPёPjPIP°CГC,P°C,PёPSCз*

PŸCзPjC-CÍPSPμ P·P°CГC,PsCГCзPIP°PSPSCЦ P'PsC,ЧГC-C"PSC,CГ<sup>PŸPн</sup> C,P° CГPёPjPIP°CГC,P°C,PёPSCr P·P±C-P»ЧБC€CГC" C±P°CГC,PsC,Cr PíC-PrPIPёC%PμPSPSCЦ ЧГC-PIPSCЦ PнP·PŸ. PμC-Pr C±P°CГ PеP»C-PSC-C±PSPёC... PrPsCГP»C-PrP¶PμPSCн PjPsPSPsC,PμCГP°PíC-C— P'PsC,ЧГC-C"PSC,PsPj<sup>PŸPн</sup> P·P±C-P»ЧБC€PμPSPSCЦ ЧГC-PIPSCЦ PнP·PŸ Cr 3 ЧГP°P·Pё PIPёC%Pμ P'PнPк CГPíPsCГC,PμCГC-PiP°P»PsCГЧB Cr 126 C-P· 895 PíP°CГC-C"PSC,C-PI (14 %), CÍPЕC- PSPμ PíCГPёPNёPjP°P»Pё CГC,P°C,PёPSPё, PíPsCГC-PIPSCЦPSPs P· 11 C-P· 41 PíP°CГC-C"PSC,P° (27 %), CÍPЕC- CГCзPíCГC,PSCHPs PíCГPёPNёPjP°P»Pё CГPёPjPIP°CГC,P°C,PёPS. PíPеC%Ps Cr C...PIPсГPsPiPs, CÍPЕPёPNё CÍPЕ CГCзPíCГC,PSC-PNё PíCГPμPíP°CГP°C, PíCГPёPNёPjP°C" CГPёPjPIP°CГC,P°C,PёPS, PIPёPSPёPеPSPμ P·P±C-P»ЧБC€PμPSPSCЦ ЧГC-PIPSCЦ PнP·PŸ, CГP»C-Pr PеPμCГCзPIP°C,PёCГCЦ ЧГPμPеPsPjPμPSPrP°CГC-CÍPjPё P· PrPsP·CзPIP°PSPSCЦ P'PsC,ЧГC-C"PSC,CГ<sup>PŸPн</sup> C,P° PíCГPёPíPёPSPёC,Pё P·P°CГC,PsCГCзPIP°PSPSCЦ CГPёPjPIP°CГC,P°C,PёPSCr (PrPёPI. ЧГPsP·PrC-P» B«PнCГPs±P»PёPIPsCГC,C- P·P°CГC,PsCГCзPIP°PSPSCЦB»). PŸP»C-Pr P· PsP±PμCГPμP¶PSC-CГC,Ч P·P°CГC,PsCГPsPICзPIP°C,Pё P'PsC,ЧГC-C"PSC,<sup>PŸPн</sup> P· C-PSCёPёPjPё CГC,P°C,PёPSP°PjPё, PsCГPеC-P»ЧБPеPё PrP°PSPёC... CГC,PsCГPsPIPSPs PsCГC-PSPеPё ЧГPёP·PёPеCз PrP»CЦ C,P°PеPёC... PеPsPjP±C-PSP°CГC-PNё PSPμPrPsCГC,P°C,PSCHPs.

*P'PiP»PёPI C—P¶C- PSP° P'PsC,ЧГC-C"PSC,<sup>PŸPн</sup>*

P—P°CГC,PsCГCзPIP°PSPSCЦ P'PsC,ЧГC-C"PSC,CГ<sup>PŸPн</sup> ЧГP°P·PsPj C-P· C—P¶PμCн P· PIPёCГPsPеPёPj P°P±Ps PSPёP·ЧБPеPёPj PIPjC-CГC,PsPj P¶PёЧГC-PI P·CзPjPsPIP»ЧЧC" P·P±C-P»ЧБC€PμPSPSCЦ PNёPsPiPs AUC C,P° C<sub>max</sub> PíCГPёP±P»PёP·PSPs PI 2 ЧГP°P·Pё. PŞPμCГPμP· C†Pμ P'PsC,ЧГC-C"PSC,<sup>PŸPн</sup> PíPsPIPёPSPμPS PíCГPёP·PSP°C±P°C,PёCГCЦ PíCГPёPSP°PNёPjPSC- P·P° 1 PiPsPrPёPSCr PrPs PíCГPёPNёPsPjCr C—P¶C- P°P±Ps C±PμCГPμP· 2 PiPsPrPёPSPё PíC-CГP»CЦ PSCHPsPiPs (PrPёPI. ЧГPsP·PrC-P» B«PŸPíPsCГC-P± P·P°CГC,PsCГCзPIP°PSPSCЦ C,P° PrPsP·PёB»).

*P>C-PeP°CГCГЧBPeC- P·P°CГPsP±Pё, C%Ps PIPiP»PёPIP°ЧЧC,ЧБ PSP° ЧГPк CёP»CзPSPeP°*

PŸCзPjC-CÍPSPμ P·P°CГC,PsCГCзPIP°PSPSCЦ PíP°P·PsPíP°PSC-P±Cз P· PμP·PsPjPμPíCГP°P·PsP»PsPj P·PjPμPSC€CГC" P±C-PsPrPsCГC,CзPíPSC-CГC,ЧB PíP°P·PsPíP°PSC-P±Cз PíCГPёP±P»PёP·PSPs PSP° 40 % (AUC C,P° C<sub>max</sub>), C,PsPjCr CГP»C-Pr CзPSPёPеP°C,Pё P·P°CГC,PsCГCзPIP°PSPSCЦ PíP°P·PsPíP°PSC-P±Cз ЧГP°P·PsPj P· P»C-PeP°CГCГЧBPePёPjPё P·P°CГPsP±P°PjPё, C%Ps PíC-PrPIPёC%CrCЧC,ЧБ ЧГPк CёP»CзPSPeP°. Pj ЧГP°P·C- PSPμPsP±C...C-PrPSPsCГC,C- CГCзPjC-CÍPSPsPiPs P·P°CГC,PsCГCзPIP°PSPSCЦ P· C-PSPiC-P±C-C,PsCГPsPj PíCГPsC,PsPSPSPsPiPs PSP°CГPsCГP° ЧГPμPеPsPjPμPSPrCзC"ЧБCГCЦ PrPsP·Cз PíP°P·PsPíP°PSC-P±Cз PíCГPёPNёPjP°C,Pё 1 ЧГP°P· PSP° PrPμPSCн P±PμP· C—P¶C- PIPiPμC†PμCГC- ЧГP°P·PsPj P· C-PSPiC-P±C-C,PsCГPsPj PíCГPsC,PsPSPSPsPiPs PSP°CГPsCГP°. Pj ЧГP°P·C- PSPμPsP±C...C-PrPSPsCГC,C- CГCзPjC-CÍPSPsPiPs P·P°CГC,PsCГCзPIP°PSPSCЦ P· P°PSC,P°PiPsPSC-CГC,PsPj Pк₂-ЧГPμC†PμPíC,PsCГP° ЧГPμPеPsPjPμPSPrCзC"ЧБCГCЦ PrPsP·Cз PíP°P·PsPíP°PSC-P±Cз PíCГPёPNёPjP°C,Pё P±PμP· C—P¶C- C...PsC±P° P± P·P° 2 PiPsPrPёPSPё PrPs P°P±Ps C±PμCГPμP· 10 PiPsPrPёPS PíC-CГP»CЦ PíCГPёPNёPsPjCr P°PSC,P°PiPsPSC-CГC,P° Pк₂-ЧГPμC†PμPíC,PsCГP°. PμP°P·PsPíP°PSC-P± CГP»C-Pr PíCГPёPNёPjP°C,Pё C...PsC±P° P± P·P° 1 PiPsPrPёPSCr PrPs

$P^{\circ}P \pm Ps$   $C \nmid P_{\mu}C \nmid P_{\mu}P \cdot 2$   $PiPsPrP \ddot{e}PSP \ddot{e}$   $PiC - C \nmid P \gg C \nmid P \ddot{e}C \nmid P \ddot{e}PN_{\circ}PsPjC \nmid$   
 $PePsC \nmid PsC, PePsPrC - C \nmid C \nmid P \ddot{e}C \dots$   $P^{\circ}PSC, P^{\circ}C \nmid P \ddot{e}PrC - PI$ .

**$PhC \nmid PsP \pm P \gg P \ddot{e}PIP sC \nmid C, C - P \cdot P^{\circ}C \nmid C, PsC \nmid C \nmid PIP^{\circ}PSPSC \nmid$ .**

$P'PiP \gg P \ddot{e}PI$   $PSP^{\circ}$   $PiP_{\mu}C \nmid C - PSPeC \nmid$ .

$P_{\mu}PsPIC - PrPsPjP \gg C \nmid P \gg PsC \nmid C \nmid P \ddot{e}C \nmid Ps$   $PIP \ddot{e}PiP^{\circ}PrPeP \ddot{e}$   $C \nmid PsP \cdot PIP \ddot{e}C, PeC \nmid$   
 $PiP_{\mu}C \nmid C - PSPePsPIP sC -$   $PSP_{\mu}PrPsC \nmid C, P^{\circ}C, PSPsC \nmid C, C -$   $(PI$   $C, PsPjC \nmid C \nmid P \ddot{e}C \nmid P \gg C -$   
 $P \gg P_{\mu}C, P^{\circ}P \gg CHPsC -)$   $PSP^{\circ}$   $C, P \gg C -$   $P \cdot P^{\circ}C \nmid C, PsC \nmid C \nmid PIP^{\circ}PSPSC \nmid$   $P'PsC, C \nmid C - C''PSC, C \nmid P \ddot{e}P^{\nabla}$ .  $Pj$   
 $PeP \gg C - PSC - C \nmid PSP \ddot{e}C \dots$   $PrPsC \nmid P \gg C - PrP \nmid P_{\mu}PSPSC \nmid C \dots$   $P \cdot P'PsC, C \nmid C - C''PSC, PsPj^{\nabla}$   $PSP^{\circ}$   $C, P \gg C -$   
 $PN_{\circ}PsPiPs$   $PiC \nmid P \ddot{e}PN_{\circ}PsPjC \nmid C \nmid P \ddot{e}PiPsC \nmid C, P_{\mu}C \nmid C - PiP^{\circ}P \gg PsC \nmid C \nmid P \ddot{e}C \nmid P \ddot{e}PN_{\circ}PsPSPSC \nmid$   
 $C \nmid P \ddot{e}C \nmid PsPIP^{\circ}C, PePsPIP \ddot{e}C \dots$   $C \nmid C - PIPSC - PI$   $C, C \nmid P^{\circ}PSC \nmid P^{\circ}PjC - PSP^{\circ}P \cdot$   $(P \nmid P \nmid P \ddot{y},$   
 $P^{\circ}C \nmid PiP^{\circ}C \nmid C, P^{\circ}C, P^{\circ}PjC - PSPsC, C \nmid P^{\circ}PSC \nmid C, P_{\mu}C \nmid P^{\circ}P \cdot P \ddot{e}$   $[P \nmid P \ddot{y}P \ddot{y}])$   $C, P^{\circ}$   
 $P \pm C - P \gg C - C \nmid C \nmid P \pm C - PSC \nmid$   $(PrP \ddot{e}PI. C \nmid PsP \cdot PrC - P \gg B \nmid P_{\mu}PsP \pm C - C \nmid PSC -$   $C \nmid P_{\mu}P^{\circ}PeC \nmid C - C - B \gg)$ .  $Pj$   
 $P \pm C - P \gg CHC \nmid PsC \nmid C, C -$   $PIP \ddot{e}PiP^{\circ}PrPeC - PI$   $PiPsPIC - PrPsPjP \gg C \nmid P \gg PsC \nmid C \nmid P \ddot{e}C \nmid P \ddot{e}PN_{\circ}Ps$   
 $C - P \cdot PsP \gg CHPsPIP^{\circ}PSP_{\mu}$   $P \cdot P \pm C - P \gg CHC \nmid P_{\mu}PSPSC \nmid$   $C \nmid C - PIPSC - PI$   $P \nmid P \nmid P \ddot{y}$   $C, P^{\circ}$   $P \nmid P \ddot{y}P \ddot{y}$   $P \pm P_{\mu}P \cdot$   
 $C \nmid C \nmid P \ddot{e}C \nmid C, PSC \nmid PsPiPs$   $PiC - PrPIP \ddot{e}C \nmid P_{\mu}PSPSC \nmid$   $C \nmid C - PIPSC - PI$   $P \gg C \nmid P \nmid PSPsC -$   
 $C, PsC \nmid C, P^{\circ}C, P^{\circ}P \cdot P \ddot{e}$   $P^{\circ}P \pm Ps$   $P \pm C - P \gg C - C \nmid C \nmid P \pm C - PSC \nmid$ .  $Pj$   $PiP^{\circ}C \nmid C - C''PSC, C - PI$   $PIC - PePsPj$   
 $PiPsPSP^{\circ}Pr$   $60$   $C \nmid PsPeC - PI$   $P \pm C - P \gg CHC \nmid P \ddot{e}PN_{\circ}$   $C \nmid P \ddot{e}P \cdot P \ddot{e}Pe$   $PiPsPjC - C \nmid PSPsPiPs$   $(P \nmid P \nmid P \ddot{y} > 3$   
 $P'P \nmid P \nmid K)$   $P^{\circ}P \pm Ps$   $P \cdot PSP^{\circ}C \nmid PSPsPiPs$   $(P \nmid P \nmid P \ddot{y} > 8$   $P'P \nmid P \nmid K)$   $PiC - PrPIP \ddot{e}C \nmid P_{\mu}PSPSC \nmid$   $P \nmid P \nmid P \ddot{y}$ .  
 $P_{\mu}P^{\circ}C \nmid C - C''PSC, P \ddot{e}$   $C \nmid PsC$   $C''$   $PSPsC \nmid C - C \nmid PjP \ddot{e}$   $HLA - B * 57 : 01$   $P^{\circ}P \gg P_{\mu}P \gg C \nmid C, C, P^{\circ}PePsP \nmid$   
 $PjP^{\circ}C \nmid C, CH$   $P \pm C - P \gg CHC \nmid P \ddot{e}PN_{\circ}$   $C \nmid P \ddot{e}P \cdot P \ddot{e}Pe$   $PiC - PrPIP \ddot{e}C \nmid P_{\mu}PSC \nmid$   $C \nmid C - PIPSC \nmid$   $P \nmid P \nmid P \ddot{y}$ ,  
 $PiPsPiB \nmid C \nmid P \cdot P^{\circ}PSPsPiPs$   $C - P \cdot P \cdot P^{\circ}C \nmid C, PsC \nmid C \nmid PIP^{\circ}PSPSC \nmid Pj$   $P'PsC, C \nmid C - C''PSC, C \nmid P \ddot{e}P^{\nabla}$ .  
 $P \ddot{y}P \gg C - Pr$   $PePsPSC, C \nmid PsP \gg C \nmid PIP^{\circ}C, P \ddot{e}$   $C, C \nmid PSPeC \nmid C - C \nmid PiP_{\mu}C \nmid C - PSPeP \ddot{e}$   $C \nmid PIC \nmid C - C \dots$   
 $PiP^{\circ}C \nmid C - C''PSC, C - PI$   $C \nmid PsC$   $PsC, C \nmid P \ddot{e}PjC \nmid C \nmid C, CH$   $P \gg C - PeC \nmid PIP^{\circ}PSPSC \nmid$   
 $P'PsC, C \nmid C - C''PSC, PsPj^{\nabla}$   $PSP_{\mu}P \cdot P^{\circ}P \gg P_{\mu}P \nmid PSPs$   $PIC - Pr$   $C - C \dots$   $PiP_{\mu}PSPsC, P \ddot{e}PiC \nmid P^{\circ}P \pm Ps$   
 $PIC - PeC \nmid$ .

$P \nmid P_{\mu}PsP \pm C \dots C - PrPSPs$   $PIP \ddot{e}P \cdot PSP^{\circ}C \nmid P^{\circ}C, P \ddot{e}$   $C \nmid P \ddot{e}C \nmid PsPIP^{\circ}C, PePsPIP \ddot{e}PN_{\circ}$   $PIPjC - C \nmid C,$   
 $PiP_{\mu}C \nmid C - PSPePsPIP \ddot{e}C \dots$   $C, P_{\mu}C \nmid PjP_{\mu}PSC, C - PI$   $PiP_{\mu}C \nmid PjP_{\mu}Pr$   $PiPsC \nmid P^{\circ}C, PePsPj$   
 $P \gg C - PeC \nmid PIP^{\circ}PSPSC \nmid$   $P'PsC, C \nmid C - C''PSC, PsPj^{\nabla}$   $C, P^{\circ}$   $PSP^{\circ}$   $3, 5, 7$   $C, P^{\circ}$   $9$   $C, P \ddot{e}P \nmid PSC -$   
 $P \gg C - PeC \nmid PIP^{\circ}PSPSC \nmid$   $PiC \nmid P_{\mu}PiP^{\circ}C \nmid P^{\circ}C, PsPj$ .  $P_{\mu}PsC, C - Pj$   $PePsPSC, C \nmid PsP \gg CH$   $C \nmid P \gg C - Pr$   
 $PiC \nmid PsPIP sPrP \ddot{e}C, P \ddot{e}$   $PSP^{\circ}$   
 $3 - PsPjC \nmid C, P^{\circ}$   $4 - PsPjC \nmid PjC - C \nmid C \nmid C \nmid C -$   $P \gg C - PeC \nmid PIP^{\circ}PSPSC \nmid$   $C -$   $PrPsPrP^{\circ}C, PePsPIP s$   $P \cdot P^{\circ}$   
 $PeP \gg C - PSC - C \nmid PSP \ddot{e}PjP \ddot{e}$   $PiPsPeP^{\circ}P \cdot P^{\circ}PSPSC \nmid PjP \ddot{e}$ .  $P_{\mu}C - C \nmid P \gg C \nmid C$   $4$   $PjC - C \nmid C \nmid C \nmid C \nmid$   
 $C, P_{\mu}C \nmid P^{\circ}PiC - C - B$   $C \nmid P \gg C - Pr$   $PiC \nmid PsPrPsPIP \nmid C \nmid PIP^{\circ}C, P \ddot{e}$   $PiP_{\mu}C \nmid C - PsPrP \ddot{e}C \nmid PSP \ddot{e}PN_{\circ}$   
 $PePsPSC, C \nmid PsP \gg CH$   $C \nmid C - PIPSC \nmid$   $PiP_{\mu}C \nmid C - PSPePsPIP \ddot{e}C \dots$   $C, P_{\mu}C \nmid PjP_{\mu}PSC, C - PI,$   
 $PIC \nmid P^{\circ}C \dots PsPIC \nmid C \nmid C -$   $PeP \gg C - PSC - C \nmid PSC -$   $PiPsPeP^{\circ}P \cdot P^{\circ}PSPSC \nmid$ .

$P''P \gg C \nmid P \ddot{e}PiP^{\circ}C \nmid C - C''PSC, C - PI$   $P \cdot PIP \ddot{e}C \dots C - PrPSP \ddot{e}PjP \ddot{e}$   $(PrPs$   $PiPsC \nmid P^{\circ}C, PeC \nmid$   
 $P \gg C - PeC \nmid PIP^{\circ}PSPSC \nmid$   $PiC \nmid P_{\mu}PiP^{\circ}C \nmid P^{\circ}C, PsPj)$   $C \nmid C - PIPSC \nmid PjP \ddot{e}$   $P \cdot P^{\circ}PiP^{\circ}P \gg CHPsPsPiPs$   
 $P \pm C - P \gg C - C \nmid C \nmid P \pm C - PSC \nmid$   
 $\leq 1,5$   $P'P \nmid P \nmid K$   $C, P^{\circ}$   $P \nmid P \ddot{y}P \ddot{y}$   $C -$   $P \nmid P \nmid P \ddot{y} \leq B$   $2$   $P'P \nmid P \nmid K$   $C \nmid P \gg C - Pr$   $PrPsC, C \nmid P \ddot{e}PjC \nmid PIP^{\circ}C, P \ddot{e}C \nmid C \nmid$   
 $C, P^{\circ}PeP \ddot{e}C \dots$   $C \nmid P_{\mu}PePsPjP_{\mu}PSP^{\circ}C \nmid C - PN_{\circ}$ .

$P_{\mu}P^{\circ}C \nmid C - C''PSC, P \ddot{e}$   $P \cdot C - P \cdot PsP \gg CHPsPIP^{\circ}PSP \ddot{e}Pj$   $PiC - PrPIP \ddot{e}C \nmid P_{\mu}PSPSC \nmid Pj$   $C \nmid C - PIPSC \nmid$   $P \nmid P \nmid P \ddot{y}$   
 $PI$   $PrC - P^{\circ}PiP^{\circ}P \cdot PsPSC -$   $PjC - P \nmid 3$   $P'P \nmid P \nmid K$   $C, P^{\circ}$   $8$   $P'P \nmid P \nmid K$   $PjPsP \nmid C \nmid C, CH$   $PiC \nmid PsPrPsPIP \nmid C \nmid PIP^{\circ}C, P \ddot{e}$   
 $P \gg C - PeC \nmid PIP^{\circ}PSPSC \nmid$   $P'PsC, C \nmid C - C''PSC, PsPj^{\nabla}$   $P \cdot P^{\circ}$   $C \nmid PjPsPI$   $C \nmid PsC, P \ddot{e}P \nmid PSP_{\mu}PIP sPiPs$   
 $PePsPSC, C \nmid PsP \gg CH$   $C \nmid C, P^{\circ}PSC \nmid$   $PiP_{\mu}C \nmid C - PSPePsPIP sC -$   $C, C \nmid PSPeC \nmid C - C -$ ,  $PiPsPeP \ddot{e}$

PhPeC $\overline{\text{C}}$ C-Pj C $\overline{\text{C}}$ P $\mu$ PePsPjP $\mu$ PSPrP $^{\circ}$ C $\dagger$ C-PN $\text{e}$ , C% $\text{o}$ Ps P $\ddot{\text{i}}$ P $^{\circ}$ C $\dagger$ C-C''PSC,P $^{\circ}$ Pj P $\cdot$  PSP $\mu$ P $\cdot$ PSP $^{\circ}$ C $\ddagger$ PSP $\ddot{\text{e}}$ PjP $\ddot{\text{e}}$  P $\cdot$ PjC-PSP $^{\circ}$ PjP $\ddot{\text{e}}$  P $\ddot{\text{i}}$ P $\mu$ C $\ddagger$ C-PSPePsPIP $\ddot{\text{e}}$ C... P $\ddot{\text{i}}$ C $\overline{\text{C}}$ PsP $\pm$  (PIP $\ddot{\text{e}}$ P $\cdot$ PSP $^{\circ}$ C $\ddagger$ P $^{\circ}$ C''C,C $\overline{\text{H}}$ C $\overline{\text{r}}$ C $\overline{\text{C}}$  C $\overline{\text{C}}$ Pe P $\ddot{\text{i}}$ C-PrPIP $\ddot{\text{e}}$ C% $\text{o}$ P $\mu$ PSPSC $\overline{\text{C}}$  C $\overline{\text{C}}$ C-PIPSC $\overline{\text{C}}$  P $\text{h}$ P $\cdot$ P $\ddot{\text{y}}$  P $\ddot{\text{i}}$ C $\overline{\text{C}}$ P $\ddot{\text{e}}$  PSPsC $\overline{\text{C}}$ PjP $^{\circ}$ P $\gg$ C $\overline{\text{H}}$ PSPsPjC $\overline{\text{r}}$  C $\overline{\text{C}}$ C-PIPSC-P $\pm$ C-P $\gg$ C-C $\overline{\text{C}}$ C $\overline{\text{r}}$ P $\pm$ C-PSC $\overline{\text{r}}$  P $^{\circ}$ P $\pm$ Ps C $\overline{\text{C}}$ Pe P $\ddot{\text{i}}$ C-PrPIP $\ddot{\text{e}}$ C% $\text{o}$ P $\mu$ PSPSC $\overline{\text{C}}$  C $\overline{\text{C}}$ C-PIPSC $\overline{\text{C}}$  P $\pm$ C-P $\gg$ C-C $\overline{\text{C}}$ C $\overline{\text{r}}$ P $\pm$ C-PSC $\overline{\text{r}}$  PI 1,5 C $\overline{\text{C}}$ P $^{\circ}$ P $\cdot$ P $^{\circ}$  PIP $\ddot{\text{e}}$ C% $\text{o}$ P $\mu$  P' $\text{P}_{\text{H}}\text{P}_{\text{K}}$  PSP $\mu$ P $\cdot$ P $^{\circ}$ P $\gg$ P $\mu$ P $\overline{\text{I}}$ PSPs PIC-Pr

C<sub>7</sub>H<sub>5</sub>C-PIPSCH<sub>2</sub> P<sub>h</sub>P>P<sub>h</sub>) C<sub>7</sub>P>C-Pr P<sub>i</sub>C<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P·PSP°C<sub>7</sub>P°C, P<sub>e</sub> 800 P<sub>j</sub>P<sub>i</sub> P'P<sub>s</sub>C, C<sub>7</sub>H<sub>5</sub>C-C" PSC, C<sub>7</sub>P<sup>P<sub>h</sub></sup> 1  
 C<sub>7</sub>H<sub>5</sub>P°P· PSP° PrP<sub>u</sub>PSCH<sub>2</sub> C, P° C... PIPsC<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P<sub>j</sub> P· P<sub>i</sub>PsP<sub>j</sub>C-C<sub>7</sub>H<sub>5</sub>PSCH<sub>2</sub> P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>C-PSPePsPIPsCH<sub>2</sub>  
 PSP<sub>u</sub>PrPsC<sub>7</sub>C, P°C, PSC-C<sub>7</sub>C, C<sub>7</sub> (C<sub>7</sub>H<sub>5</sub>C-PIP<sub>u</sub>PSCH<sub>2</sub> P<sub>±</sub>C-P>C-C<sub>7</sub>C<sub>7</sub>P<sub>±</sub>C-PSC<sub>7</sub>  
 P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>P<sub>i</sub>P<sub>e</sub>C%<sub>0</sub>C<sub>7</sub>C" PI 1, 5-3 C<sub>7</sub>H<sub>5</sub>P°P·P° P'P<sub>h</sub>P<sub>k</sub> PSP<sub>u</sub>P·P°P>P<sub>u</sub>P<sub>h</sub>PSPs PIC-Pr C<sub>7</sub>H<sub>5</sub>C-PIPSCH<sub>2</sub>  
 P<sub>h</sub>P>P<sub>h</sub>) C<sub>7</sub>P>C-Pr P·P<sub>j</sub>P<sub>u</sub>PSCH<sub>2</sub>C<sub>7</sub>P<sub>i</sub>P°C, P<sub>e</sub> P<sub>i</sub>PsC<sub>7</sub>P°C, P<sub>e</sub>PsPIC<sub>7</sub> PrPsP·C<sub>7</sub> PrPs 200 P<sub>j</sub>P<sub>i</sub> PSP°  
 PrP<sub>u</sub>PSCH<sub>2</sub>, P<sub>i</sub>PsPrP°P>CH<sub>2</sub>C<sub>7</sub>P<sub>e</sub>C... C<sub>7</sub>H<sub>5</sub>P<sub>u</sub>PePsP<sub>j</sub>P<sub>u</sub>PSPrP°C<sub>7</sub>C-PN<sub>e</sub> C%<sub>0</sub>PsPrPs  
 P<sub>j</sub>PsPrP<sub>e</sub>C,, C-PeP°C<sub>7</sub>C-C— PrPsP·P<sub>e</sub> P· PsP<sub>i</sub>P>C<sub>7</sub>PrC<sub>7</sub> PSP° C<sub>7</sub>H<sub>5</sub>P<sub>u</sub>P·C<sub>7</sub>P>CH<sub>2</sub>C, P°C, P<sub>e</sub>  
 P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>C-PSPePsPIP<sub>e</sub>C... C, P<sub>u</sub>C<sub>7</sub>C, C-PI PrP>C<sub>7</sub> C... PIPsC<sub>7</sub>H<sub>5</sub>P<sub>e</sub>C... P· C<sub>7</sub>P<sub>h</sub>P<sub>u</sub> C-C<sub>7</sub>PSC<sub>7</sub>C<sub>7</sub>C<sub>7</sub>PsCH<sub>2</sub>  
 P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>C-PSPePsPIPsCH<sub>2</sub> PSP<sub>u</sub>PrPsC<sub>7</sub>C, P°C, PSC-C<sub>7</sub>C, C<sub>7</sub> P<sub>i</sub>PsPeP<sub>e</sub> C%<sub>0</sub>Ps PSP<sub>u</sub>  
 C<sub>7</sub>H<sub>5</sub>PsP·C<sub>7</sub>H<sub>5</sub>PsP<sub>±</sub>P>P<sub>u</sub>PSPs. P<sub>u</sub>P°P·PsP<sub>i</sub>P°PSC-P<sub>±</sub> PSP<sub>u</sub> C<sub>7</sub>H<sub>5</sub>P<sub>u</sub>PePsP<sub>j</sub>P<sub>u</sub>PSPrC<sub>7</sub>C" C, CH<sub>2</sub>C<sub>7</sub>C<sub>7</sub>  
 P<sub>i</sub>P°C<sub>7</sub>C-C" PSC, P°P<sub>j</sub> P· C, C<sub>7</sub>P<sub>h</sub>P<sub>u</sub>PeP<sub>e</sub>P<sub>j</sub> P<sub>i</sub>PsC<sub>7</sub>H<sub>5</sub>C<sub>7</sub>C<sub>7</sub>P<sub>u</sub>PSCH<sub>2</sub>P<sub>j</sub> C,, C<sub>7</sub>PSPeC<sub>7</sub>C-C—  
 P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>C-PSPeP<sub>e</sub> (P·P°P<sub>i</sub>P°P>CH<sub>2</sub>PSCH<sub>2</sub>PN<sub>e</sub> P<sub>±</sub>C-P>C-C<sub>7</sub>C<sub>7</sub>P<sub>±</sub>C-PS P<sub>±</sub>C-P>CH<sub>2</sub>C<sub>7</sub> PSC-P<sub>h</sub> C<sub>7</sub> 3  
 C<sub>7</sub>H<sub>5</sub>P°P·P<sub>e</sub> PIP<sub>e</sub>C%<sub>0</sub>P<sub>e</sub>PN<sub>e</sub> P·P° P'P<sub>h</sub>P<sub>k</sub> PSP<sub>u</sub>P·P°P>P<sub>u</sub>P<sub>h</sub>PSPs PIC-Pr C<sub>7</sub>H<sub>5</sub>C-PIPSCH<sub>2</sub> P<sub>h</sub>P>P<sub>h</sub>) (PrP<sub>e</sub>PI.  
 C<sub>7</sub>H<sub>5</sub>PsP·PrC-P> B<P<sub>h</sub>P<sub>i</sub>PsC<sub>7</sub>C-P<sub>±</sub> P·P°C<sub>7</sub>C, PsC<sub>7</sub>C<sub>7</sub>P<sub>i</sub>P°PSPSC<sub>7</sub> C, P° PrPsP·P<sub>e</sub>B>).

*P<sub>h</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub> PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>PSCH<sub>2</sub>C-C<sub>7</sub>.*

P<sub>u</sub>C-Pr C<sub>7</sub>P°C<sub>7</sub> PeP>C-PSC-C<sub>7</sub>PSP<sub>e</sub>C... PrPsC<sub>7</sub>P>C-PrP<sub>h</sub>P<sub>u</sub>PSCH<sub>2</sub> P<sub>i</sub>P°P·PsP<sub>i</sub>P°PSC-P<sub>±</sub>C<sub>7</sub>  
 C<sub>7</sub>P<sub>i</sub>PsC<sub>7</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-PiP°P>P<sub>e</sub>C<sub>7</sub>C<sub>7</sub> PIP<sub>e</sub>PiP°PrPeP<sub>e</sub> P°C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub>—  
 PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>PSCH<sub>2</sub>C-C—, PIPeP>CH<sub>2</sub>C<sub>7</sub>P°C<sub>7</sub>C<sub>7</sub>P<sub>e</sub> PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, PsPSC-C<sub>7</sub>PSC- PeC<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P·P<sub>e</sub>.  
 P<sub>h</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub>PN<sub>e</sub> C, P<sub>e</sub>C<sub>7</sub>P<sub>e</sub> P<sub>j</sub>P°C" P<sub>±</sub>C<sub>7</sub>C, P<sub>e</sub> PrPsP<sub>±</sub>C<sub>7</sub>H<sub>5</sub>P<sub>u</sub>  
 PePsPSC, C<sub>7</sub>H<sub>5</sub>PsP>CH<sub>2</sub>PsPIP°PSP<sub>e</sub>P<sub>j</sub> C%<sub>0</sub>P<sub>u</sub> PrPs P<sub>i</sub>PsC<sub>7</sub>P°C, PeC<sub>7</sub> P>C-PeC<sub>7</sub>PiP°PSPSC<sub>7</sub>  
 P<sub>i</sub>P°P·PsP<sub>i</sub>P°PSC-P<sub>±</sub>PsP<sub>j</sub>. P<sub>j</sub> P<sub>i</sub>P°C<sub>7</sub>C-C" PSC, C-PI P<sub>i</sub>PsC, C<sub>7</sub>H<sub>5</sub>C-P<sub>±</sub>PSPs PePsPSC, C<sub>7</sub>H<sub>5</sub>PsP>CH<sub>2</sub>PIP°C, P<sub>e</sub>  
 C<sub>7</sub>H<sub>5</sub>C-PIP<sub>u</sub>PSCH<sub>2</sub> P°C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub>PiPs C, P<sub>e</sub>C<sub>7</sub>P<sub>e</sub>C<sub>7</sub> PSP° C<sub>7</sub>P°P<sub>j</sub>PsP<sub>j</sub>C<sub>7</sub> P<sub>i</sub>PsC<sub>7</sub>P°C, PeC<sub>7</sub>  
 P>C-PeC<sub>7</sub>PiP°PSPSC<sub>7</sub> (PSP<sub>u</sub> PiC-P·PSC-C<sub>7</sub>P<sub>u</sub> PSC-P<sub>h</sub> P·P° C, P<sub>e</sub>P<sub>h</sub>P<sub>u</sub>PSCH<sub>2</sub> PiC-C<sub>7</sub>P>C<sub>7</sub>  
 P<sub>i</sub>PsC<sub>7</sub>P°C, PeC<sub>7</sub> P>C-PeC<sub>7</sub>PiP°PSPSC<sub>7</sub> P'PsC, C<sub>7</sub>H<sub>5</sub>C-C" PSC, PsP<sub>j</sub><sup>P<sub>h</sub></sup>) C- P<sub>i</sub>PsC, C-P<sub>j</sub> P·  
 C<sub>7</sub>P°C<sub>7</sub>C, PsC, PsCH<sub>2</sub>, PSP<sub>u</sub>PsP<sub>±</sub>C... C-PrPSPsCH<sub>2</sub> PrP>C<sub>7</sub> P·P°P<sub>±</sub>P<sub>u</sub>P·P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>P<sub>u</sub>PSCH<sub>2</sub>  
 PePsPSC, C<sub>7</sub>H<sub>5</sub>PsP>CH<sub>2</sub> P·P° P°C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub>P<sub>j</sub> C, P<sub>e</sub>C<sub>7</sub>P<sub>e</sub>PsP<sub>j</sub> PeC<sub>7</sub>H<sub>5</sub>PsPIC- C, P°  
 C<sub>7</sub>PiP<sub>e</sub>PrPePs P<sub>i</sub>C<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P·PSP°C<sub>7</sub>P°C, P<sub>e</sub> C<sub>7</sub>C, P°PSPrP°C<sub>7</sub>H<sub>5</sub>C, PSC<sub>7</sub>  
 P°PSC, P<sub>e</sub>PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>PSCH<sub>2</sub>P<sub>e</sub>PIPSC<sub>7</sub> C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>P°PiC-C<sub>7</sub> C<sub>7</sub> PePsP<sub>j</sub>P<sub>±</sub>C-PSP°C<sub>7</sub>C-C— P·C-  
 P·PSP<sub>e</sub>P<sub>h</sub>P<sub>u</sub>PSCH<sub>2</sub>P<sub>j</sub> PrPsP·P<sub>e</sub> P°P<sub>±</sub>Ps P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>P<sub>u</sub>PSCH<sub>2</sub> C<sub>7</sub> C<sub>7</sub> P>C-PeC<sub>7</sub>PiP°PSPSC-  
 P'PsC, C<sub>7</sub>H<sub>5</sub>C-C" PSC, PsP<sub>j</sub><sup>P<sub>h</sub></sup> PIC-PrP<sub>i</sub>PsPIC-PrPSPs PrPs PeP>C-PSC-C<sub>7</sub>PSPsPiPs C<sub>7</sub>C, P°PSC<sub>7</sub>  
 C... PIPsC<sub>7</sub>H<sub>5</sub>PsPiPs (PrP<sub>e</sub>PI. C<sub>7</sub>H<sub>5</sub>PsP·PrC-P>P<sub>e</sub> B<P<sub>h</sub>P<sub>i</sub>PsC<sub>7</sub>C-P<sub>±</sub> P·P°C<sub>7</sub>C, PsC<sub>7</sub>C<sub>7</sub>P<sub>i</sub>P°PSPSC<sub>7</sub> C, P°  
 PrPsP·P<sub>e</sub>B> C, P° B<P<sub>u</sub>PsP<sub>±</sub>C-C<sub>7</sub>PSC-B C<sub>7</sub>H<sub>5</sub>P<sub>u</sub>P°PeC<sub>7</sub>C-C-B>). P<sub>h</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub>  
 PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>PSCH<sub>2</sub>C-C<sub>7</sub> (C<sub>7</sub>H<sub>5</sub>C-PIP<sub>u</sub>PSCH<sub>2</sub> C<sub>7</sub>P<sub>e</sub>C<sub>7</sub>C, PsP>C-C<sub>7</sub>PSPsPiPs C, P<sub>e</sub>C<sub>7</sub>P<sub>e</sub>C<sub>7</sub> PeC<sub>7</sub>H<sub>5</sub>PsPIC-  
 ≥ 150 P°P<sub>±</sub>Ps PrC-P°C<sub>7</sub>C, PsP>C-C<sub>7</sub>PSPsPiPs ≥ 100 P<sub>j</sub>P<sub>j</sub> C<sub>7</sub>H<sub>5</sub>C, C<sub>7</sub>C, ) PSP° C, P>C-  
 P>C-PeC<sub>7</sub>PiP°PSPSC<sub>7</sub> P'PsC, C<sub>7</sub>H<sub>5</sub>C-C" PSC, PsP<sub>j</sub><sup>P<sub>h</sub></sup> C<sub>7</sub>H<sub>5</sub>PsP·PIP<sub>e</sub>PIP°C" C, CH<sub>2</sub>C<sub>7</sub>C<sub>7</sub> C<sub>7</sub> C<sub>7</sub>P°PSPSC-  
 C<sub>7</sub>C, C<sub>7</sub>H<sub>5</sub>PsPeP<sub>e</sub> (C<sub>7</sub> P<sub>i</sub>C<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P<sub>±</sub>P>P<sub>e</sub>P·PSPs C<sub>7</sub> 40 % PIP<sub>e</sub>PiP°PrPeC-PI PIPsPSP°  
 C<sub>7</sub>H<sub>5</sub>PsP·PIP<sub>e</sub>PIP°C" C, CH<sub>2</sub>C<sub>7</sub>C<sub>7</sub> PrPs 9 PrPsP<sub>±</sub>P<sub>e</sub>, C<sub>7</sub> P<sub>i</sub>C<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P<sub>±</sub>P>P<sub>e</sub>P·PSPs 90 % PIP<sub>e</sub>PiP°PrPeC-PI  
 B<sub>7</sub>" C<sub>7</sub> P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C- 18 C, P<sub>e</sub>P<sub>h</sub>PSCH<sub>2</sub>-PI). P'PsC, C<sub>7</sub>H<sub>5</sub>C-C" PSC, <sup>P<sub>h</sub></sup> PSP<sub>u</sub>PsP<sub>±</sub>C... C-PrPSPs  
 PIC-PrP<sub>j</sub>C-PSP<sub>e</sub>C, P<sub>e</sub>, C<sub>7</sub>P<sub>e</sub>C%<sub>0</sub>Ps C" PsP·PSP°PeP<sub>e</sub> PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, PsPSC-C<sub>7</sub>PSPsPiPs PeC<sub>7</sub>H<sub>5</sub>P<sub>e</sub>P·C<sub>7</sub>  
 P°P<sub>±</sub>Ps P°C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C-P°P>CH<sub>2</sub>PSCH<sub>2</sub> PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>PSCH<sub>2</sub>C-C<sub>7</sub> C, C<sub>7</sub>P<sub>h</sub>P<sub>u</sub>PeP° C- P<sub>i</sub>C<sub>7</sub>H<sub>5</sub>P<sub>e</sub>  
 C<sub>7</sub>CH<sub>2</sub>PsP<sub>j</sub>C<sub>7</sub> P<sub>i</sub>P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C<sub>7</sub>P<sub>e</sub>C<sub>7</sub>C, C<sub>7</sub>C", PSP<sub>u</sub>P·PIP°P<sub>h</sub>P°C<sub>7</sub>C<sub>7</sub>P<sub>e</sub> PSP°  
 P°PSC, P<sub>e</sub>PiC-PiP<sub>u</sub>C<sub>7</sub>H<sub>5</sub>C, P<sub>u</sub>PSCH<sub>2</sub>P<sub>e</sub>PIPSC<sub>7</sub> C, P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>P°PiC-C<sub>7</sub> C- P·PSP<sub>e</sub>P<sub>h</sub>P<sub>u</sub>PSCH<sub>2</sub> PrPsP·P<sub>e</sub>  
 P'PsC, C<sub>7</sub>H<sub>5</sub>C-C" PSC, C<sub>7</sub>P<sup>P<sub>h</sub></sup>.

*P<sub>h</sub>P<sub>e</sub>PSPPrC<sub>7</sub>H<sub>5</sub>PsP<sub>j</sub> P·P°PrPSCH<sub>2</sub>PsC— PsP<sub>±</sub>P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>PSCH<sub>2</sub>PSCH<sub>2</sub>— P<sub>u</sub>PSCH<sub>2</sub>P<sub>u</sub>C,, P°P>PsPiP°C, C-C—/  
 P·P°PrPSCH<sub>2</sub>PsC— PsP<sub>±</sub>P<sub>u</sub>C<sub>7</sub>H<sub>5</sub>PSCH<sub>2</sub>PSCH<sub>2</sub>— P>P<sub>u</sub>PN<sub>e</sub>PePsP<sub>u</sub>PSCH<sub>2</sub>P<sub>u</sub>C,, P°P>PsPiP°C, C-C—.*

P<sub>u</sub>C-Pr C<sub>7</sub>P°C<sub>7</sub> P·P°C<sub>7</sub>C, PsC<sub>7</sub>C<sub>7</sub>P<sub>i</sub>P°PSPSC<sub>7</sub> P'PsC, C<sub>7</sub>H<sub>5</sub>C-C" PSC, C<sub>7</sub>P<sup>P<sub>h</sub></sup>  
 P<sub>i</sub>PsPIC-PrPsP<sub>j</sub>P>C<sub>7</sub>P>PsC<sub>7</sub>CH<sub>2</sub> P<sub>i</sub>C<sub>7</sub>H<sub>5</sub>Ps PIP<sub>e</sub>PiP°PrPeP<sub>e</sub> C<sub>7</sub>P<sub>e</sub>PSPrC<sub>7</sub>H<sub>5</sub>PsP<sub>j</sub>C<sub>7</sub> P·P°PrPSCH<sub>2</sub>PsC—

PsP±PμCḡPSPμPSPSc— PμPSC†PμC,,P°P»PsPīP°C,C-C—/ P·P°PrPSCḡPsC—  
PsP±PμCḡPSPμPSPSc— P»PμPNḡPePsPμPSC†PμC,,P°P»PsPīP°C,C-C—. PŸPēPSPrCḡPsPj PjPsP¶Pμ  
PīCḡPsCḡPIP»CḡC,PēCḡCḡ PīPsP»PsPIPSPēPj P±PsP»PμPj, P°CḡC,PμCḡC-P°P»CḡPSPScḡ  
PiC-PīPμCḡC,PμPSP·C-C”Cḡ, CḡCḡPrPsPjP°PjPē, P»PμC,P°CḡPiC-C”Cḡ,  
CḡPīP»CḡC,P°PSC-CḡC,Cḡ CḡPIC-PrPsPjPsCḡC,C-, CḡP»C-PīPsC,PsCḡ C,P° C-PSCēPēPjPē  
CḡPsP·P»P°PrP°PjPē P·PsCḡCḡ C,P° PSPμPICḡPsP»PsPiC-C†PSPēPjPē PīPsCḡCḡCēPμPSPSCḡPjPē  
C- PjPsP¶Pμ PjP°C,Pē P»PμC,P°P»CḡPSPēPNḡ PSP°CḡP»C-PrPsPe. PJ CḡP°P·C-  
PIPēPSPēPePSPμPSPSCḡ C†CḡPsPiPs CḡPēPSPrCḡPsPjCḡ P»C-PeCḡPIP°PSPSCḡ  
P’PsC,CḡC-C”PSC,PsPj<sup>PŸPḡ</sup> CḡP»C-Pr PīCḡPēPīPēPSPēC,Pē PSP°P·P°PIP¶PrPē.

*P†PSC,PμCḡCḡC,PēC†C-PNḡPSPμ P·P°C...PIPScḡCḡPIP°PSPSCḡ P»PμPiPμPSC-PI  
(P†P—P·)/PīPSPμPIPjPsPSC-C,*

P©PsPrPs P†P—P·, CḡPePμ PjPsP¶Pμ P±CḡC,Pē P·C- CḡPjPμCḡC,PμP»CḡPSPēPj  
PSP°CḡP»C-PrPePsPj, P±CḡP»Ps PīPsPIC-PrPsPjP»PμPSPSCḡ PīCḡPs CḡPsP·PIPēC,PsPe P†P—P·,  
C%Ps PīPsPiḡḡ<sup>TM</sup> CḡP·P°PSPs P· PīP°P·PsPīP°PSC-P±PsPj (PrPēPI. CḡPsP·PrC-P»  
B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C—B»). PŸP»C-Pr PICḡC,P°PSPsPIPēC,Pē PīPēP»CḡPSPēPNḡ  
PSP°PiP»CḡPr P·P° PīP°C†C-C”PSC,P°PjPē P· C-PSPrPēPeP°C,PēPIPSPēPjPē CḡPēPjPiC,PsPjP°PjPē  
C%PsPrPs P†P—P·/PīPSPμPIPjPsPSC-C,Cḡ C,P° PīCḡPēPīPēPSPēC,Pē P»C-PeCḡPIP°PSPSCḡ  
PīP°P·PsPīP°PSC-P±PsPj PīP°C†C-C”PSC,C-PI, PI CḡPePēC... PICḡC,P°PSPsPIP»PμPSPēPNḡ  
CḡPsP·PIPēC,PsPe P†P—P· P°P±Ps PīPSPμPIPjPsPSC-C,Cḡ.

*PμPsCḡCḡCēPμPSPSCḡ C,,CḡPSPeC†C-C— CḡPμCḡC†Cḡ / CḡPμCḡC†PμPIP°  
PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ*

PŸP»C-Pr PsC†C-PSPēC,Pē CḡPiC-PIPIC-PrPSPScēPμPSPSCḡ CḡPēP·PēPeC-PI C,P°  
PePsCḡPēCḡC,C- P»C-PeCḡPIP°PSPSCḡ PīP°P·PsPīP°PSC-P±PsPj PīPμCḡPμPr PīPsC†P°C,PePsPj  
C,PμCḡP°PiC-C— Cḡ PīP°C†C-C”PSC,C-PI, Cḡ CḡPePēC... PI P°PSP°PjPSPμP·C-  
CḡPiPsCḡC,PμCḡC-PiP°P»PēCḡCḡ PīPsCḡCḡCēPμPSPSCḡ C,,CḡPSPeC†C-C— CḡPμCḡC†Cḡ.  
P’PμP·PīPμPeP° C,P° C,,P°CḡPjP°PePsPeC-PSPμC,PēPeP° PīP°P·PsPīP°PSC-P±Cḡ Cḡ  
PīP°C†C-C”PSC,C-PI P· PīPsPjC-CḡPSPScḡ P°P±Ps C,CḡP¶PePsCḡ CḡPμCḡC†PμPiPsCḡ  
PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ P°P±Ps Cḡ PīP°C†C-C”PSC,C-PI P· C,,CḡP°PeC†C-C”Cḡ  
PIPēPePēPrCḡ P»C-PIPsPiPs CēP»CḡPSPSc†PeP° PSPēP¶C†Pμ PSPScḡPjP°P»CḡPSPsPiPs  
CḡC-PIPSCḡ PSPμ PrPsCḡP»C-PrP¶CḡPIP°P»PēCḡCḡ.

PJ PeP»C-PSC-C†PSPēC... PrPsCḡP»C-PrP¶PμPSPSCḡC... P· PīP°P·PsPīP°PSC-P±PsPj  
CḡPiPsCḡC,PμCḡC-PiP°P»PēCḡCḡ PIPēPīP°PrPePē PīPsCḡCḡCēPμPSPSCḡ C,,CḡPSPeC†C-C—  
CḡPμCḡC†Cḡ, C,P°PeC- CḡPe P·P°CḡC,C-PNḡPSP° CḡPμCḡC†PμPIP°  
PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ C,P° P·PjPμPSCēPμPSPSCḡ C,,CḡP°PeC†C-C— PIPēPePēPrCḡ  
P»C-PIPsPiPs CēP»CḡPSPSc†PeP°. P’ CḡP°PSPrPsPjC-P·PsPIP°PSPsPjCḡ PeP»C-PSC-C†PSPsPjCḡ  
PrPsCḡP»C-PrP¶PμPSPSC- P»C-PeCḡPIP°PSPSCḡ C...PIPScḡPēC... PSP°  
PSPēCḡPePsPiPsPeP»C-C,PēPSPSCḡ PeP°CḡC†PēPSPsPjCḡ PīP°P·PsPīP°PSC-P±PsPj PI  
PīPsCḡC-PIPSCḡPSPSC- P· CḡCḡPSC-C,PēPSC-P±PsPj, Cḡ PīP°C†C-C”PSC,C-PI, CḡPeC- PjP°P»Pē  
PePsPSC,CḡPsP»Cḡ P·P° C,,CḡP°PeC†C-C”Cḡ PIPēPePēPrCḡ P»C-PIPsPiPs CēP»CḡPSPSc†PeP° P·  
PīPsC†P°C,PeCḡ C,P° PīCḡPsC,CḡPiPsPj PrPsCḡP»C-PrP¶PμPSPSCḡ, PīPsCḡCḡCēPμPSPSCḡ  
C,,CḡPSPeC†C-C— PjC-PsPeP°CḡPrP° CḡPiPsCḡC,PμCḡC-PiP°P»Pē Cḡ 13 % (47/362)  
PīP°C†C-C”PSC,C-PI PiCḡCḡPīPē PīP°P·PsPīP°PSC-P±Cḡ, PI PīPsCḡC-PIPSCḡPSPSC- P· 11%  
(42/369) PīP°C†C-C”PSC,C-PI PiCḡCḡPīPē CḡCḡPSC-C,PēPSC-P±Cḡ. P—P°CḡC,C-PNḡPSP°  
CḡPμCḡC†PμPIP° PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ CḡPiPsCḡC,PμCḡC-PiP°P»P°CḡCḡ Cḡ 0,5 %  
PīP°C†C-C”PSC,C-PI Cḡ PePsP¶PSC-PNḡ PiCḡCḡPiC- PīP°C†C-C”PSC,C-PI. P—P°CḡC,C-PNḡPSP°  
CḡPμCḡC†PμPIP° PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ CḡPiPsCḡC,PμCḡC-PiP°P»P°CḡCḡ Cḡ 3 P· 240  
PīP°C†C-C”PSC,C-PI (1 %) Cḡ C...PsPrC- PeP»C-PSC-C†PSPēC... PrPsCḡP»C-PrP¶PμPSCḡ P†P†P†

C,,P°P·Pë C...PIPsCḡPëC... PSP° CḡP°CḡPePsPjCḡ Pjḡḡ™ CḡPePëC... C,PeP°PSPëPS. Pj C†CHḡPsPjCḡ PrPsCḡP»C-PrPḡPḡPSPSC- P·PjPḡPSCëPḡPSPSCḡ C,,CḡP°PeC†C-C— PIPëPePëPrCḡ P»C-PIPsPiPs CëP»CḡPSPsC†PeP° Cḡ CḡCḡP±ḡḡ™ C”PeC,C-PI PrPsCḡP»C-PrPḡPḡPSPSCḡ, CḡPeC- PīCḡPsC...PsPrPëP»Pë PIPëPjC-CḡCḡPIP°PSPSCḡ PSP° PīPsC†P°C,PeCḡ C,P° PI PīCḡPsC†PḡCḡC- P»C-PeCḡPIP°PSPSCḡ, CḡPīPsCḡC,PḡCḡC-PiP°P»PsCḡCḡ Cḡ 11 % (15/140) Cḡ PiCḡCḡPīC-, C%Ps PsC,CḡPëPjCḡPIP°P»P° P’PsC,CḡC-C”PSC,<sup>PḡPḡ</sup>, PīPsCḡC-PIPSCḡPSPs P· 3 % (1/39) Cḡ PiCḡCḡPīC-, C%Ps PsC,CḡPëPjCḡPIP°P»P° PīP»P°C†PḡP±Ps.

*PḡP°PeC,PsCḡPë CḡPëP·PëPeCḡ*

13 P· 15 CḡCḡP±ḡḡ™ C”PeC,C-PI Cḡ PiCḡCḡPīC- PīP°P·PsPīP°PSC-P±Cḡ PīC-Pr C†P°Cḡ PrPsCḡP»C-PrPḡPḡPSPSCḡ C,,P°P·Pë P†P†P† PīCḡPë PḡPḡPḡ PjP°P»Pë CḡCḡPīCḡC,PSCḡ PiC-PiPḡCḡC,PḡPSP·C-Cḡ, C%Ps PjPsPiP»Ps PīPsCḡPëP»PëC,Pë CḡPḡCḡC†PḡPICḡ PrPëCḡC,,CḡPSPeC†C-Cḡ Cḡ PīP°C†C-C”PSC,C-PI PiCḡCḡPīPë CḡPëP·PëPeCḡ PIPSP°CḡP»C-PrPsPe P·P±C-P»CHCëPḡPSPSCḡ CḡPḡCḡC†PḡPIPsPiPs PīPsCḡC,PSP°PIP°PSC,P°PḡPḡPSPSCḡ. 99 % PīP°C†C-C”PSC,C-PI (243/246), CḡPeC- P±CḡP°P»Pë CḡC†P°CḡC,CH Cḡ PrPsCḡP»C-PrPḡPḡPSPSC- C,,P°P·Pë P†P†P† PīCḡPë PḡPḡPḡ, PIPëP»CHC†P°CHC†Pë 15 CḡCḡP±ḡḡ™ C”PeC,C-PI, PsC,CḡPëPjCḡPIP°P»Pë P°PSC,CḡP°C†PëPeP»C-PS. PḡPsPīPḡCḡPḡPrPSCḡ C,PḡCḡP°PīC-Cḡ P°PSC,CḡP°C†PëPeP»C-PSP°PjPë PjPsPḡPḡ P±CḡC,Pë C,,P°PeC,PsCḡPsPj CḡPëP·PëPeCḡ CḡPḡCḡC†PḡPIPsC— PrPëCḡC,,CḡPSPeC†C-C—.

*P PḡP·CḡP»CHC,P°C,Pë*

4 P· 15 CḡCḡP±ḡḡ™ C”PeC,C-PI PīPsPIPSC-CḡC,CH PsPrCḡPḡP°P»Pë (Cḡ PjPḡPḡP°C... 5 % PIC-Pr PIPëC...C-PrPSPsPiPs CḡC-PIPsCḡ), P° 5 PsPrCḡPḡP°P»Pë C†P°CḡC,PePsPiPs (Cḡ PjPḡPḡP°C... PSPsCḡPjPë, P°P»Pḡ PSP° > 5 % PSPëPḡC†Pḡ PIPëC...C-PrPSPsPiPs CḡC-PIPsCḡ). PhPrPëPS CḡCḡP±ḡḡ™ C”PeC, PSPḡ PsPrCḡPḡPI, P° C%PsPrPs C-PSCëPëC... 5 CḡCḡP±ḡḡ™ C”PeC,C-PI PrP°PSC- CḡPīPsCḡC,PḡCḡPḡPḡPSPSCḡ P±CḡP»Pë PSPḡPrPsCḡC,CḡPīPSC-.

*P>C-PeCḡPIP°PSPSCḡ*

Pj PīP°C†C-C”PSC,C-PI P·C- P·PSP°C†PSPëPj P·PSPëPḡPḡPSPSCḡPj C,,CḡP°PeC†C-C— PIPëPePëPrCḡ P»C-PIPsPiPs CëP»CḡPSPsC†PeP° (PḡP’P»Pë) PīPḡCḡPḡCḡPëPIP°PSPSCḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ C,P°/P°P±Ps P·PSPëPḡPḡPSPSCḡ PrPsP·Pë PīP°P·PsPīP°PSC-P±Cḡ CḡP»C-Pr PīPsC”PrPSCḡPIP°C,Pë P· P»C-PeCḡPIP°PSPSCḡPj PiC-PiPḡCḡC,PḡPSP·C-C— (CḡPeC%Ps PIPsPSP° PīCḡPëCḡCḡC,PSCḡ, PrPëPI. PīPsPīPḡCḡPḡPrPḡPḡPSPSCḡ PīCḡPs PiC-PiPḡCḡC,PḡPSP·C-Cḡ PIPëC%Pḡ) PIC-PrPīPsPIC-PrPSPs PrPs PeP»C-PSC-C†PSPëC... PīPsPeP°P·P°PSCḡ.

*PḡPsPrPsPIPḡPḡPSPSCḡ C-PSC,PḡCḡPIP°P»Cḡ QT C- PīPsP»C-PjPsCḡC,,PSP° CëP»CḡPSPsC†PePsPIP° C,P°C...C-PeP°CḡPrC-Cḡ C,PëPīCḡ B«PīC-CḡCḡPḡC,B» (torsade de pointes).*

PḡC-Pr C†P°Cḡ PeP»C-PSC-C†PSPëC... PrPsCḡP»C-PrPḡPḡPSCḡ C%PsPrPs PIPëPIC†PḡPSPSCḡ P’PsC,CḡC-C”PSC,Cḡ<sup>PḡPḡ</sup> P±CḡP»Pë PIPëPīP°PrPePë PīPsPrPsPIPḡPḡPSPSCḡ C-PSC,PḡCḡPIP°P»Cḡ QT C- CḡPsP·PIPëC,PeCḡ torsade de pointes PSP° C,P»C- PīCḡPëPḡPsPjCḡ PīCḡPḡPīP°CḡP°C,Cḡ (PrPëPI. CḡPsP·PrC-P» B«PḡPsP±C-C†PSC- CḡPḡP°PeC†C-C—B»). P’PsC,CḡC-C”PSC,<sup>PḡPḡ</sup> CḡP»C-Pr P·P°CḡC,PsCḡPsPICḡPIP°C,Pë P· PsP±PḡCḡPḡPḡPSC-CḡC,CH PīP°C†C-C”PSC,P°Pj, CḡPeC- PjP°P»Pë PīPsPrPsPIPḡPḡPSPSCḡ C-PSC,PḡCḡPIP°P»Cḡ QTB PI P°PSP°PjPSPḡP·C-, CḡPeC- PīCḡPëPḡPjP°CHC,CH PīCḡPsC,PëP°CḡPëC,PjC-C†PSC- PīCḡPḡPīP°CḡP°C,Pë P°P±Ps C-PSCëC- P»C-PeP°CḡCḡCHPeC- P·P°CḡPsP±Pë, C%Ps PjPsPḡCḡC,CH P±CḡC,Pë

РiРsC,РμPSC†C-PM<sub>0</sub>PSPsC<sub>Н</sub> РiC<sub>Н</sub>РeC†PēPSPsC<sub>Н</sub> РiРsPrРsPIР¶PμPSPSC‡ C-PSC,РμC<sub>Н</sub>PIР°P»C<sub>Г</sub>QT, P°P±Ps C‡P<sub>0</sub>PeC- PjP°C<sub>Н</sub>C,Ч P·PSP°C†C<sub>Г</sub>C%<sub>0</sub>C- C‡PμC<sub>Н</sub>C†PμPIРs-C‡C<sub>Г</sub>PrPēPSPSC- P·P°C...PIРsC<sub>Н</sub>C<sub>Н</sub>PIР°PSPSC‡. РμC<sub>Н</sub>Рe P·P°C‡C,PsC‡C<sub>Г</sub>PIР°PSPSC- P'PsC,C<sub>Н</sub>C-C''PSC,C<sub>Г</sub><sup>РyР<sub>Н</sub></sup>C<sub>Н</sub>РμPePsPjPμPSPPrРsPIР°PSPs P·C<sub>Н</sub>PsP±PēC,Pē РμP»PμPeC,C<sub>Н</sub>PsPeP°C<sub>Н</sub>PrC-PsPiC<sub>Н</sub>P°PjC<sub>Г</sub>РiРμC<sub>Н</sub>РμPr РiРsC†P°C,PePsPj P»C-PeC<sub>Г</sub>PIР°PSPSC‡ C- РiРsPIC,PsC<sub>Н</sub>C<sub>Н</sub>PIР°C,Pē C—C— РiРμC<sub>Н</sub>C-PsPrPēC†PSPs РiC<sub>Н</sub>PsC,C‡PiРsPj C,РμC<sub>Н</sub>P°PiC—C,P° РiC-PrC,C<sub>Н</sub>РePjC<sub>Г</sub>PIР°C,Pē C<sub>Н</sub>C-PIРSC- РμP»PμPeC,C<sub>Н</sub>PsP»C-C,C-PI (PeP°P»C<sub>Н</sub>C†C-C<sub>Н</sub>, PjP°PiРSC-C<sub>Н</sub>, PeP°P»C-C<sub>Н</sub>) PI PjPμP¶P°C... PSPsC<sub>Н</sub>PjP°P»C<sub>Н</sub>PSPsPiРs PrC-P°РiР°P·PsPSC<sub>Г</sub> P·PSP°C†PμPSC<sub>Н</sub> C†PēC... РiРsPeP°P·PSPēPeC-PI.

*Р<sub>Н</sub>C<sub>Н</sub>C,РμC<sub>Н</sub>C-P°P»C<sub>Н</sub>PSPēPN<sub>0</sub> C,C<sub>Н</sub>PsPjP±PsP.*

РμC-Pr C†P°C‡ PeP»C-PSC-C†PSPēC... PrPsC‡P»C-PrP¶PμPSC<sub>Н</sub> C%<sub>0</sub>PsPrPs PIРēPIC†PμPSPSC‡ P'PsC,C<sub>Н</sub>C-C''PSC,C<sub>Г</sub><sup>РyР<sub>Н</sub></sup> C‡РiРsC‡C,РμC<sub>Н</sub>C-РiР°P»PēC‡C‡ PIРēРiР°PrPePē C<sub>Н</sub>PsP·PIРēC,PeC<sub>Г</sub>C-PSC,,P°C<sub>Н</sub>PeC,C<sub>Г</sub> PjC-PsPeP°C<sub>Н</sub>PrP°, C-CēPμPjC-C— PjC-PsPeP°C<sub>Н</sub>PrP°, B C‡C,РμPSPsPeP°C<sub>Н</sub>PrC-C—, C-CēPμPjC-C†PSPsPiРs C-PSC‡C<sub>Г</sub>P»C<sub>Н</sub>C,C<sub>Г</sub> C,P° C,C<sub>Н</sub>P°PSP·PēC,PsC<sub>Н</sub>PSPēC... C-CēPμPjC-C†PSPēC... P°C,P°Pe PSP° C,P»C- РiC<sub>Н</sub>РePN<sub>0</sub>PsPjC<sub>Г</sub>РiC<sub>Н</sub>РμРiР°C<sub>Н</sub>P°C,C<sub>Г</sub> (PrPēPI. C<sub>Н</sub>PsP·PrC-P» B«РμPsP±C-C†PSC- C<sub>Н</sub>РμP°PeC†C-C-B»). Р<sub>Н</sub>P°P»Pē PjC-C‡C†Pμ P»PμC,P°P»C<sub>Н</sub>PS- PIРēРiР°PrPePē PI C<sub>Н</sub>РμP·C<sub>Г</sub>P»C<sub>Н</sub>C,P°C,C- C†PēC... C<sub>Г</sub>C‡PeP»P°PrPSPμPSC<sub>Н</sub>. P'PsC,C<sub>Н</sub>C-C''PSC,<sup>РyР<sub>Н</sub></sup> C‡P»C-Pr P·P°C‡C,PsC‡PsPIC<sub>Г</sub>PIР°C,Pē P·PsP±PμC<sub>Н</sub>РμP¶PSC-C‡C,C<sub>Н</sub> РiР°C†C-C''PSC,P°Pj, C‡P<sub>0</sub>PeC- PjP°C<sub>Н</sub>C,Ч РiC-PrPIРēC%<sub>0</sub>РμPSPēPN<sub>0</sub> C<sub>Н</sub>РeP·PēPe C,C<sub>Н</sub>PsPjP±PsC,PēC†PSPēC... C‡PIРēC%<sub>0</sub> P°P±Ps PjP°P»Pē C,P°PeC- C‡PIРēC%<sub>0</sub>P° PI P°PSP°PjPSPμP·C-. РμP°P·PsРiР°PSC-P± PSPμ PIРēPIC†P°P»Pē PrP»C‡ P»C-PeC<sub>Г</sub>PIР°PSPSC‡ РiР°C†C-C''PSC,C-PI, C‡P<sub>0</sub>PeC- PjP°P»Pē C,C<sub>Н</sub>PsPjP±PsC,PēC†PSC- C‡PIРēC%<sub>0</sub>P° P·P° РiРsPiРμC<sub>Н</sub>РμPrPSC- 6 PjC-C‡C‡C†C-PI. P C-CēPμPSPSC‡ РiC<sub>Н</sub>Ps РiC<sub>Н</sub>РeP·PSP°C†PμPSPSC‡ P»C-PeC<sub>Г</sub>PIР°PSPSC‡ C†PēPj РiC<sub>Н</sub>РμРiР°C<sub>Н</sub>P°C,PsPj PjP°C'' Т'C<sub>Н</sub>C<sub>Г</sub>PS,C<sub>Г</sub>PIР°C,PēC‡C‡ PSP° PsC†C-PSC†C- C‡РiC-PIРIC-PrPSPsCēPμPSPSC‡ PePsC<sub>Н</sub>РeC‡C,Ч/С<sub>Н</sub>РeP·PēPe PrP»C‡ PePsP¶PSPsPiРs PsPeC<sub>Н</sub>РμPjPsPiРs РiР°C†C-C''PSC,P°.

*P'РμPSPsP·PSP° C,C<sub>Н</sub>PsPjP±PsPμPjP±PsP»C-C‡.*

РμC-Pr C†P°C‡ PeP»C-PSC-C†PSPēC... PrPsC‡P»C-PrP¶PμPSC<sub>Н</sub> PrC-C— P'PsC,C<sub>Н</sub>C-C''PSC,C<sub>Г</sub><sup>РyР<sub>Н</sub></sup> C‡РiРsC‡C,РμC<sub>Н</sub>C-РiР°P»PēC‡C‡ PIРēРiР°PrPePē C<sub>Н</sub>PsP·PIРēC,PeC<sub>Г</sub>PIРμPSPsP·PSPsC— C,C<sub>Н</sub>PsPjP±PsPμPjP±PsP»C-C—, PIРeP»C<sub>Н</sub>C†P°C<sub>Н</sub>C†Pē PIРμPSPsP·PSPēPN<sub>0</sub> C,C<sub>Н</sub>PsPjP±PsP· C,P° P»PμC,P°P»C<sub>Н</sub>PS- PIРēРiР°PrPePē C,C<sub>Н</sub>PsPjP±PsPμPjP±PsP»C-C— P»PμPiРμPSPμPIРsC— P°C<sub>Н</sub>C,РμC<sub>Н</sub>C-C—. P<sub>Н</sub>P°C‡C,PsC,P° C†PēC... PIРēРiР°PrPeC-PI C<sub>Г</sub> РiC<sub>Н</sub>C<sub>Г</sub>РiC- РiР°C†C-C''PSC,C-PI C-P· PeP°C<sub>Н</sub>C†PēPSPsPjPsC<sub>Н</sub> Рj<sub>В</sub>™ C‡P<sub>0</sub>PeC... C,PeP°PSPēPS P±C<sub>Г</sub>P»P° PIРēC%<sub>0</sub>PsC<sub>Н</sub> (5 %), PSC-P¶ C<sub>Г</sub> РiC<sub>Н</sub>C<sub>Г</sub>РiC- P· PSPēC<sub>Н</sub>PePsPIРsPeP»C-C,PēPSPSPsC<sub>Н</sub> PeP°C<sub>Н</sub>C†PēPSPsPjPsC<sub>Н</sub> (2 %).

*РyC<sub>Н</sub>PsPjP±PsC,PēC†PSP° PjC-PeC<sub>Н</sub>PsP°PSPiC-PsРiР°C,C-C‡.*

РμPsPIC-PrPsPjP»C‡P»PsC‡C<sub>Н</sub> РiC<sub>Н</sub>Ps PIРēРiР°PrPePē C,C<sub>Н</sub>PsPjP±PsC,PēC†PSPsC— PjC-PeC<sub>Н</sub>PsP°PSPiC-PsРiР°C,C-C— C<sub>Г</sub> C...PsPrC- PeP»C-PSC-C†PSPēC... PrPsC‡P»C-PrP¶PμPSC<sub>Н</sub> P·P°C‡C,PsC‡C<sub>Г</sub>PIР°PSPSC‡ P'PsC,C<sub>Н</sub>C-C''PSC,C<sub>Г</sub><sup>РyР<sub>Н</sub></sup> C‡P<sub>0</sub>Pe PjPsPSPsC,РμC<sub>Н</sub>P°PiC-C—, C<sub>Г</sub> PePsPjP±C-PSP°C†C-C— P· P±PμPIР°C†PēP·C<sub>Г</sub>PjP°P±PsPj C,P° C<sub>Г</sub> PePsPjP±C-PSP°C†C-C— P· C,PsPiРsC,РμPeP°PSPsPj (PrPēPI. C<sub>Н</sub>PsP·PrC-P» B«РμPsP±C-C†PSC- C<sub>Н</sub>РμP°PeC†C-C-B»). PJ C<sub>Н</sub>P°P·C- PIРēPSPēPePSPμPSPSC‡ C<sub>Г</sub> C...PIРsC<sub>Н</sub>PsPiРs C,C<sub>Н</sub>PsPjP±PsC,PēC†PSPsC— PjC-PeC<sub>Н</sub>PsP°PSPiC-PsРiР°C,C-C— P»C-PeC<sub>Г</sub>PIР°PSPSC‡ P'PsC,C<sub>Н</sub>C-C''PSC,PsPj<sup>РyР<sub>Н</sub></sup> C‡P»C-Pr РiC<sub>Н</sub>РeРiРēPSPēC,Pē PSP°P·P°PIР¶PrPē. РμC-C‡P»C‡ РiC<sub>Н</sub>РeРiРēPSPμPSPSC‡ P»C-PeC<sub>Г</sub>PIР°PSPSC‡ P'PsC,C<sub>Н</sub>C-C''PSC,PsPj<sup>РyР<sub>Н</sub></sup> C‡РiРsC‡C,РμC<sub>Н</sub>C-РiР°PIC‡C‡ P·PIРsC<sub>Н</sub>PsC,PSPēPN<sub>0</sub> C<sub>Н</sub>PsP·PIРēC,PsPe РμC,,РμPeC,C<sub>Г</sub> PIC-Pr

C, C<sub>7</sub>PsPjP±PsC, PēC±PSPsC— PjC—PeC<sub>7</sub>PsP°PSPiC—PsP<sub>i</sub>P°C, C—C—. P'PsC, C<sub>7</sub>C—C''PSC, <sup>P<sub>Y</sub>P<sub>H</sub></sup> PSPμ  
PīC<sub>7</sub>PēP·PSP°C±PμPSPēPN<sub>2</sub> PrP»C<sub>7</sub> P»C—PeC<sub>7</sub>PiP°PSPSC<sub>7</sub> C<sub>7</sub> PePsPjP±C—PSP°C<sub>7</sub>C— P·  
C—PSCēPēPjPē P»C—PeP°C<sub>7</sub>C<sub>7</sub>CHPePēPjPē P·P°C<sub>7</sub>PsP±P°PjPē.

*P°PμPjPsC<sub>7</sub>P°PiC—C±PSC— C<sub>7</sub>C<sub>7</sub>PeP»P°PrPSPμPSPSC<sub>7</sub>.*

P—P° PrP°PSPēPjPē PeP»C—PSC—C±PSPēC... PrPsC<sub>7</sub>P»C—PrP<sub>7</sub>μPSC<sub>H</sub>, C%<sub>00</sub>PsPrPs  
PIPēPIC±PμPSPSC<sub>7</sub> P'PsC, C<sub>7</sub>C—C''PSC, C<sub>7</sub><sup>P<sub>Y</sub>P<sub>H</sub></sup> PīPsPIC—PrPsPjP»C<sub>7</sub>IP»PsC<sub>7</sub>C<sub>7</sub> PīC<sub>7</sub>Ps  
PIPēPīP°PrPePē PīPsC<sub>7</sub>PIPē PīPμPjPsC<sub>7</sub>P°PiC—C±PSPēC... C<sub>7</sub>C<sub>7</sub>PeP»P°PrPSPμPSC<sub>H</sub> PSP° C, P»C—  
PīC<sub>7</sub>PēPN<sub>2</sub>PsPjC<sub>7</sub> PīC<sub>7</sub>PμPīP°C<sub>7</sub>P°C, C<sub>7</sub> (PrPēPI. C<sub>7</sub>PsP·PrC—P» B«PμPsP±C—C±PSC—  
C<sub>7</sub>PμP°PeC<sub>7</sub>C—C—B»). P<sub>H</sub>P°P»Pē PjC—C<sub>7</sub>C<sub>7</sub>Pμ P»PμC, P°P»CH<sub>7</sub>PSC— PSP°C<sub>7</sub>P»C—PrPePē C<sub>7</sub>  
C<sub>7</sub>PμP·C<sub>7</sub>P»CH<sub>7</sub>C, P°C, C— PīPμPjPsC<sub>7</sub>P°PiC—C±PSPēC... C<sub>7</sub>C<sub>7</sub>PeP»P°PrPSPμPSC<sub>H</sub>.  
P'PsC, C<sub>7</sub>C—C''PSC, <sup>P<sub>Y</sub>P<sub>H</sub></sup> PSPμ PIPēPIC±P°PIC<sub>7</sub>C<sub>7</sub> C<sub>7</sub> PīP°C<sub>7</sub>C—C''PSC, C—PI, C<sub>7</sub>PeC— PI  
P°PSP°PjPSPμP·C— PjP°P»Pē PμPīC—P·PsPrPē PeC<sub>7</sub>PsPIPsC...P°C<sub>7</sub>PeP°PSPSC<sub>7</sub>,  
PIPSC<sub>7</sub>C, C<sub>7</sub>C—CēPSC<sub>H</sub>PsC±PμC<sub>7</sub>PμPīPSC— PeC<sub>7</sub>PsPIPsPIPēP»PēPIPē P°P±Ps PeP»C—PSC—C±PSPs  
P·PSP°C±C<sub>7</sub>C%<sub>00</sub>C— CēP»C<sub>7</sub>PSPePsPIPs—PePēCēPePsPIC— PeC<sub>7</sub>PsPIPsC, PμC±C— PīC<sub>7</sub>PsC, C<sub>7</sub>PIPsPj  
PīPsPīPμC<sub>7</sub>PμPrPSC—C... 6 PjC—C<sub>7</sub>C<sub>7</sub>C<sub>7</sub>C—PI. P'PsC, C<sub>7</sub>C—C''PSC, <sup>P<sub>Y</sub>P<sub>H</sub></sup> C<sub>7</sub>P»C—Pr  
P·P°C<sub>7</sub>C, PsC<sub>7</sub>PsPIC<sub>7</sub>PiP°C, Pē P· PsP±PμC<sub>7</sub>PμP<sub>7</sub>PSC—C<sub>7</sub>C, C<sub>7</sub> PīP°C<sub>7</sub>C—C''PSC, P°Pj, C<sub>7</sub>PeC—  
PjP°C<sub>7</sub>C, C<sub>7</sub> C<sub>7</sub>C<sub>7</sub>C, C<sub>7</sub>C<sub>7</sub>PIPēPN<sub>2</sub> C<sub>7</sub>PēP·PēPe PīPμPjPsC<sub>7</sub>P°PiC—C±PSPēC... C<sub>7</sub>PIPēC%<sub>00</sub>.

P<sub>H</sub>PSPμPIC<sub>7</sub>PēP·PjPē C, P° C<sub>7</sub>PsP·CēP°C<sub>7</sub>C<sub>7</sub>PiP°PSPSC<sub>7</sub> P°C<sub>7</sub>C, PμC<sub>7</sub>C—PN<sub>2</sub>

P—P°C<sub>7</sub>C, PsC<sub>7</sub>C<sub>7</sub>PiP°PSPSC<sub>7</sub> C—PSPiC—P±C—C, PsC<sub>7</sub>C—PI VEGF C<sub>7</sub> PīP°C<sub>7</sub>C—C''PSC, C—PI P·  
P°C<sub>7</sub>C, PμC<sub>7</sub>C—P°P»CH<sub>7</sub>PSPsC<sub>H</sub> PiC—PīPμC<sub>7</sub>C, PμPSP·C—C''C<sub>7</sub> P°P±Ps P±PμP· PSPμC— PjPsP<sub>7</sub>μ  
C<sub>7</sub>PiC<sub>7</sub>PēC<sub>7</sub>C, Pē C<sub>7</sub>C, PIPsC<sub>7</sub>PμPSPSC<sub>H</sub> P°PSPμPIC<sub>7</sub>PēP·Pj C, P°/P°P±Ps  
C<sub>7</sub>PsP·CēP°C<sub>7</sub>C<sub>7</sub>PiP°PSPSC<sub>H</sub> P°C<sub>7</sub>C, PμC<sub>7</sub>C—PN<sub>2</sub>. PμPμC<sub>7</sub>Cē PSC—P<sub>7</sub>  
P·P°C<sub>7</sub>C, PsC<sub>7</sub>PsPIC<sub>7</sub>PiP°C, Pē PīP°P·PsPīP°PSC—P±, C<sub>7</sub>PμPN<sub>2</sub> C<sub>7</sub>PēP·PēPe C<sub>7</sub>P»C—Pr  
C<sub>7</sub>PμC, PμP»CH<sub>7</sub>PSPs C<sub>7</sub>PsP·PiP»C<sub>7</sub>PSC<sub>7</sub>C, Pē C<sub>7</sub> PīP°C<sub>7</sub>C—C''PSC, C—PI P· C, P°PePēPjPē  
C, P°PeC, PsC<sub>7</sub>P°PjPē C<sub>7</sub>PēP·PēPeC<sub>7</sub>, C<sub>7</sub>Pe P°C<sub>7</sub>C, PμC<sub>7</sub>C—P°P»CH<sub>7</sub>PSP°  
PiC—PīPμC<sub>7</sub>C, PμPSP·C—C<sub>7</sub> P°P±Ps P°PSPμPIC<sub>7</sub>PēP·PjP° PI P°PSP°PjPSPμP·C—.

*PμPμC<sub>7</sub>C, PsC<sub>7</sub>P°C<sub>7</sub>C— C, P° C, C—C<sub>7</sub>C, C<sub>7</sub>P»Pē CēP»C<sub>7</sub>PSPePsPIPs—PePēCēPePsPIPsPiPs  
C, C<sub>7</sub>P°PeC, C<sub>7</sub> (PēP<sub>7</sub>P<sub>Y</sub>).*

PμC—Pr C±P°C<sub>7</sub> PeP»C—PSC—C±PSPēC... PrPsC<sub>7</sub>P»C—PrP<sub>7</sub>μPSC<sub>H</sub> C%<sub>00</sub>PsPrPs PIPēPIC±PμPSPSC<sub>7</sub>  
P'PsC, C<sub>7</sub>C—C''PSC, C<sub>7</sub><sup>P<sub>Y</sub>P<sub>H</sub></sup> P±C<sub>7</sub>P»Pē PIPēPīP°PrPePē PīPμC<sub>7</sub>C, PsC<sub>7</sub>P°C<sub>7</sub>C—PN<sub>2</sub> C, P°  
C<sub>7</sub>C, PIPsC<sub>7</sub>PμPSPSC<sub>7</sub> C, C—C<sub>7</sub>C, C<sub>7</sub>P» PēP<sub>7</sub>P<sub>Y</sub> PSP° C, P»C— PīC<sub>7</sub>PēPN<sub>2</sub>PsPjC<sub>7</sub>  
PīC<sub>7</sub>PμPīP°C<sub>7</sub>P°C, C<sub>7</sub> (PrPēPI. C<sub>7</sub>PsP·PrC—P» B«PμPsP±C—C±PSC— C<sub>7</sub>PμP°PeC<sub>7</sub>C—C—B»).  
P<sub>H</sub>P°P»Pē PjC—C<sub>7</sub>C<sub>7</sub>Pμ P»PμC, P°P»CH<sub>7</sub>PSC— PIPēPīP°PrPePē PīC—C<sub>7</sub>P»C<sub>7</sub>  
PīPμC<sub>7</sub>C, PsC<sub>7</sub>P°C<sub>7</sub>C—PN<sub>2</sub>. P'PsC, C<sub>7</sub>C—C''PSC, <sup>P<sub>Y</sub>P<sub>H</sub></sup> C<sub>7</sub>P»C—Pr P·P°C<sub>7</sub>C, PsC<sub>7</sub>PsPIC<sub>7</sub>PiP°C, Pē P·  
PsP±PμC<sub>7</sub>PμP<sub>7</sub>PSC—C<sub>7</sub>C, C<sub>7</sub> PīP°C<sub>7</sub>C—C''PSC, P°Pj, C<sub>7</sub>PeC— PjP°C<sub>7</sub>C, C<sub>7</sub> C<sub>7</sub>PēP·PēPe  
PIPēPSPēPePSPμPSPSC<sub>7</sub> PīPμC<sub>7</sub>C, PsC<sub>7</sub>P°C<sub>7</sub>C—PN<sub>2</sub> C, P° C<sub>7</sub>C, PIPsC<sub>7</sub>PμPSPSC<sub>7</sub> C, C—C<sub>7</sub>C, C<sub>7</sub>P»  
PēP<sub>7</sub>P<sub>Y</sub>.

*P—P°PiPsC''PSPSC<sub>7</sub> C<sub>7</sub>P°PS.*

P'PsC<sub>7</sub>P»C—PrP<sub>7</sub>μPSPSC<sub>7</sub> C%<sub>00</sub>PsPrPs PIPēPIC±PμPSPSC<sub>7</sub> PIPiP»PēPIC<sub>7</sub> P'PsC, C<sub>7</sub>C—C''PSC, C<sub>7</sub><sup>P<sub>Y</sub>P<sub>H</sub></sup>  
PSP° P·P°PiPsC''PSPSC<sub>7</sub> C<sub>7</sub>P°PS PIC—PrC<sub>7</sub>C<sub>7</sub>C, PSC—. P<sub>H</sub>C<sub>7</sub>PeC—P»CH<sub>7</sub>PePē  
C—PSPiC—P±C—C, PsC<sub>7</sub>Pē C, P°PeC, PsC<sub>7</sub>P° C<sub>7</sub>PsC<sub>7</sub>C, C<sub>7</sub> PμPSPPrPsC, PμP»C—C<sub>7</sub> C<sub>7</sub>C<sub>7</sub>PrPēPS  
PjPsP<sub>7</sub>C<sub>7</sub>C, C<sub>7</sub> PīPsPiC—C<sub>7</sub>CēC<sub>7</sub>PiP°C, Pē PīC<sub>7</sub>PsC<sub>7</sub>PμC<sub>7</sub> P·P°PiPsC''PSPSC<sub>7</sub> C<sub>7</sub>P°PS,

PJ PeP»C-PSC-C‡PSPëC... PrPsCÍP»C-PrP¶PuPSPSC¶C... C-P· P·P°P»CrC‡PuPSPSC¶Pj  
PiP°C‡C-C°PSC,C-PI C-P· C¶PsP·PiPsPICÍC¶PrP¶PuPSPsC¶ CÍP°C¶PePsPjPsC¶

Pjбґ™ CҚPePëC... C,PeP°PSPëPS PİPsPIC-PrPsPjP»CҚP»PsCІ́CH PİCґPs PIPëPİP°PrPePë  
PİPSPµPIPjPsC,PsCґP°PeCІ́Cр (PrPëPI. CґPsP·PrC-P» B«PµPsP±C-C±PSC- CґPµP°PeC†C-C—B»).

PµC-Pr C±P°CІ́ P»C-PeCрPIP°PSPSCҚ PİP°P·PsPİP°PSC-P±PsPj PİP°C†C-C”PSC,C-PI CІ́P»C-Pr  
CґPµC,PµP»CHbPSPs PsP±CІ́C,PµP¶CрPIP°C,Pë PSP° PSP°CҚIPSC-CІ́C,CH PsP·PSP°Pe C,P°  
CІ́PëPjPİC,PsPjC-PI PİPSPµPIPjPsC,PsCґP°PeCІ́Cр.B

*P†PSC,,PµPeC†C-C—.*

PµPsPIC-PrPsPjP»CҚP»PsCІ́CH PİCґPs PIPëPİP°PrPePë CІ́PµCґPNµPsP·PSPëC...  
C-PSC,,PµPeC†C-PNµ (P· PSPµPNµC,CґPsPİPµPSC-C”Cґ P°P±Ps P±PµP· PSPµC—), C-PSPsPrC-  
P»PµC,P°P»CHbPSC-.

*PµPsPjP±C-PSP°C†C-CҚ P· C-PSC€PëPjPë CІ́PëCІ́C,PµPjPSPëPjPë  
PİCґPsC,PëPİCзC...P»PëPSPSPëPjPë PİCґPµPİP°CґP°C,P°PjPë.*

PµP»C-PSC-C±PSC- PrPsCІ́P»C-PrP¶PµPSPSCҚ PrC-C— P’PsC,CґC-C”PSC,Cр<sup>PÿPґ</sup> (Cр  
PePsPjP±C-PSP°C†C-C— P· PİPµPjPµC,CґPµPeCІ́PµPrPsPj, P»P°PİP°C,PëPSC-P±PsPj B C,P°  
PİPµPjP±CґPsP»C-P·CрPjP°P±PsPj) P±CрP»Pë PİCґPëPİPëPSPµPSC- CґP°PSC-C€Pµ C±PµCґPµP·  
P·P°CІ́C,PµCґPµP¶PµPSPSCҚ C°°PsPrPs PİPµCґPµPIPëC°°PµPSPsC— C,PsPeCІ́PëC±PSPsCІ́C,C-  
C,P°/P°P±Ps CІ́PjPµCґC,PSPsCІ́C,C-. P’PµP·PİPµC±PSPsC— C,P° PµC,,PµPeC,PëPIPSPsC—  
PePsPjP±C-PSP°C†C-C— PrPsP· C†PëC... PİCґPµPİP°CґP°C,C-PI PICІ́C,P°PSPsPIPëC,Pë PSPµ  
PIPрP°P»PsCІ́CҚ. P’PsC,CґC-C”PSC,<sup>PÿPґ</sup> PSPµ PİCґPëP·PSP°C±PµPSPëPNµ PrP»CҚ  
P·P°CІ́C,PsCІ́CрPIP°PSPSCҚ Cр PePsPjP±C-PSP°C†C-C— P· C†PëPjPë PİCґPµPİP°CґP°C,P°PjPë.

*P®PIPµPSC-P»CHbPSP° C,PsPeCІ́PëC±PSC-CІ́C,CH Cз C,PIP°CґPëPS.*

P— PsPİP»CҚPrCр PSP° PjPµC...P°PSC-P·Pj PrC-C—, P’PsC,CґC-C”PSC,<sup>PÿPґ</sup> PjPsP¶Pµ  
CІ́PëP»CHbPSPs PİPİP»PëPIP°C,Pë PSP° CґPsP·PIPëC,PsPe PsCґPİP°PSC-PI C,P°  
PrPsP·CґC-PIP°PSPSCҚ Cр CґP°PSPSCHbPsPjCр PİPsCІ́C,PSP°C,P°P»CHbPSPsPjCр  
PİPµCґC-PsPrC-, C,PsPjCр P’PsC,CґC-C”PSC,<sup>PÿPґ</sup> PSPµ PjPsP¶PSP° PİCґPëP·PSP°C±P°C,Pë  
PrC-C,CҚPj PrPs 2 CґPsPeC-PI.

*P’P°PiC-C,PSC-CІ́C,CH.*

P’PsPeP»C-PSC-C±PSC- PrPsCІ́P»C-PrP¶PµPSPSCҚ PSP° C,PIP°CґPëPSP°C... PİPsPeP°P·P°P»Pë  
CґPµPİCґPsPrCрPeC,PëPIPSCр C,PsPeCІ́PëC±PSC-CІ́C,CH PİCґPµPİP°CґP°C,Cр. PİPeC°°Ps  
P’PsC,CґC-C”PSC,<sup>PÿPґ</sup> P·P°CІ́C,PsCІ́PsPICрC”C,CHCІ́CҚ PİC-Pr C±P°CІ́ PIP°PiC-C,PSPsCІ́C,C-  
P°P±Ps CҚPeC°°Ps PİP°C†C-C”PSC,PeP° P·P°PIP°PiC-C,PSC-P»P° PİC-Pr C±P°CІ́  
P»C-PeCрPIP°PSPSCҚ C†PëPj PİCґPµPİP°CґP°C,PsPj, PSPµPsP±C...C-PrPSPs  
C-PSC,,PsCґPjCрPIP°C,Pë PİP°C†C-C”PSC,PeCр PİCґPs PİPsC,PµPSC†C-PNµPSCр  
PSPµP±PµP·PİPµPeCр PİCґPµPİP°CґP°C,Cр PrP»CҚ PİP»PsPrP°. P-C-PSPeP°Pj  
PrC-C,PsCґPsPrPSPsPİPs PIC-PeCр CІ́P»C-Pr CґPµPePsPjPµPSPрCрPIP°C,Pë  
P·P°PİPsP±C-PİP°C,Pë PIP°PiC-C,PSPsCІ́C,C- PİC-Pr C±P°CІ́ P»C-PeCрPIP°PSPSCҚ  
PİP°P·PsPİP°PSC-P±PsPj C,P° PİCґPsC,CҚPİPsPj 2 C,PëP¶PSC-PI PİC-CІ́P»CҚ PNµPsPİPs  
PİCґPëPİPëPSPµPSPSCҚ (PrPëPI. CґPsP·PrC-P» B«P—P°CІ́C,PsCІ́CзPIP°PSPSCҚ Cз  
PİPµCґC-PsPr PIP°PiC-C,PSPsCІ́C,C- P°P±Ps PİPsPrCзPIP°PSPSCҚ PİCґCзPrPrCґB»).

*P’P·P°C”PjPsPrC-C—.*

PŸP»C-Pr CрPSPëPeP°C,Pë CІ́CрPjC-CІ́PSPsPİPs P·P°CІ́C,PsCІ́CрPIP°PSPSCҚ P·  
CІ́PëP»CHbPSPëPjPë C-PSPİC-P±C-C,PsCґP°PjPë CYP3A4, P -gp P°P±Ps BCRP C±PµCґPµP·  
CґPëP·PëPe PİC-PrPIPëC°°PµPSPSCҚ PµPeCІ́PİPsP·PëC†C-C— PİP°P·PsPİP°PSC-P±Cр (PrPëPI.

$P''PsC, P_{\mu}P_{\bar{\mu}}C_{\bar{\eta}} PIC - PrC\bar{I}C\bar{r}C, PSC - \bar{P}\bar{P}_{\mu}C_{\bar{\eta}}P_{\mu}PePsPSP \gg P\bar{e}PIC - PrPsPeP^{\circ}P \cdot PsPIC - PrP^{\circ}PSC -$   
 $C^{\circ}_{\%}PsPrPs P \cdot P^{\circ}C\bar{I}C, PsC\bar{I}C\bar{r}PIP^{\circ}PSPSC \sqcup P'PsC, C_{\bar{\eta}}C - C''PSC, C\bar{r}^{PyP_{\bar{\eta}}} PIP^{\circ}PiC - C, PSP\bar{e}Pj P \parallel C - PSPeP^{\circ}Pj.$   
 $B P \cdot PeC\bar{I}P_{\bar{\mu}}C_{\bar{\eta}}P\bar{e}PjP_{\mu}PSC, P^{\circ}P \gg CH\bar{P}SC - PrPsC\bar{I}P \gg C - PrP \parallel P_{\mu}PSPSC \sqcup C\bar{r} C, PIP^{\circ}C_{\bar{\eta}}P\bar{e}PS$   
 $PiC_{\bar{\eta}}PsPrP_{\mu}PjPsPSC\bar{I}C, C_{\bar{\eta}}C\bar{r}PIP^{\circ}P \gg P\bar{e} C_{\bar{\eta}}P_{\mu}PiC_{\bar{\eta}}PsPrC\bar{r}PeC, P\bar{e}PIPSC\bar{r} C, PsPeC\bar{I}P\bar{e}C\ddagger PSC - C\bar{I}C, CH$   
 $PiC_{\bar{\eta}}P_{\mu}P\bar{i}P^{\circ}C_{\bar{\eta}}P^{\circ}C, C\bar{r}. P_{\mu}PsC, P_{\mu}PSC\ddagger C - PN_{\bar{e}}PSP\bar{e}PN_{\bar{e}} C_{\bar{\eta}}P\bar{e}P \cdot P\bar{e}Pe PiC_{\bar{\eta}}P_{\mu}P\bar{i}P^{\circ}C_{\bar{\eta}}P^{\circ}C, C\bar{r} PrP \gg C \sqcup$   
 $P \gg CHPrP\bar{e}PSP\bar{e} PiPsPeP\bar{e} C^{\circ}_{\%}Ps P \cdot P^{\circ}P \gg P\bar{e}C\bar{e}P^{\circ}C''C, CHC\bar{I}C \sqcup PSP_{\mu}PIC - PrPsPjP\bar{e}Pj.$   
 $P'PsC, C_{\bar{\eta}}C - C''PSC, P^{PyP_{\bar{\eta}}} PSP_{\mu} P\bar{i}PsPIP\bar{e}PSP_{\mu}PS P \cdot P^{\circ}C\bar{I}C, PsC\bar{I}PsPIC\bar{r}PIP^{\circ}C, P\bar{e}C\bar{I}C \sqcup PiC - Pr C\ddagger P^{\circ}C\bar{I}$

PIP°PiC-C,PSPsCfC,C-, P·P° PIPëPSCfC,PePsPj PIPëPïP°PrPeC-PI, PePsP»Pë  
PïPsC,PμPSC†C-PNëPSP° PePsCfPëCfC,CH PIC-Pr P·P°CfC,PsCfCfPIP°PSPSCfC  
PïPμCfPμPIP°P¶P°C” CfPëP·PëPe. PïPeC%Ps P’PsC,CfC-C”PSC,<sup>PÿPñ</sup>  
P·P°CfC,PsCfPsPICfC”C,CHCfCfCf PïC-Pr C†P°Cf PIP°PiC-C,PSPsCfC,C- P°P±Ps CfPeC%Ps  
PïP°C†C-C”PSC,PeP° P·P°PIP°PiC-C,PSC-P»P° PSP° C,,PsPSC- PïCfPëPNëPsPjCf PrP°PSPsPiPs  
PïCfPμPïP°CfP°C,Cf, PSPμPsP±C...C-PrPSPs PïPsCfCfPSPëC,Pë PïP°C†C-C”PSC,C†C- PïCfPs  
PïPsC,PμPSC†C-PNëPSCf PSPμP±PμP·PïPμPeCf PïCfPμPïP°CfP°C,Cf PrP»Cf PïP»PsPrP°.

P— PjPμC,PsCf P·P°PïPsP±C-PïP°PSPSCf PIP°PiC-C,PSPsCfC,C- PïCfPë C,PμCfP°PïC-C—  
PïP°P·PsPïP°PSC-P±PsPj P¶C-PSPeP°Pj CfPμPïCfPsPrCfPeC,PëPIPSPsPiPs PIC-PeCf C†P»C-Pr  
CfPμPePsPjPμPSPPrCfPIP°C,Pë P·P°CfC,PsCfPsPICfPIP°C,Pë PμC,,PμPeC,PëPIPSC- PjPμC,PsPrPë  
PePsPSC,CfP°C†PμPïC†C-C— PïC-Pr C†P°Cf P·P°CfC,PsCfCfPIP°PSPSCf PïP°P·PsPïP°PSC-P±Cf  
C,P° PïCfPsC,CfPiPsPj 2 C,PëP¶PSC-PI PïC-C†P»Cf PïCfPëPïPëPSPμPSPSCf  
P·P°CfC,PsCfCfPIP°PSPSCf PïP°P·PsPïP°PSC-P±Cf.

PμP°C†C-C”PSC,Pë C†PsP»PsPIC-C†PsC— CfC,P°C,C- (PI C,PsPjCf C†PëCfP»C- C,C-, PePsPjCf  
PïCfPsPiPsPrPëP»Pë PIP°P·PμPeC,PsPjC-Cf) PïPsPïPëPSPSC- PIPëPePsCfPëCfC,PsPICfPIP°C,Pë  
PïCfPμP·PμCfPIP°C,PëPIPë PïC-Pr C†P°Cf CfC,P°C,PμPiPsPiPs P°PeC,Cf PI PïPμCfC-PsPr  
P»C-PeCfPIP°PSPSCf PïP°P·PsPïP°PSC-P±PsPj C- PïCfPsC,CfPiPsPj PïCfPëPSP°PNëPjPSC- 2  
C,PëP¶PSC-PI PïC-C†P»Cf PïCfPëPNëPsPjCf PsCfC,P°PSPSCHPsC— PrPsP·Pë  
PïP°P·PsPïP°PSC-P±Cf, C%PsP± CfPSPëPePSCfC,Pë PjPsP¶P»PëPiPsPiPs PïP»PëPICf  
PïCfPμPïP°CfP°C,Cf PSP° PïP°CfC,PSPμCfC-PI ðf” PIP°PiC-C,PSPëC... P¶C-PSPsPe  
CfPμPïCfPsPrCfPeC,PëPIPSPsPiPs PIC-PeCf.

*PμPμCfC-PsPr PiPsPrC¿PIP°PSPSCf PïCfC¿PrPrCf.*

PkP° CfCHPsPiPsPrPSC- P±PμP·PïPμC†PSC-CfC,CH P·P°CfC,PsCfCfPIP°PSPSCf  
P’PsC,CfC-C”PSC,Cf<sup>PÿPñ</sup> Cf PïPμCfC-PsPr PiPsPrCfPIP°PSPSCf PïCfCfPrPrCf PSPμ  
PrPsCfP»C-PrP¶PμPSP°. PkPμ PIC-PrPsPjPs, C†Pë PμPeCfPeCfPμC,CfC”C,CHCfCfCf  
PïP°P·PsPïP°PSC-P± Cf PïCfCfPrPSPμ PjPsP»PsPePs P»CfPrPëPSPë, C,PsPjCf PïC-Pr C†P°Cf  
P»C-PeCfPIP°PSPSCf P’PsC,CfC-C”PSC,PsPj<sup>PÿPñ</sup> PSPμPsP±C...C-PrPSPs PïCfPëPïPëPSPëC,Pë  
PiPsPrCfPIP°PSPSCf PïCfCfPrPrCf.

*P—PrP°C,PSC-CfC,CH PIPïP»PëPIP°C,Pë PSP° CëPIPëPrPeC-CfC,CH CfPμP°PeC†C-C— PïCfPë  
PePμCfC¿PIP°PSPSC- P°PIC,PsC,CfP°PSCfPiPsCfC,PsPj P°P±Ps CfPsP±PsC,C- P· C-PSCëPëPjPë  
PjPμC...P°PSC-P·PjP°PjPë.*

P’PsC,PμPïPμCf PSPμ PïCfPsPiPsPrPëP»PsCfCf PrPsCfP»C-PrP¶PμPSCf C%PsPrPs  
PIPïP»PëPICf P’PsC,CfC-C”PSC,Cf<sup>PÿPñ</sup> PSP° P·PrP°C,PSC-CfC,CH PePμCfCfPIP°C,Pë  
P°PIC,PsPjPsP±C-P»PμPj P°P±Ps PSP° PjPsP¶P»PëPIC-CfC,CH PïCfP°C†CfPIP°C,Pë P·  
CfC-P·PSPëPjPë PjPμC...P°PSC-P·PjP°PjPë. P’CfP°C...PsPICfCHC†Pë  
C,,P°CfPjP°PePsP»PsPiC-C†PSC- PIP»P°CfC,PëPiPsCfC,C- PïP°P·PsPïP°PSC-P±Cf, PNëPsPiPs  
PSPμCfPïCfPëCfC,P»PëPIPëPNë PIPïP»PëPI PSP° C,P°PeC- PIPëPrPë PrC-CfP»CHPSPsCfC,C-  
PjP°P»PsPNëPjPsPIC-CfPSPëPNë. PμCfPë PsC†C-PSC†C- P·PrP°C,PSPsCfC,C- PïP°C†C-C”PSC,P°  
PIPëCfC-CëCfPIP°C,Pë P·P°PIPPrP°PSPSCf, C%Ps PïPsC,CfPμP±CfCfC,CH  
PïCfPëPNëPSCfC,C,Cf CfC-CëPμPSCf, CfC-PIPSCf PNëPsPiPs PjPsC,PsCfPSPëC... C-  
PePsPiPSC-C,PëPIPSPëC... PSP°PIPëC†PsPe, PïPsPïPëPSPμPS PICfP°C...PsPICfPIP°C,PëCfCf  
PeP»C-PSC-C†PSPëPNë CfC,P°C,CfCf C...PiPsCfPsPiPs C,P° PïCfPsC,,C-P»CH  
PïPsP±C-C†PSPëC... CfPμP°PeC†C-PNë P’PsC,CfC-C”PSC,Cf<sup>PÿPñ</sup>.



C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCř PïP°P·PsPïP°PSC-P±Cř, PICḡP°C...PsPICřCḡC±Pë  
PSPëP·CHPePëPNë CḡC-PIPµPSCḡ PµPeCřPeCḡPµC†C-C— PïP°P·PsPïP°PSC-P±Cř C,P° PNëPsPiPs  
PjPµC,P°P±PsP»C-C,PI C†PµCḡPµP· PSPëCḡPePë, PePsCḡPëPiCřPIP°PSPSCḡ PrPsP·Pë  
PïCḡPµPïP°CḡP°C,Cř PïCḡPë C†CHPeSjCř PSPµ PïPsC,CḡC-P±PSPµ C...PIPsCḡPëPj P·  
PeP»C-CḡPµPSCḡPsPj PeCḡPµP°C,PëPSC-PSCř ≥ 30 PjP»/C...PI (PrPëPI. CḡPsP·PrC-P»  
B«PαP°CḡPjP°PePsPeC-PSPµC,PëPeP°B»).

*PµPµC†C-PSPePsPIP° PSPµPrPsCřC,P°C,PSC-CřC,CH.*

P'PµP·PïPµC†PSC-CřC,CH P·P°CřC,PsCřCřPIP°PSPSCḡ PïP°P·PsPïP°PSC-P±Cř C,P°  
PsCřPsP±P»PëPIPsCřC,C- PNëPsPiPs C,,P°CḡPjP°PePsPeC-PSPµC,PëPePë Cř PïP°C†C-C"PSC,C-PI  
P· C-CřPSCřCḡC±PsCḡ PïPµC†C-PSPePsPIPsCḡ PSPµPrPsCřC,P°C,PSC-CřC,Cḡ PrPsC,PµPïPµCḡ  
PIPëPIC†PµPSC- PSPµPrPsCřC,P°C,PSCHPeS (PrPëPI. CḡPsP·PrC-P» B«PḡCřPsP±P»PëPIPsCřC,C-  
P·P°CřC,PsCřCřPIP°PSPSCḡB»).

P'CřC-Pj PïP°C†C-C"PSC,P°Pj CřP»C-Pr P·CḡPsP±PëC,Pë PïPµC†C-PSPePsPIC- PïCḡPsP±Pë  
C%PsPrPs PïPsCḡCřCëPµPSPSCḡ C,,CřPSPeC†C-C— PïPµC†C-PSPePë PïPµCḡPµPr  
PïPsC†P°C,PePsPj C,P° PïC-Pr C†P°Cř P»C-PeCřPIP°PSPSCḡ PïP°P·PsPïP°PSC-P±PsPj.  
PµP°C†C-C"PSC,P°Pj P· PïPsCḡCřCëPµPSPSCḡPj C,,CřPSPeC†C-C— PïPµC†C-PSPePë  
P»PµPiPePsPiPs C,P° PïPsPjC-CḡPSPsPiPs CřC,CřPïPµPSCḡ CřP»C-Pr  
P·P°CřC,PsCřPsPICřPIP°C,Pë PïP°P·PsPïP°PSC-P± P· PsP±PµCḡPµP¶PSC-CřC,Cḡ, P° C,P°PePsP¶  
PïCḡPsPIPsPrPëC,Pë CḡPµC,PµP»CHPePSPëPNë PePsPSC,CḡPsP»CH  
PïPµCḡPµPSPsCřPëPjPsCřC,C-.

P"P»Cḡ C...PIPsCḡPëC... P· PSPµP·PSP°C†PSPëPjPë P·PjC-PSP°PjPë PïPµC†C-PSPePsPIPëC...  
PïCḡPsP±, C%Ps PIPëP·PSP°C†P°CḡC,CHCřCḡ CḡPe PïC-PrPIPëC%PµPSPSCḡ CḡC-PIPsCḡ  
PḡP»Pḡ PïCḡPë PSPsCḡPjP°P»CHPeSjCř CḡC-PIPsC- P±C-P»C-CḡCřP±C-PSCř P°P±Ps CḡPe  
PïC-PrPIPëC%PµPSPSCḡ CḡC-PIPsCḡ P±C-P»C-CḡCřP±C-PSCř PI 1,5 CḡP°P·P° PIPëC%Pµ  
P'PḡPḡ PSPµP·P°P»PµP¶PSPs PIC-Pr CḡC-PIPsCḡ PḡP»Pḡ, PrPsP·P° PïCḡPµPïP°CḡP°C,Cř  
CřC,P°PSPsPIPëC,CH 800 PjPi 1 CḡP°P· PSP° PrPµPSCḡ.

PJ PïP°C†C-C"PSC,C-PI P· PïPsPjC-CḡPSPsCḡ PrPëCřC,,CřPSPeC†C-C"CH PïPµC†C-PSPePë  
(P·P°PiP°P»CHPePSPëPNë P±C-P»C-CḡCřP±C-PS PI 1,5-3 CḡP°P·Pë PIPëC%PëPNë P·P° P'PḡPḡ  
PSPµP·P°P»PµP¶PSPs PIC-Pr CḡC-PIPsCḡ PḡP»Pḡ) PrPsP·Cř P'PsC,CḡC-C"PSC,Cř<sup>PḡPḡ</sup>  
PSPµPsP±C...C-PrPSPs P·PSPëP·PëC,Pë PrPs 200 PjPi PSP° PrPsP±Cř. P"PsC,PµPïPµCḡ  
PSPµPrPsCřC,P°C,PSCHPeS PrP°PSPëC... PïCḡPs P·P°CřC,PsCřCřPIP°PSPSCḡ  
PïCḡPµPïP°CḡP°C,Cř PïP°C†C-C"PSC,P°Pj P· C,CḡP¶PePsCḡ PïPµC†C-PSPePsPIPsCḡ  
PSPµPrPsCřC,P°C,PSC-CřC,Cḡ (P·P°PiP°P»CHPePSPëPNë P±C-P»C-CḡCřP±C-PS P±C-P»CHCë  
PSC-P¶ Cř 3 CḡP°P·Pë PIPëC%PëPNë P·P° P'PḡPḡ PSPµP·P°P»PµP¶PSPs PIC-Pr CḡC-PIPsCḡ  
PḡP»Pḡ); Cř P·PIBḡ™ CḡP·PeCř P· C†PëPj PïCḡPëP·PSP°C†PµPSPSCḡ P'PsC,CḡC-C"PSC,Cř<sup>PḡPḡ</sup>  
C,P°PePëPj PïP°C†C-C"PSC,P°Pj PSPµ CḡPµPePsPjPµPSPPrCřC"C,CHCřCḡ.

*PIPIPSCḡC- P»C-C,PSCHPeSPiPs PIC-PeCé.*

PµP°C†C-C"PSC,Pë CřC,P°CḡCëPµ 65 CḡPsPeC-PI PSPµ PïPsC,CḡPµP±CřCḡC,CH  
PePsCḡPµPeC†C-C— PrPsP·Pë, C†P°CřC,PsC,Pë C,P° CřPïPsCřPsP±Cř PïCḡPëPNëPsPjCř  
PïCḡPµPïP°CḡP°C,Cř.

*P"C-C,Pë.*

P'PµP·PïPµC†PSC-CřC,CH C,P° PµC,,PµPeC,PëPIPsC-CřC,CH P·P°CřC,PsCřCřPIP°PSPSCḡ  
P'PsC,CḡC-C"PSC,Cř<sup>PḡPḡ</sup> Cř PrC-C,PµPNë PrPsC,PµPïPµCḡ PSPµ PIPëPIC†PµPSC- (PrPëPI.

$$\text{C}_7\text{H}_5\text{PsP} \cdot \text{PrC-P} \gg \text{B} \ll \text{PhCl}^+\text{PsP} \pm \text{P} \gg \text{P} \ddot{\text{e}} \text{PIP} \text{PsCl}^+\text{C,C-} \text{P} \cdot \text{P}^\circ \text{Cl}^+\text{C,PsCl}^+\text{CrPIP}^\circ \text{PSPSClB} \gg).$$

***PμPμCΠPμPΓPsP·CζPIP°PSPSCΠ.***

PJ PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSPSC¶C... PIPëPIC†P°P»PëCÍC¶ PrPsP·Pë  
P'PsC,C¶C-C" PSC,CÍ<sup>PyPb</sup> PrPs 2000 PjPi. PJ 1 P· 3 PiP°C†C-C" PSC,C-PI, C%Ps  
PsC,C¶PëPjCÍPIP°P»Pë PiC¶PµPiP°C¶P°C, CÍ PrPsP·P°C... 2000 PjPi C,P° 1000 PjPi PSP°  
PrPsP±CÍ, CÍPiPsCÍC,PµC¶C-PiP°P»PëCÍC¶ PiC-PrPIPëC%PµPSP°  
PIC,PsPjP»C¶PIP°PSC-CÍC,C¶ 3-PiPs CÍC,CÍPiPµPSC¶ C,C¶P¶PePsCÍC,C-  
(PrPsP·PsP»C-PjC-C,CÍC¶C†P° C,PsPeCÍPëC†PSC-CÍC,C¶) C,P° P°C¶C,PµC¶C-P°P»C¶PSP°  
PiC-PiPµC¶C,PµPSP·C-C¶ 3-PiPs CÍC,CÍPiPµPSC¶ C,C¶P¶PePsCÍC,C- PIC-PrPiPsPIC-PrPSPs.

$$P\check{Y}P\ddot{e}PjP\ddot{i}C,PsPjP\ddot{e} \ C,P^{\circ} \ PsP\cdot PSp^{\circ}PeP\ddot{e}.$$
$$P''PsC, P_{\mu}P_{\bar{\mu}}P_{\mu}C\bar{\eta} \quad P_rPsC\bar{\Gamma}PIC-P_r \quad P_{\bar{\mu}}P_{\mu}C\bar{\eta}P_{\mu}P_rPsP \cdot C\acute{r}PIP^{\circ}PSPSC\bar{\eta} \quad P'PsC, C\bar{\eta}C-C''PSC, C\acute{r}^{P\bar{P}P_{\bar{\mu}}}$$

$$PsP \pm P_jP_{\mu}P_{\bar{\mu}}P_{\mu}PSP\bar{P}N_{\circ}.$$
$$P \succ C - P \epsilon C \acute{z} PIP^{\circ} P S P S C \downarrow.$$

PŸPİPıC†PĖC,,C-C‡PSPsPiPs P°PSC,PēPrPsC,Cr PİCḤPē PİPıCḤPıPrPsP·CrPIP°PSPSC-  
PİP°P·PsPİP°PSC-P±Cr PSPıPjP°C". P—P°CÍC,PsCÍPsPICrCḤC,CHCÍCı P·PIPēC‡P°PN₂PSC-  
PİC-PrC,CḤPēPjCrCḤC‡C- P·P°CÍPsP±Pē P·P°P»PıP¶PSPs PIC-Pr PeP»C-PSC-C‡PSPēC...  
PİPsPeP°P·P°PSCḤ. P"PıPjPsPrC-P°P»C·P PSP°PICḤCıPr C‡Pē P±CrPrPı CÍPİCḤPēCıC,Pē  
PİPsPeCḤP°C%ıPıPSPSCḤ PıP»C-PjC-PSP°C†C-C— PİP°P·PsPİP°PSC-P±Cr, PsCÍPeC-P»CHPePē  
C†PıPN₂ PİCḤPıPİP°CḤP°C, CÍCrC,C,C"PIPs PSPı PıPeCÍPeCḤPıC,CrC"C,CHCÍCı  
PSPēCḤPeP°PjPē C,P° P·PSP°C‡PSPsCḤ PjC-CḤPsCḤ P·PIḇḥ™ CıP·CrC"C,CHCÍCı P·  
P±C-P»PeP°PjPē PİP»P°P·PjPē PeCḤPsPIC-.

**$P_{\psi}P_{\sigma}P_{\pm}C-C\neq PSC-C\bar{H}P_{\mu}P^{\circ}P_{\epsilon}C\neq C-C-$ .**

P—PIP<sub>μ</sub>PrP<sub>μ</sub>PSC- PrP°PSC-, PsC, C<sub>7</sub>P<sub>6</sub>P<sub>6</sub>P°PSC- PI PsC<sub>7</sub>PSPsPIPSPsPjC<sub>7</sub>  
PrPsC<sub>7</sub>P»C-PrP<sub>¶</sub>P<sub>μ</sub>PSPSC- C<sub>7</sub> P<sub>6</sub>P°C<sub>7</sub>C-C°PSC, C-PI P· P<sub>6</sub>P<sub>6</sub>P<sub>6</sub> (VEG105192, n=290),  
C<sub>7</sub>P<sub>6</sub>P·C<sub>6</sub>P<sub>6</sub>C<sub>7</sub>P<sub>μ</sub>PSPsPjC<sub>7</sub> PrPsC<sub>7</sub>P»C-PrP<sub>¶</sub>P<sub>μ</sub>PSPSC- (VEG107769, n=71),  
PrPsP<sub>6</sub>P<sub>6</sub>PjC-P<sub>¶</sub>PSPsPjC<sub>7</sub> PrPsC<sub>7</sub>P»C-PrP<sub>¶</sub>P<sub>μ</sub>PSPSC- C<sub>7</sub>, P°P·P<sub>6</sub> II (VEG102616, n=225) C, P°  
C<sub>7</sub>P°PSPPrPsPjC-P·PsPIP°PSPsPjC<sub>7</sub> PIC-PrPeC<sub>7</sub>P<sub>6</sub>C, PsPjC<sub>7</sub> PrPsC<sub>7</sub>P»C-PrP<sub>¶</sub>P<sub>μ</sub>PSPSC-  
PSP<sub>μ</sub>PjP<sub>μ</sub>PSC<sub>6</sub>PsC— P<sub>μ</sub>C<sub>7</sub>, P<sub>μ</sub>PeC, P<sub>6</sub>PIPSPsC<sub>7</sub>C, C- PI P<sub>6</sub>P°C<sub>7</sub>P°P»P<sub>μ</sub>P»C<sub>7</sub>PSP<sub>6</sub>C... PiC<sub>7</sub>C<sub>7</sub>P<sub>6</sub>P°C...  
C<sub>7</sub>, P°P·P<sub>6</sub> III (VEG108844, n=557), P±C<sub>7</sub>P»P<sub>6</sub> PiC<sub>7</sub>P<sub>6</sub>P°PSP°P»C-P·PsPIP°PSC- PI PjP<sub>μ</sub>P<sub>¶</sub>P°C...  
P·P°PiP°P»C<sub>7</sub>PSPsC— PsC<sub>7</sub>C-PSPeP<sub>6</sub> P±P<sub>μ</sub>P·P<sub>6</sub>P<sub>μ</sub>PeP<sub>6</sub> C, P° P<sub>6</sub>P<sub>μ</sub>C<sub>7</sub>P<sub>μ</sub>PSPsC<sub>7</sub>P<sub>6</sub>PjPsC<sub>7</sub>C, C-  
P<sub>6</sub>P°P·PsP<sub>6</sub>P°PSC-P±C<sub>7</sub> (PIC<sub>7</sub>C<sub>7</sub>P<sub>6</sub>P<sub>6</sub> n=1149) PI PsC<sub>7</sub>C-P± P· P<sub>6</sub>P<sub>6</sub>P<sub>6</sub>.

P—PIP<sub>μ</sub>PrP<sub>μ</sub>PSC- PrP°PSC-, PsC, C<sub>7</sub>H<sub>5</sub>PëPjP°PSC- PI P±P°P·PsPIP<sub>μ</sub>PjC<sub>7</sub> PrPsC<sub>7</sub>P»C-PrP<sub>¶</sub>P<sub>μ</sub>PSPSC-  
C<sub>7</sub> PiP°C<sub>7</sub>C-C°PSC, C-PI P· C<sub>7</sub>P°C<sub>7</sub>PePsPjPsC<sub>7</sub> Pj<sub>5</sub>H<sub>7</sub><sup>TM</sup> C<sub>7</sub>IPePëC... PeP»C-C, PëPS (P<sub>Y</sub>P<sub>H</sub>P<sub>Y</sub>)  
(VEG110727, n=369) C- PrPsPiPsPjC-P<sub>¶</sub>PSPsPjC<sub>7</sub> PrPsC<sub>7</sub>P»C-PrP<sub>¶</sub>P<sub>μ</sub>PSPSC- C,,P°P·Pë II  
(VEG20002, n=142), P±C<sub>7</sub>P»Pë PiC<sub>7</sub>PsP°PSP°P»C-P·PsPIP°PSC- PI PjP<sub>μ</sub>P<sub>¶</sub>P°C...  
P·P°PiP°P»CH<sub>5</sub>PSPsC— PsC<sub>7</sub>C-PSPePë P±P<sub>μ</sub>P·PiP<sub>μ</sub>PePë C,P° PiP<sub>μ</sub>C<sub>7</sub>P<sub>μ</sub>PSPsC<sub>7</sub>PëPjPsC<sub>7</sub>C,C-  
PiP°P·PsPiP°PSC-P±C<sub>7</sub> (P·P°PiP°P»CH<sub>5</sub>PSP° PiPsPiC<sub>7</sub>P»C<sub>7</sub>C<sub>7</sub>C-C<sub>7</sub> PrP»C<sub>7</sub> PsC<sub>7</sub>C-PSPePë  
P±P<sub>μ</sub>P·PiP<sub>μ</sub>PePë n=382) PI PsC<sub>7</sub>C-P± P· P<sub>Y</sub>P<sub>H</sub>P<sub>Y</sub>.

PkP°PN±C-P»CHBC€ PIP°P¶P»PëPIPëPJpë CÍPµCĤPN±PsP·PSPëPJpë PSPµP±P°P¶P°PSPëPJpë  
CĤPµP°PeC†C-CĬPJpë, C-PrPµPSC,PëC,,C-PePsPIP°PSPëPJpë PI PrPsCÍP»C-PrP¶PµPSPSCĬC... Cr  
PiP°C†C-C”PSC,C-PI P· PkPŁPŁ P°P±Ps PŸPŁPŸ, P±CrP»Pë C,CĤP°PSP·PëC,PsCĤPSP°  
C-C€PµPjC-C‡PSP° P°C,P°PeP°, C-C€PµPjC-C‡PSPëPN± C-PSCÍCrP»CHBC,, C-C€PµPjC-CĬ  
PjC-PsPeP°CĤPPrP°, C-PSC,,P°CĤPeC, PjC-PsPeP°CĤPPrP° C,P° C-PSC,,P°CĤPeC, PjPsP·PeCr,  
CÍPµCĤC†PµPIP° PrPëCÍC,,CÍPSPeC†C-CĬ, PiPµCĤC,,PsCĤP°C†C-CĬ C,P° C,,C-CÍC,CrP»Pë PI  
PËPŁPŸ, PiPsPrPsPIP¶PµPSPSCĬ C-PSC,PµCĤPIP°P»Cr QT, C€P»CrPSPsC‡PePsPIP°  
C,P°C...C-PeP°CĤPPrC-CĬ C,PëPiCr B«PiC-CĤCrPµC,B» C,P° PeCĤPsPIPsPIPëP»PëPI PI  
P»PµPiPµPSCĬC..., PËPŁPŸ C- PiPsP»PsPIPSpsPjCr PjPsP·PeCr. P’CÍC- PSPµP±P°P¶P°PSC-  
CĤPµP°PeC†C-C— PIPëPSPëPeP°P»Pë Cr <1% PiP°C†C-C”PSC,C-PI, CĬPeC-  
PsC,CĤPëPJCrPIP°P»Pë P»C-PeCrPIP°PSPSCĬ. P†PSC€C- PIP°P¶P»PëPIC- CÍPµCĤPN±PsP·PSC-  
PSPµP±P°P¶P°PSC- CĤPµP°PeC†C-C—, C-PrPµPSC,PëC,,C-PePsPIP°PSC- PI  
PrPsCÍP»C-PrP¶PµPSPSCĬC... Cr PiP°C†C-C”PSC,C-PI P· PŸPŁPŸ, PIPeP»CHC‡P°P»Pë  
PIPµPSPsP·PSC- C,CĤPsPjP±PsPµPjP±PsP»C-C‡PSC- CĬPIPëC‰P°, PrPëCÍC,,CÍPSPeC†C-CĤ  
P»C-PIPsPiPs C€P»CrPSPsC‡PeP° C,P° PiPSPµPIpjPsC,PsCĤP°PeCÍ.

PkP°PN₂P±C-P»CH₃C€ PiPsC€PēCḡPμPSC- PSpμP±P°P¶P°PSC- CḡPμP°PeC†C-C—  
 (PIPēPSPēPeP»Pē C%oPsPSP°PN₂PjPμPSC€Pμ Cr 10% PīP°C†C-C”PSC,C-PI) P±CrPrCH₃-  
 C‡PePsPiPs C†C,CrPiPμPSC‡, C‡PeC- P±CrP»Pē P·P°CḡPμC”C†C,CḡPsPIP°PSC- Cr  
 PIPēPiCḡPsP±CrPIP°PSPSC‡C... Cr PīP°C†C-C”PSC,C-PI P· PkPḡPḡ C,P° PŸPḡPŸ:  
 PrC-P°CḡPμC‡, P·PjC-PSP° PePsP»CH₃PsCḡCr PIPsP»PsC†C†C‡,  
 PiC-PiPsPiC-PiPjPμPSC,P°C†C-C‡ C€PeC-CḡPē, PμPeC†C,,PsP»C-P°C,PēPIPSPēPN₂ PIPēC†PēPi,  
 PiC-PiPμCḡC,PμPSP·C-C‡, PSC†PrPsC,P°, PiPsP»PsPIPSPēPN₂ P±C-P»CH₃,  
 PIC,PsPjP»CḡPIP°PSC-C†C,CH₃, P°PSPsCḡPμPeC†C-C‡, P±P»CḡPIP°PSPSC‡,  
 PrPēC†PiPμPIP·C-C‡, C†C,PsPjP°C,PēC,, P·PjPμPSC€PμPSPSC‡ PjP°C†Pē C,C-P»P°, P±C-P»CH₃,  
 PiC-PrPIPēC%oPμPSPSC‡ CḡC-PIPC-PI P°P»P°PSC-PSP°PjC-PPSsC,CḡP°PSC†C,,PμCḡP°P·Pē  
 C,P° P°C†PiP°CḡC,P°C,P°PiC-PPSsC.CḡP°PSC†C,,PμCḡP°P·Pē.

$$\text{P}_{\text{b}}\text{P}^{\circ}\text{C}, \text{P}_{\text{u}}\text{P}\text{i}\text{P}\text{sC}\text{H}\text{C}-\text{C}-\text{P}\text{I}\text{P}\text{eP}\cdot\text{P}\text{S}\text{P}^{\circ}\text{C}\ddagger\text{P}_{\text{u}}\text{P}\text{S}\text{C}-\text{P}\text{S}\text{P}^{\circ}\text{P}\ddot{\text{C}}-\text{P}\text{r}\text{C}\dot{\text{I}}\text{C}, \text{P}^{\circ}\text{P}\text{I}\text{C}-\text{P}^{\circ}\text{P}\pm\text{C}\dot{\text{I}}\text{P}\text{sP}\gg\text{C}\text{H}\text{C}, \text{P}\text{S}\text{P}\text{S}\text{C}-\text{C}\ddagger\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}, \text{P}\text{s}\text{C}, \text{P}\ddot{\text{e}}\text{P}\ddot{\text{I}}\text{P}\text{S}\text{P}\pm\text{C}-\text{C}\ddagger\text{P}\text{S}\text{P}\ddot{\text{e}}\text{C}\dots\text{C}\text{H}\text{P}_{\text{u}}\text{P}^{\circ}\text{P}\text{e}\text{C}\ddagger\text{C}-\text{P}\text{N}_{\text{e}}\text{P}\cdot\text{P}^{\circ}\text{P}\text{r}\text{P}^{\circ}\text{P}\text{S}\text{P}\ddot{\text{e}}\text{P}\text{i}\text{P}\ddot{\text{e}}$$

**PkPμP±P°P¶P°PSC- C̄H̄PμP°PeC†C-C—, PīPsPIвҒ™ CII·P°PSC- P· P»C-PeCfPIP°PSPSCIIpj,  
CII·PeC- P±CfP»Pē P·P°C̄H̄PμC”CfC,C̄H̄PsPIP°PSC- PI PrPsCfP»C-PrP¶PμPSPSCIIc... Cf  
PīP°C†C-C”PSC,C-PI P· PkPлPл (n=1149) P°P±Ps PiC-Pr C‡P°Cf  
PiC-CfP»CIIСH̄PμC”CfC,C̄H̄P°C†C-PN₂PSPsPiPs P·P°CfC,PscfCfPIP°PSPSCII**

[illegible]

|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |            |           |   |
|----------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|-----------|---|
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>CfCfPrP6PS                                                                                                | PrCfP¶Ru<br>C±P°CfC,Ps | PbC7C,PuC7C-P°P»CHbPSP° PiC-PiPµC7C,PµPSP-C-ClI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 473 (41 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 115 (10 %) | 1 (< 1 %) |   |
|                                                                                                                                              | C±P°CfC,Ps             | PuC7P6PiP»P6PiP6<br>P°PµPSPsP-PSRµ C,C7PpsPjP±PsPµjP±PsP»C-C±PSPµ<br>CUIPIP6C°Pµ¶ <sup>†</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 16 (1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµPsC±PµC7PiPsPSC-PSPSCUI PsP±P»P6C±C±ClI<br>P°C-PiPµC7C,PµPSP-P6PiPSP6Pµ PeC7P6P°                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 13 (1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 6 (< 1 %)  | 7 (< 1 %) |   |
|                                                                                                                                              | C7C-PrPePs             | PµPsC±PµC7PiPsPSC-PSPSCUI PsP±P»P6C±C±ClI<br>P°C7C,PµC7C-Pµ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 12 (1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              |                        | P°C-PiPµC7C,PµPSP-P6PiPSP6Pµ PeC7P6P°<br>PµC7PpsPiPsPiP6P»P6Pi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 6 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0          | 2 (< 1 %) |   |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>PrP6C...P°P»CHbPSPsC—<br>CfP6CfC,PµjP6, PiC7CfPrPSPsC—<br>PeP»C-C,PeP6 C,P°<br>CfPµC7PµPrPpsCfC,C-PSPSCII | C±P°CfC,Ps             | PkPsCfPsPiP° PeC7PpsPiPsC,PµC±P°<br>P°P6CfC,PsPSC-ClI<br>P—P°PrP6C6PeP°<br>PµC7PpsPiPsC...P°C7P6P°PSPSCUI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 50 (4 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1 (< 1 %)  | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | P P6PSPsC7PµClI<br>P»PµPiPµPSµPiPiP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PµPSµPiPiPjPsC,PsC7P°PeCf                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 48 (4 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              |                        | PµPSµPiPiPjPsC,PsC7P°PeCf<br>P C-PrPePs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 42 (4 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 8 (< 1 %)  | 1 (< 1 %) |   |
|                                                                                                                                              |                        | P P6PSPsC7PµClI<br>P»PµPiPµPSµPiPiP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PµPSµPiPiPjPsC,PsC7P°PeCf                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 15 (1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | P C-PrPePs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | PtPSC,PµC7CfC,P6C±C-P°P»CHbPSP° C...PiPsC7PpsP±P°<br>P»PµPiPµPSPsC7PµPiPiPjPsPSC-C,7P                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1 (< 1 %)  | 0         | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | P°CfP¶Pµ<br>C±P°CfC,Ps | P°C-P°C7PµClI<br>PkCfPrPsC,P°<br>P°P»CHbPiP°PSPSCUI<br>P°C-P»CHb Pi C6P»CfPSPeCf°                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 614 (53 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 65 (6 %)   | 2 (< 1 %) |   |
|                                                                                                                                              | C±P°CfC,Ps             | PµC,PµPjP°C,P6C,<br>P°P6CfPµCfC-ClI<br>PµPµC,PµPsC7P6P-Pj<br>P—PrCfC,C,ClI P¶P6PiPsC,P°<br>PiC,PiPsC7PµPSPSCUI PiP6C7P°P-PsPe Pi<br>C7PpsC,PsPiC-Pµ PiPsC7PpsP¶PSP6PSC-<br>PµCfC...C-CfC,CHb Pi C7PpsC,-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 96 (8 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | PµPµP»PµPSP°<br>PSP°CfC,C- PiP6PiPsC7PpsP¶PSPµPSPSCUI<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi | 27 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                         | 8 (< 1 %)  | 4 (< 1 %) | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | C±P°CfC,Ps             | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 225 (20 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 18 (2 %)   | 1 (< 1 %) |   |
|                                                                                                                                              |                        | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 139 (12 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 15 (1 %)   | 0         |   |
|                                                                                                                                              |                        | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 96 (8 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                         | 83 (7 %)   | 2 (< 1 %) | 0 |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi | 43 (4 %)   | 0         | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | C±P°CfC,Ps             | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 36 (3 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 2 (< 1 %)  | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 28 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 3 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 27 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                         | 8 (< 1 %)  | 4 (< 1 %) | 0 |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi | 8 (< 1 %)  | 2 (< 1 %) | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | C±P°CfC,Ps             | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 27 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                         | 8 (< 1 %)  | 2 (< 1 %) | 0 |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi | 8 (< 1 %)  | 4 (< 1 %) | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | C±P°CfC,Ps             | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 27 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                         | 8 (< 1 %)  | 4 (< 1 %) | 0 |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi | 8 (< 1 %)  | 4 (< 1 %) | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | C±P°CfC,Ps             | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 27 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                         | 8 (< 1 %)  | 4 (< 1 %) | 0 |
|                                                                                                                                              |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi | 8 (< 1 %)  | 4 (< 1 %) | 0 |
| RuPsC7CfC6RuPSPSCII P. P±PsPeCf<br>C6P»CfPSPePsPiPs-PeP6C6PePsPiPsPiPs<br>C,C7P°PeC,Cf                                                       | C±P°CfC,Ps             | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7PpsPiPsPiP6P»P6Pi Cf PiPµC7C...PSC-C...<br>PiC-PrPrC-P»P°C... C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPiPs C,C7P°PeC,Cf<br>P—PsPiPSC-C6PSCUI PeP6C6PePsPiP° C,C-CfC,CfP»P°<br>PµC7P6PiP°PiPµ P±P»CHbPiP°PSPSCUI<br>P°PµPiPsC7PpsC—PrP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi<br>PµPiC7C,PsC7P°CfC-ClI PeP»CfP±PsPiPsC—<br>PeP6C6PeP6<br>PµC7PpsPiPsPiP6P»P6Pi Pi CfC,C7P°PiPsC...PsPrC-<br>P PµC,C7PpsPiPµC7P6C,PsPSPµP°P»CHbPSP6Pµ<br>PeC7PpsPiPsPiP6P»P6Pi                                                                                                         | 27 (2 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0          | 0         |   |
|                                                                                                                                              | PSRµC±P°CfC,Ps         | PµP°PSPeC7PµP°C,P6C,<br>P PµPeC,P°P»CHbPSP6Pµ PeC7PpsPiPsPiP6P»P6Pi<br>PkP°ClIPIPSC-CfC,CHb CfPiC-P¶PsC— PeC7PpsPiC- Pi<br>PeP°P»C—<br>PµC7PpsPiPsPiP6P»P6Pi Pi C6P»CfPSPePsPiPs-<br>PeP6C6PePsPiPsPjCf C,C7P°PeC,C-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 8 (< 1 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 4 (< 1 %)  | 0         |   |
|                                                                                                                                              |                        | PµPµC7C,PsC7P°CfC-ClI C,PsPiCfC,PsPiPs<br>PeP6C6PµC±PSP6PeP°<br>PµC7PpsPiPsPiP6P»P6Pi Pi C7PpsC,PsPiC-Pµ<br>PiPsC7PpsP¶PSP6PSC-<br>PµC7Pps                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |            |           |   |





|                                                                                                                 |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |           |           |           |
|-----------------------------------------------------------------------------------------------------------------|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------|-----------|
| <b>РnPsCҗCfCӨPnPPSPSCII P· P±PsPeCf<br/>CӨPeC-CHPө C, P°<br/>PiC-PrCӨPeC-CHPSPөC... C, PeP°PSPөPS</b>           | P°CfP¶Pµ<br>C±P°CTC, Ps | P—PjC-PSP° PePsP»CHPsCҗCf PIPsP»PsCfCTCII<br>P°C-PIPsPiC-PijPµPSC, P°CtC-CII CӨPeC-CHPө<br>P•PeCTC, PsP»C-P°C, PөPIPSPөP№ PIPөCTPөPi                                                                                                                                                                                                                                                                                                                                                     | 93 (24 %) | 0         | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PҗP»PsPiPµCTC-CII<br>PjCҗP°P¶PµPSPSCII CӨPeC-CHPө <sup>и</sup><br>PVCfC...C-CTC, C, H CӨPeC-CHPө<br>P°C-PIPiCҗPiC-PrCҗPsP·<br>PjCҗP°P¶PµPSPSCII PSC-PiC, C-PI<br>PYPiPµCҗP±C-P¶<br>P·CҗPөC, PµPjP°                                                                                                                                                                                                                                                                                       | 30 (8 %)  | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 26 (7 %)  | 4 (1 %)   | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PҗPөPµP»PµC, PSPs-Pjвҗ <sup>и</sup> CIIP-PsPIPөP№ P±C-P»CHҗ<br>PнC-P°P°PiC-CII<br>Pнвҗ <sup>и</sup> CIIP-PsPIC- CTPIP°P·PjPө                                                                                                                                                                                                                                                                                                                                                             | 18 (5 %)  | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 13 (3 %)  | 0         | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PҗPөPµP»PµC, PSPs-Pjвҗ <sup>и</sup> CIIP-PsPIPөP№ P±C-P»CHҗ<br>PнC-P°P°PiC-CII<br>Pнвҗ <sup>и</sup> CIIP-PsPIC- CTPIP°P·PjPө                                                                                                                                                                                                                                                                                                                                                             | 11 (3 %)  | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 4 (1 %)   | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 3 (< 1 %) | 1 (< 1 %) | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 3 (< 1 %) | 1 (< 1 %) | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 3 (< 1 %) | 1 (< 1 %) | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 3 (< 1 %) | 1 (< 1 %) | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 3 (< 1 %) | 1 (< 1 %) | 0         |
| <b>РnPsCҗCfCӨPnPPSPSCII P· P±PsPeCf<br/>PSPөCHPsPe C-<br/>CTPµC±PsPIPөPIC-PrPSPөC...<br/>CӨP»CIICT...C-PI</b>   | PrCfP¶Pµ<br>C±P°CTC, Ps | P°C, PsPjP»CHPIP°PSC-CTC, CHҗ                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 35 (9 %)  | 2 (< 1 %) | 0         |
|                                                                                                                 | C±P°CTC, Ps             | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 28 (7 %)  | 2 (< 1 %) | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 8 (2 %)   | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2 (< 1 %) | 0         | 0         |
| <b>Р—P°PiP°P»CHҗPSC- CHҗPsP·P»P°PrPө<br/>C, P° CHҗPµP°PeCtC-C— PI PjC-CTCtC-<br/>P·P°CTC, PsCfCTPIP°PSPSCII</b> | PrCfP¶Pµ<br>C±P°CTC, Ps | P°C, PsPjP»CHPIP°PSC-CTC, CHҗ                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 178 (47%) | 34 (9 %)  | 1 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | P°PөCҗP°P·PePө PSP° CӨPeC-CHC-<br>P°PөCTPөPi<br>PµP°PiCfP»CIICTҗPSPөP№ PIPөCTPөPi<br>P PµP»PeCtC-CII C, PsC, PsCtCfC, P»PөPIPsCTC, C-<br>P°PsP»PsPSPSPs-PiC-PrPsCөPsPIPSPөP№<br>CTPөPSPPrCҗPsPj                                                                                                                                                                                                                                                                                          | 18 (5 %)  | 1 (< 1 %) | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 12 (3 %)  | 4 (1 %)   | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 10 (3 %)  | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
|                                                                                                                 | PSPµC±P°CTC, Ps         | PµCҗPсC, PµC—PSCfCTC-CII                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1 (< 1 %) | 0         | 0         |
| <b>Р·P°P±PsCHҗP°C, PsCHҗPSC- C·P°<br/>C-PSCfC, CHҗCfPjPµPSC, P°P»CHҗPSC-<br/>PrP°PSC-<sup>и</sup></b>           | PrCfP¶Pµ<br>C±P°CTC, Ps | P—PjPµPSCөPµPSPSCII PjP°CTPө C, C-P»P°                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 86 (23 %) | 5 (1 %)   | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 29 (8 %)  | 4 (1 %)   | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 8 (2 %)   | 4 (1 %)   | 2 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 6 (2 %)   | 0         | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 5 (1 %)   | 2 (< 1 %) | 2 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 4 (1 %)   | 0         | 3 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 2 (< 1 %) | 0         | 0         |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 2 (< 1 %) | 0         | 2 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 1 (< 1 %) | 0         | 1 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 1 (< 1 %) | 0         | 1 (< 1 %) |
|                                                                                                                 | C±P°CTC, Ps             | PµP°C, PsP»PsPiC-C—, PIPөCIIPIP»PµPSC- PиCTҗPө<br>PsPiP»CIIPrC- P·PhP -PsCHҗPiP°PSC-PI <sup>и</sup><br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°P»P°PSC-PSP°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>P°C-PrC...PөP»PµPSPSCII CHҗC-PIPSCII<br>C...PsP»PµCTC, PµCHҗPөPSCf PI PөCHҗPsPIC-<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI<br>P°CTPIP°CHҗC, P°C, P°PjC-PSPsC, CHҗP°PSCfC, PµCHҗP°P·Pө<br>PµC-PrPIPөC»PµPSPSCII CHҗC-PIPSC-PI PIP°PjPjP°·<br>PiP»CHҗC, P°PjC-P»C, CHҗP°PSCfC, PµCHҗP°P·Pө | 2 (< 1 %) | 1 (< 1 %) | 0         |

Pj PïP°CTC-C”PSC, C-PI CTCT...C-PrPSPs-P°P·C-PNөCTCTHөPePsPiPs PïPsC...PsPrP¶PµPSPSCII  
C±P°CTC, C-CөPµ CTPIPsCTCT, PµCHҗC-PiP°P»Pө PSPµPNөC, CHҗPsPiPµPSC-CH,  
C, CHҗPsPjP±PsCtPөC, PsPiPµPSC-CH C, P° CTPIPөPSPPrCHҗPsPj PrPsP»PsPSPSPs-  
PiC-PrPsCөPsPIPSPс— PµCHҗPөC, CHҗPsPrPөP·PµCTCT, PµP·C-C— .

P—PIC-C, CTPIP°PSPSCII PïCHҗPs PïC-PrPsP·CHҗCHPIP°PSC- PSPµP±P°P¶P°PSC-  
CHҗPµP°PeCtC-C—

P—PIC-C, CTPIP°PSPSCII PïCHҗPs PïC-PrPsP·CHҗCHPIP°PSC- PSPµP±P°P¶P°PSC-  
CHҗPµP°PeCtC-C— PïC-CTP»CII CHҗPµC”CTCT, CHҗP°CTC-C— P»C-PөP°CTCTCTHөPePsPiPs

P·P°CÍPSP±Cí PjP°C” PIP°P¶P»PëPIPµ P·PSP°C‡PµPSPSC¶. P|Pµ P·P°P±PµP·PīPµC‡CíC”  
PīPSCÍC,C-PN₂PSPëPN₂ PjPsPSC-C,PsC¶PëPSPi CÍPīC-PIPIC-PrPSPsC€PµPSPSC¶  
PePsC¶PëCÍC,CH/C¶PëP·PëPe P·P°CÍC,PsCÍCíPIP°PSPSC¶ P»C-PeP°C¶CÍCHPePsPiPs  
P·P°CÍPSP±Cí. PŸPīPµC‡C-P°P»C-CÍC,C-PI CÍC,,PµC¶Pë PsC...PsC¶PsPSPë P·PrPsC¶PsPIB¶™ C¶  
PīC¶PsCÍC¶C,CH P·PIC-C,CíPIP°C,Pë PīC¶Ps P±CíPrCH-C¶PeC- PīC-PrPsP·C¶C¶PIP°PSC-  
PSPµP±P°P¶P°PSC- C¶PµP°PeC‡C-C— C‡PµC¶PµP· PSP°C‡C-PsPSP°P»CHPSCí CÍPëCÍC,PµPjCí  
P·PIC-C,PSPsCÍC,C- (P°PIC,PsPjP°C,PëP·PsPIP°PSP° C-PSC,,PsC¶PjP°C‡C-PN₂PSP°  
CÍPëCÍC,PµPjP° P· C,,P°C¶PjP°PePsPSP°PiP»C¶PrCí).

**PŸPµC¶PjC-PS PīC¶PëPrP°C,PSPsCÍC,C-.** 3 C¶PsPePë.

**PjPjPsPIPë P·P±PµC¶C-PiP°PSPSC¶.**

P—P±PµC¶C-PiP°C,Pë PīC¶PµPīP°C¶P°C, PīC¶Pë C,PµPjPīPµC¶P°C,CíC¶C- PSPëP¶C‡Pµ 30 B°C.  
P—P±PµC¶C-PiP°C,Pë Cí PSPµPrPsCÍC,CíPīPSPsPjCí PrP»C¶ PrC-C,PµPN₂ PjC-CÍC‡C-.

**PjPīP°PePsPIPëP°.**

PµPs 30 C,P°P±P»PµC,PsPe Cí PSPµPīC¶PsP·PsC¶PsPjCí C,,P»P°PePsPSC- P·  
PīPsP»C-PµC,PëP»PµPSCí PIPëCÍPSPePsC— C%oC-P»CHPSPsCÍC,C- P±C-P»PsPiPs  
PePsP»CHPsC¶Cí P· PīPsP»C-PīC¶PsPīC-P»PµPSPsPIPsC¶ PeC¶PëC€PePsC¶, C%oPs PjP°C”  
P·P°C...PëCÍC, PIC-Pr PrC-C,PµPN₂. PµPs 1 C,,P»P°PePsPSCí PI PeP°C¶C,PsPSPSC-PN₂  
PePsC¶PsP±C‡C-.

**PµP°C,PµPiPsC¶C-C¶ PIC-PrPīCíCÍPeCí.** P—P° C¶PµC‡PµPīC,PsPj.

**P’PëC¶PsP±PSPëPePë.**

1. P’PëPīCíCÍPe CÍPµC¶C—:

P“P»P°PeCÍPs P’PµP»P»PePsPj PŸ.P¶., P‡CÍPīP°PSC-C¶/ Glaxo Wellcome S.A., Spain;

2. P’PëPīCíCÍPe CÍPµC¶C—:

PḱPsPIP°C¶C,C-CÍ PḱP°C¶PjP°CÍCHC¶C,PëPeP°P» PḱP°PSCíC,,P°PeC,CíC¶C-PSPi P»P»PŸ,  
PŸP»PsPIPµPSC-C¶/ Novartis Pharmaceutical Manufacturing LLC, Slovenia.

**PḱC-CÍC‡PµP·PSP°C...PsPrP¶PµPSPSC¶ PIPëC¶PsP±PSPëPeC-PI C,P° P°PrC¶PµCÍPë  
PjC-CÍC‡C¶ PīC¶PsPIP°PrP¶PµPSPSC¶ C—C... PrC-C¶P»CHPSPsCÍC,C-.**

1. PḱPIPrP°. P·PeCÍC,C¶PµPjP°PrCíC¶P°, 3, PµPsP». P‡PSPr. PḱP»P»PµPSPrPµPrCíPµC¶Ps,  
PḱC¶P°PSPrP° PrPµ P”CíPµC¶Ps, P’CíC¶PiPsCÍ, 09400, P‡CÍPīP°PSC-C¶/ Avda. Extremadura, 3,

Pol. Ind. Allendeduero, Aranda de Duero, Burgos, 09400, Spain;

2. PICŕP». P'PµCĤPsPIC€PePsPIP° 57, P>CHP±P»CİPSP°, 1000, PŸP»PsPIPµPSC-Cİ/ Verovskova  
Ulica 57, Ljubljana, 1000, Slovenia.