

Р†РќРŸРŸР РЈРЉР|Р†РЇ

**РrР»CЏ РjРµРrРёC†PSPsPiPs Р·Р°CЏC,PsCЏCЏPIP°PSPSCЏ Р»C-РeР°CЏCЏCЏРePsPiPs
Р·Р°CЏPs±CЏ**

Р—РћР›РћРѠР Р·Рќ РѠРћРŸРŸ

(ZOLAFREN FAST)

РŸРeР»Р°Рr:

РrC-CЏC†Р° CЏРµC†PsPIPёPSP°: PsP»Р°PSP·Р°PіC-PS;

1 C,Р°Р±Р»РµC,РeР° РjC-CЏC,РёC,CЏ 10 РjPi Р°Р±Ps 20 РjPi PsP»Р°PSP·Р°PіC-PSCЏ;

*РrPsPiPsPjC-PЏPSC- CЏРµC†PsPIPёPSPё: РjР°PSC-C, (Р· 421), РeCЏPsCЏPіPsPIC-РrPsPS,
Р°CЏPіР°CЏC,Р°Рj (Р· 951), Р°CЏPsPjР°C,РёР·Р°C,PsCЏ Р°PіРµР»CЏCЏPёPSPsPIPёPNё,
РeCЏРµРjPSC-CЏ РrC-PsРeCЏPёРr РePsP»PsC—РrPSPёPNё Р±РµРµР·PіPsРrPSPёPNё, PSP°C,CЏC-CЏ
CЏC,РµР°CЏPёР»C„CЏРjР°CЏР°C,.*

**Р»C-РeР°CЏCЏCЏРeР° C„PsCЏРjР°. РŸР°Р±Р»РµC,РeРё, C%Ps
РrРёCЏPіРµCЏPіCЏCЏC,CЏCЏCЏ PІ CЏPsC,PsPIC-PNё PіPsCЏPsPЏPSPёPSC-.**

РћCЏPSPsPIPC- C„C-P·РёРePs-C...C-РjC-C†PSC- PIP»Р°CЏC,РёPIPсCЏC,C-:

C,Р°Р±Р»РµC,РeРё PіPs 10 РjPi: PЏPsPIC,C-, PіР»Р°CЏРeC-, РeCЏCЏPіР»C- C,Р°Р±Р»РµC,РeРё, Р·
PsРrPSPsPiPs Р±PsРeCЏ вЏ“ PіCЏР°PIC-CЏPіР°PSPSCЏ B«10B», РrC-Р°РjРµC,CЏPsPj 8 РjPj,
Р±РµРµР· PIPёРrРёРjРёC... PIPeCЏР°PіР»РµPSCH Р°Р±Ps PIPeР»CЏC†РµPSCH;

C,Р°Р±Р»РµC,РeРё PіPs 20 РjPi: PЏPsPIC,C-, PіР»Р°CЏРeC-, РeCЏCЏPіР»C- C,Р°Р±Р»РµC,РeРё, Р·
PsРrPSPsPiPs Р±PsРeCЏ вЏ“ PіCЏР°PIC-CЏPіР°PSPSCЏ B«20B», РrC-Р°РjРµC,CЏPsPj 10 РjPj,
Р±РµРµР· PIPёРrРёРjРёC... PIPeCЏР°PіР»РµPSCH Р°Р±Ps PIPeР»CЏC†РµPSCH.

**РѠР°CЏРjР°РePsC,РµCЏР°PіРµPIC,РёC†PSP° PіCЏCЏPіР°. РћPSC,РёPіCЏPёC...PsC,РёC†PSC-
Р·Р°CЏPs±Рё. РЉPsРr РћРŸРЇ N05A H03.**

РѠР°CЏРjР°РePsP»PsPіC-C†PSC- PIP»Р°CЏC,РёPIPсCЏC,C-.

РѠР°CЏРjР°РePsРrРёPSP°РjC-РeР°.

РћР»Р»Р°PSP·Р°PіC-PS C” Р°PSC,РёPіCЏPёC...PsC,РёC†PSPёРj,
Р°PSC,РёРjР°PSC-Р°РeР°Р»CЏPSPёРj Р»C-РeР°CЏCЏCЏРeРёРj Р·Р°CЏPs±PsPj, C,Р°РePsPЏ

PIC-PS CÍC,P°P±C-P»C-P·CfC" PSP°CÍC,CĤC-PN₂, PjP°C" CÍPíPµPeC,CĤ
C„P°CĤPjP°PePsP»PsPiC-C†PSPsC— PrC-C—, P·CfPjPsPIP»PµPSPsC— PIPíP»PēPIPsPj PSP°
CĤC-P·PSC- CĤPµC†PµPiC,PsCĤPē.

Pj PrPsPeP»C-PSC-C†PSPēC... PrPsCÍP»C-PrP¶PµPSPSCĬC... PIPēCĬPIP»PµPSPs
P·PIbĤ™ CĬP·CfPIP°PSPSCĬ PsP»P°PSP·P°PiC-PSCr P·C- CÍPµCĤPsC,PsPSC-PSPsPIPēPjPē
CĤPµC†PµPiC,PsCĤP°PjPē 5PĥPŸ2Pĥ/2PŸ, 5PĥPŸ3, 5PĥPŸ6, PrPsPíP°PjC-PSPsPIPēPjPē
CĤPµC†PµPiC,PsCĤP°PjPē D1, D2, D3, D4, D5, PjCfCÍPeP°CĤPēPSPsPIPēPjPē
CĤPµC†PµPiC,PsCĤP°PjPē Pĥ1-Pĥ5, P°PrCĤPµPSPµCĤPiC-C†PSPēPj CĤPµC†PµPiC,PsCĤPsPj α1
C- PiC-CÍC,P°PjC-PSPsPIPēPj Pĥ1-CĤPµC†PµPiC,PsCĤPsPj. Pj PiCĤPsC†PµCÍC-
PrPsCÍP»C-PrP¶PµPSCĤ PiPsPIPµPrC-PSPePē C,PIP°CĤPēPS, CĬPePēPj PIPsPrPēP»Pē
PsP»P°PSP·P°PiC-PS, PIPēCĬPIP»PµPSPs P°PSC,P°PiPsPSC-P·Pj PsP»P°PSP·P°PiC-PSCr CĬPe
PrPs CÍPµCĤPsC,PsPSC-PSPsPIPēC... CĤPµC†PµPiC,PsCĤC-PI 5PĥPŸ, C,P°Pe C- PrPs
PrPsPíP°PjC-PSPsPIPēC... C- C...PsP»C-PSPµCĤPiC-C†PSPēC... CĤPµC†PµPiC,PsCĤC-PI.
PĥP»P°PSP·P°PiC-PS PjP°C" PIPēC%PēPN₂ CĤC-PIPµPSCĤ P·PIbĤ™ CĬP·CfPIP°PSPSCĬ P·
CĤPµC†PµPiC,PsCĤP°PjPē CÍPµCĤPsC,PsPSC-PSCr 5PĥPŸ2, PSC-P¶ P· CĤPµC†PµPiC,PsCĤP°PjPē
PrPsPíP°PjC-PSCr D2, CÍ PjPsPrPµP»CĬC... CĬPe *in vitro*, C,P°Pe C- *in vivo*.
P·P»PµPeC,CĤPsC„C-P·C-PsP»PsPiC-C†PSC- PrPsCÍP»C-PrP¶PµPSPSCĬ PiPsPeP°P·P°P»Pē,
C%Ps PsP»P°PSP·P°PiC-PS CÍPµP»PµPeC,PēPIPsPs P·PjPµPSC€CfC" P·P±CfPrP»PēPIC-CÍC,CH
PjPµP·PsP»C-PjP±C-C†PSPēC... (Pĥ10) PrPsPíP°PjC-PSPµCĤPiC-C†PSPēC... PSPµPN₂CĤPsPSC-PI,
PiCĤPsCĬPIP»CĬCĤC†Pē PiCĤPē C†CHPsPjCf PSPµP·PSP°C†PSPēPN₂ PIPíP»PēPI PSP°
CÍC,CĤC-P°CĤPSC- (Pĥ9) C€P»CĬC...Pē, PiPsPIbĤ™ CĬP·P°PSC- P· PjPsC,PsCĤPSPsCĤ
C„CfPSPeC†C-C"CH. PĥP»P°PSP·P°PiC-PS PiP°P»CHPjCfC" CÍPjPsPIPSPēPN₂ CĤPµC„P»PµPeCÍ
CfPSPēPePSPµPSPSCĬ, C%Ps CÍPIC-PrC†PēC,CH PiCĤPs PN₂PsPiPs
P°PSC,PēPiCÍPēC...PsC,PēC†PSCr P°PeC,PēPIPsC-CÍC,CH PiCĤPē PiCĤPēPN₂PsPjC- PI
PrPsP·P°C..., PjPµPSC€PēC..., PSC-P¶ PrPsP·Pē, C%Ps CÍPiCĤPēC†PēPSCĬCĤC,CH
PeP°C,P°P»PµPiCÍC-CH, CĬPeP° C" PsP·PSP°PePsCĤ PiPsP±C-C†PSPēC... PjPsC,PsCĤPSPēC...
PµC„PµPeC,C-PI. PĥP° PIC-PrPjC-PSCr PIC-Pr C-PSC€PēC... P°PSC,PēPiCÍPēC...PsC,PēC†PSPēC...
P»C-PeP°CĤCÍCHPePēC... P·P°CÍPsP±C-PI, PsP»P°PSP·P°PiC-PS PiPsCÍPēP»CHC"
CĤPµP°PeC†C-C— PSP° PiPsPrCĤP°P·PSPēPePē PiCĤPē PiCĤPsPIPµPrPµPSPSC-
P°PSPeCÍC-PsP»C-C,PēC†PSPsPiPs C,PµCÍC,Cf.

PµCĤPē PsPrPSPsCĤP°P·PsPIPsPjCf PiPµCĤPsCĤP°P»CHPSPsPjCf PiCĤPēPN₂PsPjC- 10 PjPi
PsP»P°PSP·P°PiC-PSCr CÍ PiCĤPsC†PµCÍC- PiPsP·PēC,CĤPsPSPSPs-PµPjC-CÍC-PN₂PSPsC—
C,PsPjPsPiCĤP°C„C-C— (PµP·PŸ) P·P° CÍC†P°CÍC,C- P·PrPsCĤPsPIPēC...
PrPsP±CĤPsPIPsP»CHC†C-PI P·bĤ™ CĬCÍPsPIP°PSPs, C%Ps PsP»P°PSP·P°PiC-PS PjP°PI
P±C-P»CHC€PēPN₂ CĤC-PIPµPSCĤ P·PIbĤ™ CĬP·CfPIP°PSPSCĬ P· CĤPµC†PµPiC,PsCĤP°PjPē
5PĥPŸ2Pĥ, PSC-P¶ P· PrPsPíP°PjC-PSPsPIPēPjPē CĤPµC†PµPiC,PsCĤP°PjPē D2. PĥCĤC-Pj
C,PsPiPs, CÍ CĤPµP·CfP»CHC,P°C,C- P°PSP°P»C-P·Cf P·PsP±CĤP°P¶PµPSCĤ,
PsC,CĤPēPjP°PSPēC... PiC-Pr C†P°CÍ PrPsCÍP»C-PrP¶PµPSCĤ PiP°C†C-C"PSC,C-PI,
C...PIPsCĤPēC... PSP° C€PēP·PsC„CĤPµPSC-CH PjPµC,PsPrPsPj PsPrPSPsC„PsC,PsPSPSPsC—
PµPjC-CÍC-PN₂PSPsC— PePsPjPiPbĤ™ CHC,PµCĤPSPsC— C,PsPjPsPiCĤP°C„C-C— (PĥPαP·PĥPŸ),
P·bĤ™ CĬCÍCfPIP°P»PsCÍCĬ, C%Ps PsP»P°PSP·P°PiC-PSC†CfC,P»PēPIC- PiP°C†C-C"PSC,Pē
PIPēCĬPIP»CĬP»Pē PjPµPSC€PēPN₂ CĤC-PIPµPSCĤ P·PIbĤ™ CĬP·CfPIP°PSPSCĬ P·C-
CÍC,CĤC-P°CĤPSPēPjPē D2-CĤPµC†PµPiC,PsCĤP°PjPē, PSC-P¶ C-PSC€C-
P°PSC,PēPiCÍPēC...PsC,PēPe- C,P° CĤPµCÍPiC-CĤPēPrPsPSC†CfC,P»PēPIC- PiP°C†C-C"PSC,Pē,
PiPsCĤC-PIPsCĬPSPs P· PeP»PsP·P°PiC-PSC†CfC,P»PēPIPēPjPē PiP°C†C-C"PSC,P°PjPē.

PĥP»C-PSC-C†PSP° PµC„PµPeC,PēPIPsC-CÍC,CH

PµC-Pr C†P°CÍ PrPIPsC... C-P· PrPIPsC... PiP»P°C†PµP±Ps-PePsPSC,CĤPsP»CHPsPIP°PSPēC... C-
PrPIPsC... C-P· C,CĤCHPsC... PiPsCĤC-PIPsCĬP»CHPSPs-PePsPSC,CĤPsP»CHPsPIP°PSPēC...

PrPsCfP»C-PrP¶PµPSCĤ P·P° CřC‡P°CřC,C- PİPsPSP°Pr 2900 C...PIPsCĤPëC... PSP°
C€PëP·PsC,,CĤPµPSC-CĤ P· PİPsP·PëC,PëIPSPëPjPë C- PSPµPiP°C,PëIPSPëPjPë
CřPëPjPiC,PsPjP°PjPë PsP»P°PSP·P°PiC-PS PİPsPeP°P·P°PI CřC,P°C,PëCřC,PëC‡PSPs
PrPsCřC,PsPIC-CĤPSC- PrP°PSC- PİPsP»C-PİC€PµPSPSCİ CİPe PSPµPiP°C,PëIPSPëC..., C,P°Pe
C- PİPsP·PëC,PëIPSPëC... CřPëPjPiC,PsPjC-PI.

Pj PiCĤPsC†PµCřC- PjC-P¶PSP°CĤPsPrPSPëC... PİPsPrPIC-PMēPSPëC... CřP»C-PİPëC...
PİPsCĤC-PIPSCİP»CHPSPëC... PrPsCřP»C-PrP¶PµPSCĤ P· CřC‡P°CřC,CĤ 1484
C...PIPsCĤPëC... PSP° C€PëP·PsC,,CĤPµPSC-CĤ, C€PëP·PsP°C,,PµPeC,PëIPSC-CřC,CĤ C,P° P·
P°CřPsC†C-PMēPsPiP°PSPëPjPë P· C†PëPjPë C...PIPsCĤPsP±P°PjPë CĤPsP·P»P°PrP°PjPë P·
CĤC-P·PSPëPj CřC,CřPiPµPSPµPj PİPsCĤCřC€PµPSCĤ, C°Ps PİPsPiĤĤ™ CİP·P°PSC- P·
PrPµPiCĤPµCřPëIPSPëPjPë CřPëPjPiC,PsPjP°PjPë (16,6 PİCřPSPeC,P° P·P° C€PeP°P»PsCĤ
PĤPsPSC,PİPsPjPµCĤC--PĤCřP±PµCĤPiP° PrP»Cİ PsC†C-PSPePë PrPµPiCĤPµCřC-C—),
PiCĤPsCřPiPµPeC,PëIPSPµ PIC,PsCĤPëPSPSPµ PrPsCřP»C-PrP¶PµPSPSCİ PIC-Pr
PİPsC‡P°C,PeCř PrPs PeC-PSC†Cİ PsC†C-PSPePë P·PjC-PS PSP°CřC,CĤPsCĤ PrP°P»Ps P·PjPsPiCř
PICřC,P°PSPsPiPëC,Pë CřC,P°C,PëCřC,PëC‡PSPs P·PSP°C‡CřC°Pµ PİPsPeCĤP°C°PµPSPSCİ
B B B B B B B B (CĤ = 0,001) PiC-CřP»Cİ P»C-PeCřPiP°PSPSCİ PsP»P°PSP·P°PiC-PSPsPj (-6,0)
PİPsCĤC-PIPSCİPSPs P· C,P°PePëPj PiCĤPë P»C-PeCřPiP°PSPSC- PiP°P»PsPiPµCĤPëPrPsP»PsPj
(-3,1).

Pj PiP°C†C-C”PSC,C-PI P· PjP°PSC-P°PeP°P»CHPSPëPjPë P°P±Ps P·PjC-C€P°PSPëPjPë
PµPiC-P·PsPrP°PjPë PiCĤPë P±C-PİPsP»CİCĤPSPsPjCř CĤPsP·P»P°PrC- PsP»P°PSP·P°PiC-PS
PiCĤPsPrPµPjPsPSCřC,CĤCřPiP°PI PiPëCřPsPeCř PµC,,PµPeC,PëIPSC-CřC,CĤ Cř
P·PSPëP¶PµPSPSC- PjP°PSC-P°PeP°P»CHPSPëC... CřPëPjPiC,PsPjC-PI PiCĤPsC,CİPiPsPj 3
C,PëP¶PSC-PI PİPsCĤC-PIPSCİPSPs P· PiP»P°C†PµP±Ps C,P° PiP°P»CHPiCĤPsP°C,PsPj
PSP°C,CĤC-CĤ. PhP»P°PSP·P°PiC-PS C,P°PePsP¶ PİPsPeP°P·P°PI PİPsCĤC-PIPSCİPSPSCř
PµC,,PµPeC,PëIPSC-CřC,CĤ CĤPµP·CřP»CHC,P°C,C-PI P· PiP°P»PsPiPµCĤPëPrPsP»PsPj Cř
PiPµCĤPµCĤP°C...CřPiP°PSPSC- PSP° C‡P°CřC,PeCř PiP°C†C-C”PSC,C-PI P·C-
CřPëPjPiC,PsPjP°C,PëC‡PSPsCĤ CřC,P°PrC-C”CĤ CĤPµPjC-CřC-C—, PİPsC‡PëPSP°CĤC‡Pë P·
PjP°PSC-C— C,P° PrPµPiCĤPµCřC-C— PSP° 6 C- 12 C,PëP¶PSCİC... P»C-PeCřPiP°PSPSCİ. Pj
PiCĤPsC†PµCřC- PrPsCřP»C-PrP¶PµPSPSCİ PiC-Pr C‡P°Cř CřCřPiCřC,PSCHPsPiPs
P»C-PeCřPiP°PSPSCİ P»C-C,C-C”Pj P°P±Ps PiP°P»CHPiCĤPsP°C,PsPj PiCĤPsC,CİPiPsPj 2
C,PëP¶PSC-PI P· PrPsPrP°PiP°PSPSCİPj PsP»P°PSP·P°PiC-PSCř PI PrPsP·C- 10 PjPi
PICřC,P°PSPsPiP»PµPSPs P·PSP°C‡PSPµ P·PSPëP¶PµPSPSCİ CřPëPjPiC,PsPjC-PI PjP°PSC-C—
PİPsCĤC-PIPSCİPSPs P· C,P°PePëPj PiCĤPë PjPsPSPsC,PµCĤP°PiC-C— P»C-C,C-C”Pj P°P±Ps
PiP°P»CHPiCĤPsP°C,PsPj PiC-CřP»Cİ 6 C,PëP¶PSC-PI P»C-PeCřPiP°PSPSCİ.

Pj PiCĤPsC†PµCřC- 12-PjC-CřCİC‡PSPsPiPs PrPsCřP»C-PrP¶PµPSPSCİ
PiCĤPsC,,C-P»P°PeC,PëPePë CĤPµC†PëPrPëPIC-PI PjP°PSC-P°PeP°P»CHPSPëC...
PµPiC-P·PsPrC-PI Cř PiP°C†C-C”PSC,C-PI, CİPeC- PrPsCřCİPiP»Pë CĤPµPjC-CřC-C— P·P°
PrPsPiPsPjPsPiPsCĤ PsP»P°PSP·P°PiC-PSCř C- PI PİPsPrP°P»CHC€PsPjCř P±CřP»Pë
CĤP°PSPPrPsPjC-P·PsPiP°PSC- Cř PiCĤCřPiPë PiCĤPëPMēPsPjCř PsP»P°PSP·P°PiC-PSCř P°P±Ps
PiP»P°C†PµP±Ps, PsP»P°PSP·P°PiC-PS PiCĤPsPrPµPjPsPSCřC,CĤCřPiP°PI
CřC,P°C,PëCřC,PëC‡PSPs P·PSP°C‡CřC°Cř PiPµCĤPµPiP°PiCř PİPsCĤC-PIPSCİPSPs P·
PiP»P°C†PµP±Ps PI PeC-PSC†PµPIC-PMē C,PsC‡C†C- PeCĤPëC,PµCĤC-CĤ PsC†C-PSPePë
CĤPµC†PëPrPëPICř P±C-PİPsP»CİCĤPSPsPiPs CĤPsP·P»P°PrCř. PhP»P°PSP·P°PiC-PS C,P°PePsP¶
PİPsPeP°P·P°PI CřC,P°C,PëCřC,PëC‡PSPs P·PSP°C‡CřC°C- PiPµCĤPµPiP°PiPë PSP°Pr
PiP»P°C†PµP±Ps PI CĤP°PjPeP°C... P·P°PiPsP±C-PiP°PSPSCİ CĤPµC†PëPrPëPICř PjP°PSC-C—
P°P±Ps CĤPµC†PëPrPëPICř PrPµPiCĤPµCřC-C—.

Pj PiCĤPsC†PµCřC- PSP°CřC,CřPiPSPsPiPs 12-PjC-CřCİC‡PSPsPiPs PrPsCřP»C-PrP¶PµPSPSCİ
PiCĤPsC,,C-P»P°PeC,PëPePë CĤPµC†PëPrPëPIC-PI PjP°PSC-P°PeP°P»CHPSPëC...

$P_{\mu}P_{\bar{C}}-P \cdot P_sPrC-PI$ C_r $P_{\bar{P}}^{\circ}C^{\dagger}C-C''PSC, C-PI$, $C_{\bar{I}}PeC-$ $PrPsC^{\dagger}C_{\bar{I}}PiP \gg P_{\bar{e}} C_{\bar{H}}P_{\mu}P_jC-C^{\dagger}C-C-$ C_r
 $C_{\bar{H}}P_{\mu}P \cdot C_rP \gg CHC, P^{\circ}C, C-$ $C^{\dagger}C_rP_{\bar{C}}C_rC, PSC_{\bar{H}}PsPiPs$ $P \gg C-PeC_rPIP^{\circ}PSPSC_{\bar{I}} PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSPsP_j$
 $C, P^{\circ} P \gg C-C, C-C''P_j C-$ $P \cdot PiPsPrPsP_j P \pm C_rP \gg P_{\bar{e}} C_{\bar{H}}P^{\circ}PSP_rPsP_jC-P \cdot PsPIP^{\circ}PSC-$ C_r $P_{\bar{C}}C_{\bar{H}}C_rP_{\bar{I}}P_{\bar{e}}$
 $P_{\bar{C}}C_{\bar{H}}P_{\bar{e}}P_{\bar{N}}PsP_jC_r PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSC_r P^{\circ}P \pm Ps$ $P \gg C-C, C-C_{\bar{H}} PsPeC_{\bar{H}}P_{\mu}P_jPs$, $PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PS$
 $PSP_{\mu} P_jP^{\circ}PI$ $C^{\dagger}C, P^{\circ}C, P_{\bar{e}}C^{\dagger}C, P_{\bar{e}}C \pm PSPs$ $P \cdot PSP^{\circ}C \pm C_rC \% PsC-$ $P_{\bar{I}}P_{\mu}C_{\bar{H}}P_{\mu}PIP^{\circ}PiP_{\bar{e}} PSP^{\circ}Pr$
 $P \gg C-C, C-C''P_j C_r$ $PeC-PSC^{\dagger}P_{\mu}PIC-P_{\bar{N}} C, PsC \pm C^{\dagger}C-$ $PeC_{\bar{H}}P_{\bar{e}}C, P_{\mu}C_{\bar{H}}C-C_{\bar{H}} PsC^{\dagger}C-PSPeP_{\bar{e}}$
 $C_{\bar{H}}P_{\mu}C^{\dagger}P_{\bar{e}}PrP_{\bar{e}}PIC_r P \pm C-P_{\bar{I}}PsP \gg C_{\bar{I}}C_{\bar{H}}PSPsPiPs$ $C_{\bar{H}}PsP \cdot P \gg P^{\circ}PrC_r (PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PS$ 30% ,
 $P \gg C-C, C-P_{\bar{N}} 38,3 \%$, $C_{\bar{H}} = 0,055$).

$P_j P_{\bar{C}}C_{\bar{H}}PsC^{\dagger}P_{\mu}C^{\dagger}C-$ $18-P_jC-C^{\dagger}C_{\bar{I}}C \pm PSPsPiPs$ $PrPsC^{\dagger}P \gg C-PrP_{\bar{I}}P_{\mu}PSPSC_{\bar{I}} P_{\bar{C}}-Pr C \pm P^{\circ}C^{\dagger}$
 $C^{\dagger}C_rP_{\bar{C}}C_rC, PSC_{\bar{H}}PsPiPs$ $P \gg C-PeC_rPIP^{\circ}PSPSC_{\bar{I}} P_jP^{\circ}PSC-P^{\circ}PeP^{\circ}P \gg CH_PSP_{\bar{e}}C \dots P^{\circ}P \pm Ps$
 $P \cdot P_jC-C_{\bar{E}}P^{\circ}PSP_{\bar{e}}C \dots P_{\mu}P_{\bar{C}}-P \cdot PsPrC-PI$ $C^{\dagger}C, P^{\circ}PS$ $P_{\bar{P}}^{\circ}C^{\dagger}C-C''PSC, C-PI$
 $C^{\dagger}C, P^{\circ}P \pm C-P \gg C-P \cdot C_rPIP^{\circ}P \gg P_{\bar{e}} P \cdot P^{\circ} PrPsPiPsP_jPsPiPsC_{\bar{H}} PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSC_r$, $C_{\bar{I}}Pe$
 $C^{\dagger}C, P^{\circ}P \pm C-P \gg C-P \cdot P^{\circ}C, PsC_{\bar{H}} PSP^{\circ}C^{\dagger}C, C_{\bar{H}}PsC_{\bar{H}} P \cdot P^{\circ}C^{\dagger}C, PsC^{\dagger}PsPIC_rPIP^{\circ}P \gg P_{\bar{e}} P \gg C-C, C-P_{\bar{N}}$
 $P^{\circ}P \pm Ps$ $PIP^{\circ}P \gg CH_PiC_{\bar{H}}PsP^{\circ}C,;$ $PrPsPiPiPsC, C_{\bar{H}}P_{\bar{e}}PIP^{\circ}P \gg P_{\mu} C^{\dagger}C_rP_{\bar{C}}C_rC, PSC''$
 $P \gg C-PeC_rPIP^{\circ}PSPSC_{\bar{I}} PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSPsP_j P \cdot P \gg C-C, C-C''P_j P^{\circ}P \pm Ps$
 $PIP^{\circ}P \gg CH_PiC_{\bar{H}}PsP^{\circ}C, PsP_j PSP_{\mu} PIC^{\dagger}C, P^{\circ}PSPsPiP_{\bar{e}}P \gg Ps$ $C^{\dagger}C, P^{\circ}C, P_{\bar{e}}C^{\dagger}C, P_{\bar{e}}C \pm PSPs$
 $P \cdot PSP^{\circ}C \pm C_rC \% PsC-$ $P_{\bar{I}}P_{\mu}C_{\bar{H}}P_{\mu}PIP^{\circ}PiP_{\bar{e}} PSP^{\circ}Pr$ $P_jPsPSPsC, P_{\mu}C_{\bar{H}}P^{\circ}P_{\bar{C}}-C''C_{\bar{H}} P \gg C-C, C-C''P_j$
 $P^{\circ}P \pm Ps$ $PIP^{\circ}P \gg CH_PiC_{\bar{H}}PsP^{\circ}C, PsP_j C-$ $PIC-PrC^{\dagger}C, C_{\bar{H}}PsC \pm P_{\mu}PSPSC_{\bar{I}} C_{\bar{H}}P_{\mu}C^{\dagger}P_{\bar{e}}PrP_{\bar{e}}PIC-PI$
 $P \pm C-P_{\bar{I}}PsP \gg C_{\bar{I}}C_{\bar{H}}PSP_{\bar{e}}C \dots C_{\bar{H}}PsP \cdot P \gg P^{\circ}PrC-PI$, $PIP_{\bar{e}}P \cdot PSP^{\circ}C \pm P_{\mu}PSP_{\bar{e}}C \dots PIC-PrPiPsPIC-PrPSPs$
 $PrPs$ $C^{\dagger}P_{\bar{e}}PSP_rC_{\bar{H}}PsP_jPSPsPiPs (PrC-P^{\circ}PiPSPsC^{\dagger}C, P_{\bar{e}}C \pm PSPsPiPs) PeC_{\bar{H}}P_{\bar{e}}C, P_{\mu}C_{\bar{H}}C-C_{\bar{H}}$.

P''C-C, P_e

$P''PsC^{\dagger}PIC-Pr P \cdot P^{\circ}C^{\dagger}C, PsC^{\dagger}C_rPIP^{\circ}PSPSC_{\bar{I}} P \gg C-PeP^{\circ}C_{\bar{H}}C^{\dagger}CH_PePsPiPs$ $P \cdot P^{\circ}C^{\dagger}PsP \pm C_r$
 $P_{\bar{C}}-PrP \gg C-C, PeP^{\circ}P_j (PIC-PePsP_j PIC-Pr$ $13 PrPs$ $17 C_{\bar{H}}PsPeC-PI)$ $PsP \pm P_jP_{\mu}P_{\bar{I}}P_{\mu}PSP_{\bar{e}}P_{\bar{N}}$
 $PIC-PrPiPsPIC-PrPSPs$ $PrPs$ $PsC, C_{\bar{H}}P_{\bar{e}}P_jP^{\circ}PSP_{\bar{e}}C \dots PrP^{\circ}PSP_{\bar{e}}C \dots C \% PsPrPs$
 $P_{\mu}C, P_{\mu}PeC, P_{\bar{e}}PIPSPsC^{\dagger}C, C-$ $PePsC_{\bar{H}}PsC, PePsC, C_{\bar{H}}P_{\bar{e}}PIP^{\circ}P \gg PsPiPs$ $P \gg C-PeC_rPIP^{\circ}PSPSC_{\bar{I}}$
 $C_{\bar{E}}P_{\bar{e}}P \cdot PsC, C_{\bar{H}}P_{\mu}PSC-C-$ $(6 C, P_{\bar{e}}P_{\bar{I}}PSC-PI)$ $C, P^{\circ} P_jP^{\circ}PSC-C-$, $P_{\bar{I}}PsPi_{\bar{b}}C_{\bar{H}}^{\text{TM}} C_{\bar{I}}P \cdot P^{\circ}PSPsC-$ $P \cdot$
 $P \pm C-P_{\bar{I}}PsP \gg C_{\bar{I}}C_{\bar{H}}PSP_{\bar{e}}P_jP_{\bar{e}} C_{\bar{H}}PsP \cdot P \gg P^{\circ}PrP^{\circ}P_jP_{\bar{e}} (3 C, P_{\bar{e}}P_{\bar{I}}PSC-), P \cdot P^{\circ} C_rC \pm P^{\circ}C^{\dagger}C, C-$ $P_jP_{\mu}PSC_{\bar{E}}$
 $PSC-P_{\bar{I}} 200 P_{\bar{C}}-PrP \gg C-C, PeC-PI$. $P_{\mu}PsC \pm P^{\circ}C, PePsPIP^{\circ} PrPsP \cdot P^{\circ} PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSC_r$
 $C^{\dagger}C, P^{\circ}PSPsPiP_{\bar{e}}P \gg P^{\circ} 2,5 P_jPi C, P^{\circ} PrPsC^{\dagger}C_{\bar{I}}PiP^{\circ}P \gg P^{\circ} 20 P_jPi PSP^{\circ} PrPsP \pm C_r$. $P_{\mu}C-Pr C \pm P^{\circ}C^{\dagger}$
 $P \gg C-PeC_rPIP^{\circ}PSPSC_{\bar{I}} PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSPsP_j P_jP^{\circ}C^{\dagger}P^{\circ} C, C-P \gg P^{\circ} C_r P_{\bar{C}}-PrP \gg C-C, PeC-PI$
 $P \cdot PSP^{\circ}C \pm PSPs P \cdot P \pm C-P \gg CH_C_{\bar{E}}P_{\bar{e}}P \gg P^{\circ}C^{\dagger}C_{\bar{I}} P_{\bar{I}}PsC_{\bar{H}}C-PIPSC_{\bar{I}}PSPs P \cdot PrPsC_{\bar{H}}PsC^{\dagger}P \gg P_{\bar{e}}P_jP_{\bar{e}}$. P_j
 $P_{\bar{C}}-PrP \gg C-C, PeC-PI$ $C^{\dagger}PiPsC^{\dagger}C, P_{\mu}C_{\bar{H}}C-PiP^{\circ}P \gg PsC^{\dagger}C_{\bar{I}} P_{\bar{C}}-PrPiP_{\bar{e}}C \% P_{\mu}PSPSC_{\bar{I}} C_{\bar{H}}C-PIPSC_{\bar{I}}$
 $P \cdot P^{\circ}PiP^{\circ}P \gg CH_PSPsPiPs C \dots PsP \gg P_{\mu}C^{\dagger}C, P_{\mu}C_{\bar{H}}P_{\bar{e}}PSC_r, C \dots PsP \gg P_{\mu}C^{\dagger}C, P_{\mu}C_{\bar{H}}P_{\bar{e}}PSC_r$
 $P \gg C-P_{\bar{I}}PsPiC_{\bar{H}}PsC, P_{\mu}C-PSC-PI$ $PSP_{\bar{e}}P \cdot CH_PePsC-$ $C \% C-P \gg CH_PSPsC^{\dagger}C, C-$,
 $C, C_{\bar{H}}P_{\bar{e}}PiP \gg C-C^{\dagger}P_{\mu}C_{\bar{H}}P_{\bar{e}}PrC-PI$ $C, P^{\circ} P_{\bar{C}}C_{\bar{H}}PsP \gg P^{\circ}PeC, P_{\bar{e}}PSC_r P_{\bar{I}}PsC_{\bar{H}}C-PIPSC_{\bar{I}}PSPs P \cdot$
 $PrPsC_{\bar{H}}PsC^{\dagger}P \gg P_{\bar{e}}P_jP_{\bar{e}}$. $P''P^{\circ}PSC-$ $C \% PsPrPs$ $P_{\bar{C}}-PrC, C_{\bar{H}}P_{\bar{e}}P_jP^{\circ}PSPSC_{\bar{I}} P_{\mu}C, P_{\mu}PeC, C_r$
 $P \gg C-PeC_rPIP^{\circ}PSPSC_{\bar{I}} C, P^{\circ} PrPsPiPiPsC, C_{\bar{H}}P_{\bar{e}}PIP^{\circ}P \gg P_{\bar{e}}C \dots PrPsC^{\dagger}P \gg C-PrP_{\bar{I}}P_{\mu}PSC_{\bar{H}}$,
 $PsPrP_{\mu}C_{\bar{H}}P_{\bar{I}}P^{\circ}PSC-$ $P \cdot PIC-PrPeC_{\bar{H}}P_{\bar{e}}C, P_{\bar{e}}C \dots PSP_{\mu}PePsPSC, C_{\bar{H}}PsP \gg CH_PsPiP^{\circ}PSP_{\bar{e}}C \dots$
 $PeP \gg C-PSC-C \pm PSP_{\bar{e}}C \dots PrPsC^{\dagger}P \gg C-PrP_{\bar{I}}P_{\mu}PSC_{\bar{H}}$, $PsP \pm P_jP_{\mu}P_{\bar{I}}P_{\mu}PSC-$.

P_αP^oC_HP_jP^oPePsPeC-PSP_μC, P_ePeP^o.

$P_{\bar{H}}P \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PS$ $C_r C, PsC_{\bar{H}}P_jC-$ $C, P^{\circ}P \pm P \gg P_{\mu}C, PsPe$, $C \% Ps$ $PrP_{\bar{e}}C^{\dagger}PiP_{\mu}C_{\bar{H}}PiC_rC_{\bar{H}}C, CH_C^{\dagger}C_{\bar{I}}$
 $C_r C_{\bar{H}}PsC, PsPIC-P_{\bar{N}}$ $P_{\bar{I}}PsC_{\bar{H}}PsP_{\bar{I}}PSP_{\bar{e}}PSC-$, $P \pm C-PsP_{\mu}PePIC-PIP^{\circ}P \gg P_{\mu}PSC, PSP_{\bar{e}}P_{\bar{N}}$ $C \% PsPrPs$
 $PsP \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PSC_r C_r C, PsC_{\bar{H}}P_jC-$ $C, P^{\circ}P \pm P \gg P_{\mu}C, PsPe$, $PIPeC_{\bar{H}}P_{\bar{e}}C, P_{\bar{e}}C \dots$
 $PsP \pm PsP \gg PsPSPePsC_{\bar{H}}$, $C_{\bar{I}}PeC-$ $PrP_{\mu}P_jPsPSC^{\dagger}C, C_{\bar{H}}C_rC_{\bar{H}}C, CH_C C^{\dagger}C \dots PsP_{\bar{I}}C_r$
 $C_{\bar{E}}PiP_{\bar{e}}PrPeC-C^{\dagger}C, CH_C C, P^{\circ} C^{\dagger}C, C_rPiC-PSC_{\bar{H}} P^{\circ}P \pm C^{\dagger}PsC_{\bar{H}}P \pm C^{\dagger}C-C-$. $P_{\bar{H}}P \gg P^{\circ}PSP \cdot P^{\circ}P_{\bar{C}}-PS$ C_r
 $C, PsC_{\bar{H}}P_jC-$ $C, P^{\circ}P \pm P \gg P_{\mu}C, PsPe$, $C \% Ps$ $PrP_{\bar{e}}C^{\dagger}PiP_{\mu}C_{\bar{H}}PiC_rC_{\bar{H}}C, CH_C^{\dagger}C_{\bar{I}}$ $C_r C_{\bar{H}}PsC, PsPIC-P_{\bar{N}}$
 $P_{\bar{I}}PsC_{\bar{H}}PsP_{\bar{I}}PSP_{\bar{e}}PSC-$, $P_jPsP_{\bar{I}}P_{\mu} P \cdot P^{\circ}C^{\dagger}C, PsC^{\dagger}PsPIC_rPIP^{\circ}C, P_{\bar{e}}C^{\dagger}C_{\bar{I}} C_{\bar{I}}Pe$

P°P»CHC,PμCḡPSP°C,PëPIP° PsP»P°PSP·P°PīC-PSCr Cr C,,PsCḡPjC- C,P°P±P»PμC,PsPe,
PIPeCḡPëC,PëC... PsP±PsP»PsPSPePsCḡ.

PḡP±CḡPsCḡP±C†C-Cḡ

PμCḡPμPīP°CḡP°C, PrPsP±CḡPμ PICḡPjPsPeC,CrC''C,CHCḡCḡ PīC-CḡP»Cḡ
PīPμCḡPsCḡP°P»CHPSPsPiPs PīCḡPëPμPsPjCr, PμPsPiPs PjP°PeCḡPëPjP°P»CHPSP°
PePsPSC†PμPSC,CḡP°C†C-Cḡ (C_{max}) Cr PīP»P°P·PjC- PeCḡPsPIC- PrPsCḡCḡPīP°C''C,CHCḡCḡ
C†PμCḡPμP· 5-8 PiPsPrPëPS. P°PḡPëPIP°PSPSCḡ C-PḡC- PSPμ PIPiP»PëPIP°C'' PSP°
PICḡPjPsPeC,CrPIP°PSPSCḡ PsP»P°PSP·P°PīC-PSCr. PḡP±CḡPsP»CḡC,PSP°
P±C-PsPrPsCḡC,CrPīPSC-CḡC,CH PīPμCḡPsCḡP°P»CHPSPsC— C,,PsCḡPjPë PīCḡPëPμPsPjCr
PsP»P°PSP·P°PīC-PSCr PīPsCḡC-PIPSCḡPSPs P· PIPSCrC,CḡC-CḡPSCḡPsPIPμPSPSPsCḡ PSPμ
PICḡC,P°PSPsPIP»PμPSP°.

P PsP·PīPsPrC-P»

P C-PIPμPSCḡ P·PīBḡ™ CḡP·CrPIP°PSPSCḡ PsP»P°PSP·P°PīC-PSCr P· PīCḡPsC,PμC—PSP°PjPë
PīP»P°P·PjPë PeCḡPsPIC- CḡC,P°PSPsPIPëPI PīCḡPëP±P»PëP·PSPs 93 % PrP»Cḡ
PePsPSC†PμPSC,CḡP°C†C-C— Cr PjPμPḡP°C... PIC-Pr 7 PrPs 1000 PSPi/PjP». PhP»P°PSP·P°PīC-PS
P·PīBḡ™ CḡP·CrC''C,CHCḡCḡ PīPμCḡPμPIP°PḡPSPs P· P°P»CHP±CḡPjC-PSPsPj C- α1-
PePëCḡP»PëPj PīP»C-PePsPīCḡPsC,PμC—PSPsPj.

P'C-PsC,CḡP°PSCḡC,,PsCḡPjP°C†C-Cḡ

PhP»P°PSP·P°PīC-PS PjPμC,P°P±PsP»C-P·CrC''C,CHCḡCḡ Cr PīPμC†C-PSC†C- CḡP»CḡC...PsPj
PePsPSCḡ™ CḡPīP°C†C-C— C,P° PsPePëCḡPSPμPSPSCḡ. PhCḡPSPsPIPSPëPj
PjPμC,P°P±PsP»C-C,PsPj, C%Ps C†PëCḡPeCḡP»CḡC'', C'' 10-N-PiP»CḡPeCḡPsPSC-Pr,
CḡPePëPμ PSPμ PīCḡPsC...PsPrPëC,CH PeCḡC-P·CH PīPμPjP°C,PsPμPSC†PμC,,P°P»C-C†PSPëPμ
P±P°CḡBḡ™ C''Cḡ. PīPëC,PsC...CḡPsPjPë P450-CYP1A2 C- P450-CYP2D6 CḡPīCḡPëCḡCḡC,CH
C,,PsCḡPjCrPIP°PSPSCḡ PjPμC,P°P±PsP»C-C,C-PI N-PrPμP·PjPμC,PëP»Cr C- 2-
PiC-PrCḡPsPeCḡPëPjPμC,PëP»Cr, CḡPeC- PīCḡPsCḡPIP»CḡCḡC,CH P·PSP°C†PSPs PjPμPSCḡCr
C,,P°CḡPjP°PePsP»PsPiC-C†PSCr P°PeC,PëPIPSC-CḡC,CH *in vivo*, PSC-Pḡ PsP»P°PSP·P°PīC-PS,
Cr PīCḡPsC†PμCḡC- PrPsCḡP»C-PrPḡPμPSCḡ PSP° C,PIP°CḡPëPSP°C....
PμPμCḡPμPIP°PḡP°CḡC†P° C,,P°CḡPjP°PePsP»PsPiC-C†PSP° P°PeC,PëPIPSC-CḡC,CH
P·CrPjPsPIP»PμPSP° PīPμCḡPIPëPSPSPëPj PsP»P°PSP·P°PīC-PSPsPj.

P'PëPIPμPrPμPSPSCḡ

PμC-CḡP»Cḡ PīPμCḡPsCḡP°P»CHPSPsPiPs P·P°CḡC,PsCḡCrPIP°PSPSCḡ CḡPμCḡPμPrPSC-Pμ
PīPμCḡC-PsPr PSP°PīC-PIPIPëPIPμPrPμPSPSCḡ PsP»P°PSP·P°PīC-PSCr Cr
PrPsP±CḡPsPIPsP»CHC†C-PI PePsP»PëPIP°PICḡCḡ P·P°P»PμPḡPSPs PIC-Pr PIC-PeCr C,P°
CḡC,P°C,C-.

Pj P·PrPsCḡPsPIPëC... PrPsP±CḡPsPIPsP»CHC†C-PI P»C-C,PSCHPsPiPs PIC-PeCr (PIC-PePsPj
PIC-Pr 65 CḡPsPeC-PI) PīPsCḡC-PIPSCḡPSPs P· PjPsP»PsPrCḡPëPjPë P·P° PIC-PePsPj
PrPsP±CḡPsPIPsP»CHC†CḡPjPë CḡPμCḡPμPrPSC-Pμ PīPμCḡC-PsPr
PSP°PīC-PIPIPëPIPμPrPμPSPSCḡ P±CrPI C,CḡPëPIP°P»C-CḡPëPμ (51,8 PīCḡPsC,Pë 33,8
PiPsPrPëPSPë), PeP»C-CḡPμPSCḡ Cr PīP»P°P·PjC- PeCḡPsPIC- P±CrPI P·PSPëPḡPμPSPëPμ (17,5
PīCḡPsC,Pë 18,2 P»/PiPsPr PIC-PrPīPsPIC-PrPSPs). P°P°CḡPjP°PePsPeC-PSPμC,PëC†PSC-
PePsP»PëPIP°PSPSCḡ, C%Ps CḡPīPsCḡC,PμCḡC-PiP°P»PëCḡCḡ Cr PrPsP±CḡPsPIPsP»CHC†C-PI
P»C-C,PSCHPsPiPs PIC-PeCr, P·PSP°C...PsPrCḡC,CHCḡCḡ Cr PjPμPḡP°C... PrC-P°PīP°P·PsPSCr
PrP»Cḡ PjPsP»PsPrCḡPëC... PrPsP±CḡPsPIPsP»CHC†C-PI. Pj 44 C...PIPSCḡPëC... PSP°

C€PëP·PsC,,CḡPμPSC-Cḡ PIC-PePsPj PIC-Pr 65 CḡPsPeC-PI PrPsP·CfPIP°PSPSCḡ PIC-Pr 5 PrPs
20 PjPi PSP° PrPsP±Cf PSPμ P±CfP»Ps PİPsPIBḡ™ CḡP·P°PSPs P· PḡPsPrPSPëPj
C...P°CḡP°PeC,PμCḡPSPëPj PİCḡPsC,,C-P»PμPj PİPsP±C-CfPSPëC... CḡPμP°PeC†C-PNë.

PJ PḡC-PSPsPe PİPsCḡC-PIPSCḡPSPs P· CfPsP»PsPIC-PeP°PjPë CḡPμCḡPμPrPSC-PNë
PİPμCḡC-PsPr PSP°PİC-PIIPëPIPμPrPμPSPSCḡ P±CfPI C,CḡPëPIP°P»C-C€PëPNë (36,7
PİCḡPsC,Pë 32,3 PİPsPrPëPSPë) C,P° PeP»C-CḡPμPSCḡ Cḡ PİP»P°P·PjC- PeCḡPsPIC- P±CfPI
P·PSPëPḡPμPSPëPNë (18,9 PİCḡPsC,Pë 27,3 P»/PİPsPr). PhPrPSP°Pe PsP»P°PSP·P°PİC-PS (5-20
PjPi) PİPsPeP°P·P°PI PİPsCḡC-PIPSCḡPSPSPëPNë PİCḡPsC,,C-P»CH P±PμP·PİPμPePë CḡPe Cḡ
PḡC-PSPsPe (n = 467), C,P°Pe C- Cḡ CfPsP»PsPIC-PeC-PI (n = 869).

PμP°C†C-C°PSC,Pë P· PSPëCḡPePsPIPsCḡ PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ

PJ PİP°C†C-C°PSC,C-PI P· PSPëCḡPePsPIPsCḡ PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ (PeP»C-CḡPμPSCḡ
PeCḡPμP°C,PëPSC-PSCḡ < 10 PjP»/C...PI) PİPsCḡC-PIPSCḡPSPs P·C- P·PrPsCḡPsPIPëPjPë
PrPsP±CḡPsPIPsP»CHC†CḡPjPë PSPμ P±CfP»Ps C-CḡC,PsC,PSPsC— CḡC-P·PSPëC†C- Cḡ
PİPsPeP°P·PSPëPeP°C... CḡPμCḡPμPrPSCḡPsPİPs PİPμCḡC-PsPrCḡ
PSP°PİC-PIIPëPIPμPrPμPSPSCḡ (37,7 PİCḡPsC,Pë 32,4 PİPsPrPëPSPë) P°P±Ps
PeP»C-CḡPμPSCḡCḡ Cḡ PİP»P°P·PjC- PeCḡPsPIC- (21,2 PİCḡPsC,Pë 25,0 P»/PİPsPr).
P°PsCḡP»C-PrPḡPμPSPSCḡ PİPsPeP°P·P°P»Pë, C%Ps PİCḡPëP±P»PëP·PSPs 57 %
PsP»P°PSP·P°PİC-PSCḡ P· CḡP°PrC-PsP°PeC,PëPIPsCḡ PjC-C,PePsCḡ PSP°CḡPIPSC- PI
CḡPμC†C-, PİPsP»PsPIPsPëPj CfPëPSPsPj Cḡ PİPëPİP»CḡPrC- PjPμC,P°P±PsP»C-C,PI.

PμPsCḡCžC€PμPSPSCḡ C,,CžPSPeC†C-C— PİPμC†C-PSPePë

PJ PİCḡPsC†PμCḡC- PSPμPIPμP»PëPePsPİPs PrPsCḡP»C-PrPḡPμPSPSCḡ PİPİP»PëPICḡ
PİPsCḡCḡC€PμPSPSCḡ C,,CḡPSPeC†C-C— PİPμC†C-PSPePë Cḡ 6 PİP°C†C-C°PSC,C-PI C-P·
PeP»C-PSC-CfPSPs P·PSP°C†CḡC%PëPj (PeP»P°CḡPëC,,C-PeP°C†C-Cḡ PŠP°PNëP»PrP°-PμBḡ™ Cḡ
A (n = 5) C- B (n = 1)) C†PëCḡPsP·PsPj PİPëCḡPIP»PμPSPs PSPμP·PSP°CfPSPëPNë PİPİP»PëPI
PSP° C,,P°CḡPjP°PePsPeC-PSPμC,PëPeCḡ PİPμCḡPsCḡP»P»CHPSPsPİPs PsP»P°PSP·P°PİC-PSCḡ
(2,5Bḡ™7,5 PjPi), CḡP°P·PsPIP° PrPsP·P°): PİP°C†C-C°PSC,Pë P· P»PμPİPePsCḡ C,P°
PİPsPjC-CḡPSPsCḡ PrPëCḡC,,CḡPSPeC†C-C°Cḡ PİPμC†C-PSPePë PjP°P»Pë PrPμC%Ps
PİC-PrPIPëC%PμPSPëPNë CḡPëCḡC,PμPjPSPëPNë PeP»C-CḡPμPSCḡ C- C€PIPëPrC€PëPNë
PİPμCḡC-PsPr PSP°PİC-PIIPëPIPμPrPμPSPSCḡ PİPsCḡC-PIPSCḡPSPs P· PİP°C†C-C°PSC,P°PjPë
P±PμP· PİPμC†C-PSPePsPIPsC— PrPëCḡC,,CḡPSPeC†C-C— (n = 3). PŸPμCḡPμPr
PİP°C†C-C°PSC,C-PI C-P· C†PëCḡPsP·PsPj P±CfP»Ps P±C-P»CHC€Pμ PeCḡCḡC†C-PI (4/6; 67 %),
PSC-Pḡ CḡPμCḡPμPr PİP°C†C-C°PSC,C-PI P±PμP· PİPsCḡCḡC€PμPSPSCḡ C,,CḡPSPeC†C-C—
PİPμC†C-PSPePë (0/3; 0 %).

PμP°C†C-C°PSC,Pë, CḡPeC- PİP°P»CḡC,CH

PJ PSPμPeCḡCḡC†C-PI PİPsCḡC-PIPSCḡPSPs P· PeCḡCḡC†CḡPjPë (CfPsP»PsPIC-PePë C,P°
PḡC-PSPePë) CḡPμCḡPμPrPSC-PNë PİPμCḡC-PsPr PSP°PİC-PIIPëPIPμPrPμPSPSCḡ P±CfPI
C,CḡPëPIP°P»C-C€PëPNë (38,6 PİCḡPsC,Pë 30,4 PİPsPrPëPSPë), P° PeP»C-CḡPμPSCḡ Cḡ
PİP»P°P·PjC- PeCḡPsPIC- P±CfPI P·PSPëPḡPμPSPëPNë (18,6 PİCḡPsC,Pë B B B B B 27,7 P»/PİPsPr).

PḡP»C-CḡPμPSCḡ PsP»P°PSP·P°PİC-PSCḡ Cḡ PİP»P°P·PjC- PeCḡPsPIC- PSPëPḡCfPëPNë Cḡ
PİP°C†C-C°PSC,C-PI P»C-C,PSCHPsPİPs PIC-PeCḡ PİPsCḡC-PIPSCḡPSPs P· PjPsP»PsPrC€PëPjPë
PİP°C†C-C°PSC,P°PjPë, Cḡ PḡC-PSPsPe PİPsCḡC-PIPSCḡPSPs P· CfPsP»PsPIC-PeP°PjPë C,P° Cḡ
PSPμPeCḡCḡC†C-PI PİPsCḡC-PIPSCḡPSPs P· PeCḡCḡC†CḡPjPë. P† PICḡPμ Pḡ C,P°PeC-
C,,P°PeC,PsCḡPë CḡPe PIC-Pe, CḡC,P°C,CH C,P° PİP°P»C-PSPSCḡ PjP°P»Ps PjPsPḡCḡC,CH
PİPİP»PëPIP°C,Pë PSP° PeP»C-CḡPμPSCḡ PsP»P°PSP·P°PİC-PSCḡ Cḡ PİP»P°P·PjC- PeCḡPsPIC-

C,P° PīPμCḡC-PsPr PSP°PīC-PIPIēPIPμPrPμPSPSCḡ PīPsCḡC-PIPCḡPSPs C-P·
P·P°PīP°P»CH̄PSPsCḡ PjC-PSP»PēPIC-CḡC,Cḡ PjC-Pḡ C-PSPrPēPIC-PrCrCrPjP°PjPē.

PJ PīCḡPsC†PμCḡC- PrPsCḡP»C-PrPḡPμPSCḡ P· CrC†P°CḡC,Cḡ PīP°C†C-C”PSC,C-PI-
C”PICḡPsPīPμPNēC†C-PI, PīP°C†C-C”PSC,C-PI CḡPīPsPSCḡCḡPePsC— C,P°
PePēC,P°PNēCḡCḡPePsC— PSP°C†C-PsPSP°P»CH̄PSPsCḡC,PμPNē PIC-PrPjC-PSPSPsCḡC,PμPNē Cr
C,,P°CḡPjP°PePsPeC-PSPμC,PēC†C- PsP»P°PSP·P°PīC-PSCḡ PSPμ PIPēCḡPIIP»PμPSPs.

PμC-PrP»C-C,PePē C- PrPsCḡPsCḡP»C-

PαP°CḡPjP°PePsPeC-PSPμC,PēPeP° PsP»P°PSP·P°PīC-PSCḡ Cr PīC-PrP»C-C,PeC-PI C-
PrPsCḡPsCḡP»PēC... PīPsPrC-P±PSP°. PJ PīCḡPsC†PμCḡC- PeP»C-PSC-C†PSPēC...
PrPsCḡP»C-PrPḡPμPSCḡ CḡPμCḡPμPrPSC-PNē PIPīP»PēPI PsP»P°PSP·P°PīC-PSCḡ P±CrPI
PīCḡPēP±P»PēP·PSPs PSP° 27 % PIPēC%PēPNē Cr PīC-PrP»C-C,PeC-PI, PSC-Pḡ Cr
PrPsCḡPsCḡP»PēC... PīP°C†C-C”PSC,C-PI. P”PμPjPsPīCḡP°C,,C-C†PSC- PIC-PrPjC-PSPSPsCḡC,C-
PjC-Pḡ PīC-PrP»C-C,PeP°PjPē C- PrPsCḡPsCḡP»PēPjPē PIPeP»CḡC†P°CḡC,Cḡ PSPēPḡC†Cr
CḡPμCḡPμPrPSCḡ PjP°CḡCr C,C-P»P° C,P° PjPμPSCḡCr PeC-P»CH̄PeC-CḡC,Cḡ PeCrCḡC†C-PI
CḡPμCḡPμPr PīP°C†C-C”PSC,C-PI PīC-PrP»C-C,PePsPIPsiPs PIC-PeCr. PḡP°PeC-
C,,P°PeC,PsCḡPē, C-PjPsPIC-CḡPSPs, PIPīP»PēPIP°CḡC,Cḡ PSP° PIPēC%PēPNē
CḡPμCḡPμPrPSC-PNē PμC,,PμPeC, PsP»P°PSP·P°PīC-PSCḡ, C%Ps CḡPīPsCḡC,PμCḡC-PiP°PICḡCḡ
Cr PīC-PrP»C-C,PeC-PI.

РљР»С-РSC-С†РSC- С...Р°СḡР°РeC,РμCḡPēCḡC,PēPePē.

PμPsPeP°P·P°PSPSCḡ.

PḡP»P°PSP·P°PīC-PS PīPsPeP°P·P°PSPēPNē PrP»Cḡ P»C-PeCrPIP°PSPSCḡ
CḡPēP·PsC,,CḡPμPSC-C—.

PḡP»P°PSP·P°PīC-PS PμC,,PμPeC,PēPIPSPēPNē PrP»Cḡ PīC-PrC,CḡPēPjP°PSPSCḡ
PrPsCḡCḡPIPSCrC,PsPiPs PeP»C-PSC-C†PSPsPiPs PμC,,PμPeC,Cr PīC-Pr C†P°Cḡ
C,CḡPēPIP°P»PsC— C,PμCḡP°PīC-C— Cr PīP°C†C-C”PSC,C-PI, Cr CḡPePēC...
CḡPīPsCḡC,PμCḡC-PiP°P»P°CḡCḡ PIC-PrPīPsPIC-PrCH̄ PSP° PīPsC†P°C,PePsPICḡ
C,PμCḡP°PīC-Cḡ.

PḡP»P°PSP·P°PīC-PS PīPsPeP°P·P°PSPēPNē PrP»Cḡ P»C-PeCrPIP°PSPSCḡ
PjP°PSC-P°PeP°P»CH̄PSPēC... PμPīC-P·PsPrC-PI PīPsPjC-CḡPSPsPiPs C,P° C,CḡPḡPePsPiPs
CḡC,CrPīPμPSCḡ.

PḡP»P°PSP·P°PīC-PS PīPsPeP°P·P°PSPēPNē PrP»Cḡ PīCḡPsC,,C-P»P°PeC,PēPePē
PīPsPIC,PsCḡPSPēC... PSP°PīP°PrC-PI Cr PīP°C†C-C”PSC,C-PI P· P±C-PīPsP»CḡCḡPSPēPjPē
CḡPsP·P»P°PrP°PjPē, Cr CḡPePēC... P±CrP»Ps PsC,CḡPēPjP°PSPs PīPsP·PēC,PēPIPSCr
PIC-PrPīPsPIC-PrCH̄ PīCḡPē P»C-PeCrPIP°PSPSC- PsP»P°PSP·P°PīC-PSPsPj PjP°PSC-C—.

PμCḡPsC,PēPīPsPeP°P·P°PSPSCḡ.

PμC-PrPIPēC%PμPSP° C†CrC,P»PēPIC-CḡC,Cḡ PrPs PrC-CḡC†PsC— CḡPμC†PsPIPēPSPē P°P±Ps
PrPs PrPsPīPsPjC-PḡPSPēC... PePsPjPīPsPSPμPSC,C-PI PīCḡPμPīP°CḡP°C,Cr; PIC-PrPsPjPēPNē
CḡPēP·PēPe P·P°PeCḡPēC,PsPeCrC,PsPIPsC— PiP»P°CrPePsPjPē.

P'P·P°C''PjPsPrC-CI P·C-PSC€PëPjPë P»C-PeP°CĤCÍCHPePëPjPë P·P°CÍPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C''PjPsPrC-PN.

P''PsCÍP»C-PrP¶PµPSPSCİ PIP·P°C''PjPsPrC-C— P·C-PSC€PëPjPë P»C-PeP°CĤCÍCHPePëPjPë P·P°CÍPsP±P°PjPë PİCĤPsPIPsPrPëP»Pë C,C-P»CHPePë P·CÍC±P°CÍC,CĤ PrPsCĤPsCÍP»PëC....

P'P·P°C''PjPsPrC-C—, C%Ps PjP°CĤC,CĤ PİPsC,PµPSC†C-PN.PSPëPN PIPİP»PëPI PSP° PsP»P°PSP·P°PİC-PS

PĥCÍPeC-P»CHPePë PsP»P°PSP·P°PİC-PS PjPµC,P°P±PsP»C-P·CÍC''C,CĤCÍCİ C-P·PsC,,PµCĤPjPµPSC,PsPj CYP1A2, CĤPµC±PsPIPëPSPë, CİPeC- CÍPİPµC†PëC,,C-C±PSPs C-PSPrCÍPeCÍCĤC,CĤCÍCİ P°P±Ps C-PSPiC-P±CÍCĤC,CĤCÍCİ C†PëPj C-P·PsC,,PµCĤPjPµPSC,PsPj, PjPsP¶CÍC,CĤ PIPİP»PëPIP°C,Pë PSP° C,,P°CĤPjP°PePsPeC-PSPµC,PëPeCÍ PsP»P°PSP·P°PİC-PSCÍ.

P†PSPrCÍPeC,PsCĤPë CYP1A2

PĥPµC,P°P±PsP»C-P·Pj PsP»P°PSP·P°PİC-PSCÍ PjPsP¶Pµ P±CÍC,Pë C-PSPrCÍPePsPIP°PSPëPN PİP°P»C-PSPSCİPj C,P° P·P°CÍC,PsCÍCÍPIP°PSPSCİPj PeP°CĤP±P°PjP°P·PµPİC-PSCÍ, CİPePëPN PİCĤPëP·PIPsPrPëC,CĤ PrPs P·PSPëP¶PµPSPSCİ PePsPSC†PµPSC,CĤP°C†C-C— PsP»P°PSP·P°PİC-PSCÍ. PŸPİPsCÍC,PµCĤC-PİP°P»PsCÍCİ CÍP»P°P±PePµ P°P±Ps PİPsPjC-CĤPSPµ PİC-PrPIPëC%PµPSPSCİ PeP»C-CĤPµPSCÍCÍ PsP»P°PSP·P°PİC-PSCÍ. PĥP»C-PSC-C†PSC- PIPëCÍPSPsPIPePë PsP±PjPµP¶PµPSC-, P°P»Pµ CĤPµPePsPjPµPSPrCÍC''C,CĤCÍCİ PeP»C-PSC-C†PSPëPN PjPsPSC-C,PsCĤPëPSPİ C,P°, CİPeC%Ps PSPµPsP±C...C-PrPSPs, P·P±C-P»CHC€PµPSPSCİ PrPsP·Pë PsP»P°PSP·P°PİC-PSCÍ.

P†PSPİC-P±C-C,PsCĤPë CYP1A2

PαP»CÍPsPeCÍP°PjC-PS, CÍPİPµC†PëC,,C-C±PSPëPN C-PSPiC-P±C-C,PsCĤ CYP1A2, C-CÍC,PsC,PSPs P·PSPëP¶CÍC'' PjPµC,P°P±PsP»C-P·Pj PsP»P°PSP·P°PİC-PSCÍ. PİPµ PİCĤPëP·PIPsPrPëC,CĤ PrPs CÍPµCĤPµPrPSCĤPsPiPs P·CĤPsCÍC,P°PSPSCİ PŸ_{max} PİC-CÍP»Cİ PİCĤPëPNPsPjCÍ C,,P»CÍPsPeCÍP°PjC-PSCÍ PSP° 54 % CÍ P¶C-PSPsPe, CİPeC-PSPµ PİP°P»CİC,CĤ, C,P° PSP° 77 % CÍ C±PsP»PsPIC-PeC-PI, CİPeC- PİP°P»CİC,CĤ. PŸPµCĤPµPrPSC'' P·CĤPsCÍC,P°PSPSCİ PİP»PsC%C- PİC-Pr C,,P°CĤPjP°PePsPeC-PSPµC,PëC±PSPsCĤ PeCĤPëPIPsCĤ B«PePsPSC†PµPSC,CĤP°C†C-Cİ- C†P°CÍB» (AUC) PsP»P°PSP·P°PİC-PSCÍ CÍC,P°PSPsPIPëC,CĤ 52 % C,P° 108 % PIC-PrPİPsPIC-PrPSPs. P''P»Cİ PİP°C†C-C''PSC,C-PI, CİPeC- P·P°CÍC,PsCÍPsPICÍCĤC,CĤ C,,P»CÍPsPeCÍP°PjC-PS P°P±Ps P±CÍPrCH-CİPeC- C-PSC€C- C-PSPiC-P±C-C,PsCĤPë CYP1A2, PSP°PİCĤPëPeP»P°Pr C†PëPİCĤPsC,,P»PsPeCÍP°C†PëPS, PİPsC,CĤC-P±PSPs PİCĤPëP·PSP°C†P°C,Pë P·PSPëP¶PµPSC- PrPsP·Pë PsP»P°PSP·P°PİC-PSCÍ. PkPµPsP±C...C-PrPSPs CĤPsP·PiP»CİPSCÍC,Pë PjPsP¶P»PëPIC-CÍC,CĤ P·PSPëP¶PµPSPSCİ PrPsP·Pë PsP»P°PSP·P°PİC-PSCÍ, CİPeC%Ps C-PSC-C†C-PNPsPIP°PSPµ P»C-PeCÍPIP°PSPSCİ C-PSPiC-P±C-C,PsCĤPsPj CYP1A2.

P—PjPµPSC€PµPSPSCİ P±C-PsPrPsCÍC,CÍPİPSPsCÍC,C-

P—P°CÍC,PsCÍCÍPIP°PSPSCİ P°PeC,PëPIPsPIP°PSPsPiPs PICÍPiC-P»P»Cİ P·PSPëP¶CÍPIP°P»Ps PİPµCĤPsCĤP°P»CHPSCÍ P±C-PsPrPsCÍC,CÍPİPSC-CÍC,CĤ PİCĤPëPNPSCİC,PsPiPs PsP»P°PSP·P°PİC-PSCÍ PSP° 50-60 %, C,PsPjCÍ PNPsPiPs CÍP»C-Pr P·P°CÍC,PsCÍPsPICÍPIP°C,Pë PİCĤPsC,CİPiPsPj 2 PiPsPrPëPS PrPs PİCĤPëPNPsPjCÍ P°P±Ps C±PµCĤPµP· 2 PiPsPrPëPSPë

PiC-CI'P»CII PiCTjPePNePsPjCr PsP»P°PSP·P°PiC-PSCr.

P»P»CrPsPeCI'PμC,PēPS (C-PSPiC-P±C-C,PSCj CYP2D6), PsPrPSPsCTjP°P·PsPIP° PrPsP·P°
P°PSC,P°C†PēPrC-PI, C%oPs PjC-CI'C,CIIc,CH P°P»CTjPjC-PSC-PNē C,P° PjP°PiPSC-PNē P°P±Ps
C†PēPjPμC,PēPrPēPS, C-CI'C,PsC,PSPs PSPμ PIPiP»PēPIP°P»Pē PSP°
C,,P°CTjPjP°PePsPeC-PSPμC,PēPeCr PsP»P°PSP·P°PiC-PSCr.

PμPsP¶P»PēPIPēPNē PIPiP»PēPI PsP»P°PSP·P°PiC-PSCr PSP° C-PSC€C- P»C-PeP°CTjCI'CHPeC-
P·P°CI'PsP±Pē

PhP»P°PSP·P°PiC-PS PjPsP¶Pμ PiCTjPsCIIPIP»CIIc,Pē P°PSC,P°PiPsPSC-P·Pj PrPs PμC,,PμPeC,C-PI
PiCTjCIIPIjPēC... C,P° PSPμPiCTjCIIPIjPēC... P°PiPsPSC-CI'C,C-PI PrPsPiP°PjC-PSCr.

PhP»P°PSP·P°PiC-PS PSPμ PiCTjPēPiPSC-C†CrPIP°PI PsCI'PSPsPIPSC- C-P·PsC,,PμCTjPjPμPSC,Pē
CYP 450 (PSP°PiCTjPēPeP»P°Pr, 1A2, 2D6, 2C9, 2C19, 3A4) *in vitro*. PŷP°PePēPj C†PēPSPsPj, PSPμ
PsC†C-PeCrC" C,CHCI'CI PSC-CIIPIePēC... PsCI'PsP±P»PēPIPēC... PIP·P°C" PjPsPrC-PNē, C%oPs
PiC-PrC,PIPμCTjPrP¶PμPSPs Cr PrPsCI'P»C-PrP¶PμPSPSCIIc... *in vivo*, PrPμ PSPμ
PIC-PrP·PSP°C†P°P»PsCI'CH C-PSPiC-P±CrPIP°PSPSCII PjPμC,P°P±PsP»C-P·PjCr
PsP»P°PSP·P°PiC-PSCr PiCTjPē P·P°CI'c,PsCI'CrPIP°PSPSC- C,P°PePēC... P°PeC,PēPIPSPēC...
CTjPμC†PsPIPēPS: C,CTjPēC†PēPeP»C-C†PSC- P°PSC,PēPrPμPiCTjPμCI'P°PSC,Pē
(PiPsP»PsPIPSPēPj C†PēPSPsPj PiCTjPμPrCI'c,P°PIP»PμPSC- C-P·PsC,,PμCTjPjPμPSC,PsPj CYP2D6),
PIP°CTjC,,P°CTjPēPS (CYP2C9), C,PμPsC,,C-P»C-PS (CYP 1A2) P°P±Ps PrC-P°P·PμPiP°Pj (CYP 3P4
C,P° 2Pŷ19).

PkPμ P±CrP»Ps P·P°C,,C-PeCI'PsPIP°PSPs PIP·P°C" PjPsPrC-C— PsP»P°PSP·P°PiC-PSCr P·
P»C-C,C-C" Pj P°P±Ps P±C-PiPμCTjPēPrPμPSPsPj.

PŷPμCTjP°PiPμPIC,PēC†PSPēPNē PjPsPSC-C,PsCTjPēPSPi CTjC-PIPSCII PIP°P»CHPiCTjPsP°C,Cr Cr
PiP»P°P·PjC- PeCTjPsPIC- PSPμ PIPēCIIPIPēPI PSPμPsP±C...C-PrPSPsCI'c,C- PePsCTjPμPeC†C-C—
PrPsP·Pē PIP°P»CHPiCTjPsP°C,Cr PiCTjPē CI'CrPiCrC,PSCHPsPjCr PiCTjPēP·PSP°C†PμPSPSC- P·
PsP»P°PSP·P°PiC-PSPsPj.

P—P°PiP°P»CHPSP° P°PeC,PēPIPSC-CI'c,CH C%oPsPrPs C†PμPSC,CTjP°P»CHPSPsC—
PSPμCTjPIPsPIPsC— CI'PēCI'c,PμPjPē (PiPkPŷ)

P— PsP±PμCTjPμP¶PSC-CI'c,CH CI'P»C-Pr P·P°CI'c,PsCI'PsPICrPIP°C,Pē PsP»P°PSP·P°PiC-PS
PiP°C†C-C" PSC,P°Pj, CIIPeC- PiCTjPēPNēPjP°CTjC,CH PμC,P°PSPsP» P°P±Ps
P»C-PeP°CTjCI'CHPeC- P·P°CI'PsP±Pē, C%oPs PjPsP¶CI'c,CH CI'PiCTjPēC†PēPSPēC,Pē
PiCTjPēPiPSC-C†PμPSPSCII P|PkPŷ.

PŷCrPiCrC,PSC" P·P°CI'c,PsCI'CrPIP°PSPSCII PsP»P°PSP·P°PiC-PSCr P·
P°PSC,PēPiP°CTjPeC-PSCrPsPSC-C†PSPēPjPē PiCTjPμPiP°CTjP°C,P°PjPē PiP°C†C-C" PSC,P°Pj C-P·
C...PIPsCTjPsP±PsCH PμP°CTjPeC-PSCrPsPSP° C,P° PrPμPjPμPSC†C-C" CH PSPμ
CTjPμPePsPjPμPSPCrC" C,CHCI'CI.

P†PSC,PμCTjPIP°P» QTCI'

PŷP»C-Pr P· PsP±PμCTjPμP¶PSC-CI'c,CH PiCTjPēP·PSP°C†P°C,Pē PsP»P°PSP·P°PiC-PS P·
C-PSC€PēPjPē PiCTjPμPiP°CTjP°C,P°PjPē C-P· PIC-PrPsPjPēPj CTjPēP·PēPePsPj
PiC-PrPIPēC%oPμPSPSCII C-PSC,PμCTjPIP°P»Cr QTCI'.

PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCáPIP°PSPSCII.

PµC-Pr C†P°CÍ P°PSC,PëPiCÍPëC...PsC,PëC†PSPsC— C,PµCÍP°PíC-C— PíPsP»C-PíC€PµPSPSCII
PeP»C-PSC-C†PSPsPiPs CÍC,P°PSCí PíP°C†C-C''PSC,P° PjPsP¶Pµ C,CÍPëPIP°C,Pë PIC-Pr
PeC-P»CHPePsC... PrPSC-PI PrPs PeC-P»CHPePsC... C,PëP¶PSC-PI. PµCÍPsC,CIIPIPsPj
C†CHPePsPiPs PíPµCÍC-PsPrCí CÍP»C-Pr CÍPµC,PµP»CHPSPs CÍPíPsCÍC,PµCÍC-PíP°C,Pë P·P°
PíP°C†C-C''PSC,P°PjPë.

*PµCÍPëC...PsP· C,P° (P°P±Ps) CÍPsP·P»P°PrPë PíPsPIPµPrC-PSPePë, PíPsPI'CIIIP·P°PSC- P·
PrPµPjPµPSC†C-C''CÍ*

PhP»P°PSP·P°PíC-PS PSPµ CÍPµPePsPjPµPSPPrCíC''C,CHCÍCII P·P°CÍC,PsCÍPsPICíPIP°C,Pë
PíP°C†C-C''PSC,P°Pj P·C- CÍPëPjPíC,PsPjP°PjPë PíCÍPëC...PsP·Cí C,P°/P°P±Ps
PíPsCÍCíC€PµPSPSCIIIPjPë PíPsPIPµPrC-PSPePë, PíPsPI'CIIIP·P°PSPëPjPë P·
PrPµPjPµPSC†C-C''CÍ, Cí P·PI'CIIIP·PeCí P· PíC-PrPIPëC%PµPSPSCIIIPj
P»PµC,P°P»CHPSPsCÍC,C- C,P° CÍPëP·PëPeCí C†PµCÍPµP±CÍPsPIP°CÍPeCíP»CII CÍPSPëC...
PIPëPíP°PrPeC-PI. Pj PíCÍPsC†PµCÍC- PíP»P°C†PµP±Ps-PePsPSC,CÍPsP»CHPsPIP°PSPëC...
PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSCÍ (C,CÍPëPIP°P»C-CÍC,CÍ 6-12 C,PëP¶PSC-PI)
P·P° CíC†P°CÍC,C- PíP°C†C-C''PSC,C-PI P»C-C,PSCHPsPiPs PIC-PeCí (CÍPµCÍPµPrPSC-PNë
PIC-Pe 78 CÍPsPeC-PI), CIIPeC- CÍC,CÍP°P¶PrP°CÍC,CH PSP° PíCÍPëC...PsP· C,P°/P°P±Ps
PíPsCÍCíC€PµPSPSCII PíPsPIPµPrC-PSPePë, PíPsPIBÍ™ CIIIP·P°PSC- P· PrPµPjPµPSC†C-C''CÍ,
PeC-P»CHPeC-CÍC,CH P»PµC,P°P»CHPSPëC... PIPëPíP°PrPeC-PI P±CíP»P° Cí 2 CÍP°P·Pë
PIPëC%P° Cí PíP°C†C-C''PSC,C-PI, CIIPeC- PíCÍPëPNëPjP°P»Pë PsP»P°PSP·P°PíC-PS,
PíPsCÍC-PIPSCIIIPSPs P· PíP»P°C†PµP±Ps (3,5 % PíCÍPsC,Pë 1,5 % PIC-PrPíPsPIC-PrPSPs).
P'PëCÍPsPeP° P»PµC,P°P»CHPSC-CÍC,CH PSPµ P±CíP»P° PíPsPIBÍ™ CIIIP·P°PSP° P·
PIPµP»PëC†PëPSPsCÍ P·P°CÍC,PsCÍPsPICíPIP°PSPëC... PrPsP· PsP»P°PSP·P°PíC-PSCí
(CÍPµCÍPµPrPSCII PrPsP±PsPIP° PrPsP·P° CÍC,P°PSPsPIPëP»P° 4,4 PjPi) P°P±Ps P·
C,CÍPëPIP°P»C-CÍC,CÍ P»C-PeCíPIP°PSPSCII. PαP°PeC,PsCÍPë CÍPëP·PëPeCí, CIIPeC-
PjPsP¶CíC,CH CÍPíCÍPëC†PëPSPëC,Pë PíC-PrPIPëC%PµPSPSCII P»PµC,P°P»CHPSPsCÍC,C-,
PIPeP»CHC†P°CÍC,CH PIC-Pe PIC-Pr 65 CÍPsPeC-PI, PrPëCÍC,,P°PíC-CÍ, B CÍPµPrP°C†C-CÍ,
PSPµPrPsC—PrP°PSPSCII C,P° P·PSPµPIPsPrPSPµPSPSCII, P»PµPiPµPSPµPIC- C...PIPsCÍPsP±Pë
(PíPSPµPIPjPsPSC-CII P· P°P±Ps P±PµP· P°CÍPíC-CÍP°C†C-C—), CÍCíPíCíC,PSC''
P·P°CÍC,PsCÍCíPIP°PSPSCII P±PµPSP·PsPrC-P°P·PµPíC-PSC-PI. PµCÍPsC,Pµ PIPëPíP°PrPePë
P»PµC,P°P»CHPSPsCÍC,C- P±CíP»Pë PIPëC%P° PíCÍPë C,PµCÍP°PíC-C—
PsP»P°PSP·P°PíC-PSPsPj, PSC-P¶ PíCÍPë PíCÍPëPNëPsPjC- PíP»P°C†PµP±Ps,
PSPµP·P°P»PµP¶PSPs PIC-Pr C,,P°PeC,PsCÍC-PI CÍPëP·PëPeCí.

Pj PíCÍPsC†PµCÍC- C†PëC... PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSCÍ
CÍPíPsCÍC,PµCÍC-PíP°P»PëCÍCII PIPëPíP°PrPePë
C†PµCÍPµP±CÍPsPIP°CÍPeCíP»CII CÍPSPëC... PíPsP±C-C†PSPëC... CÍPµP°PeC†C-PNë
(PSP°PíCÍPëPeP»P°Pr, C-PSCÍCíP»CHC,, C,CÍP°PSP·PëC,PsCÍPSPëPNë
C-C€PµPjC-C†PSPëPNë C-PSCÍCíP»CHC,,) Cí C,PsPjCí C†PëCÍP»C- P·
P»PµC,P°P»CHPSPëPj PSP°CÍP»C-PrPePsPj. PµC-P»CHPeC-CÍC,CH
C†PµCÍPµP±CÍPsPIP°CÍPeCíP»CII CÍPSPëC... PíPsP±C-C†PSPëC... CÍPµP°PeC†C-PNë
P±CíP»P° Cí 3 CÍP°P·Pë PIPëC%P° Cí PíP°C†C-C''PSC,C-PI, CIIPeC- PíCÍPëPNëPjP°P»Pë
PsP»P°PSP·P°PíC-PS, PíPsCÍC-PIPSCIIIPSPs P· PíP°C†C-C''PSC,P°PjPë, CIIPeC-
PíCÍPëPNëPjP°P»Pë PíP»P°C†PµP±Ps (1,3 % PíCÍPsC,Pë 0,4 % PIC-PrPíPsPIC-PrPSPs).
PjCÍC- PíP°C†C-C''PSC,Pë, CIIPeC- PíCÍPëPNëPjP°P»Pë PsP»P°PSP·P°PíC-PS P°P±Ps
PíP»P°C†PµP±Ps C- Cí CIIPePëC... CÍPíPsCÍC,PµCÍC-PíP°P»PëCÍCII
C†PµCÍPµP±CÍPsPIP°CÍPeCíP»CII CÍPSC- PíPsP±C-C†PSC- CÍPµP°PeC†C-C—,

PjP°P»Pë C,,P°PeC,PsCḡPë CḡPëP·PëPeCř. P'C-Pe PIC-Pr 75 CḡPsPeC-PI C,P°
CÍCřPrPëPSPSPëPNë/P·PjC-C€P°PSPëPNë C,PëPi PrPµPjPµPSC†C-C— P±CřP»Pë
C-PrPµPSC,PëC,,C-PePsPIP°PSC- CḡPe C,,P°PeC,PsCḡPë CḡPëP·PëPeCř
C†PµCḡPµP±CḡPsPIP°CÍPeCřP»CḡCḡPSPëC... PİPsP±C-C†PSPëC... CḡPµP°PeC†C-PNë
PİCḡPë C,PµCḡP°PİC-C— PsP»P°PSP·P°PİC-PSPsPj. P•C,,PµPeC,PëPIPSC-CÍC,CH
PsP»P°PSP·P°PİC-PSCř PSPµ P±CřP»P° PICÍC,P°PSPsPIP»PµPSP° Cř PİCḡPsC†PµCÍC-
PrP°PSPëC... PrPsCÍP»C-PrPḡPµPSCH.

PIPIPsCḡPsP±P° PµP°CḡPeC-PSCÍPsPSP°

PkPµ CḡPµPePsPjPµPSPPrPsPIP°PSPs P·P°CÍC,PsCÍCřPIP°PSPSCḡ PsP»P°PSP·P°PİC-PSCř
Cř C,PµCḡP°PİC-C— PİCÍPëC...PsP·C-PI, C°Ps P°CÍPsC†C-PNëPsPIP°PSC- P·
P°PiPsPSC-CÍC,P°PjPë PrPsPİP°PjC-PSCř PI PİP°C†C-C''PSC,C-PI C-P·
C...PIPsCḡPsP±PsCḡ PµP°CḡPeC-PSCÍPsPSP°. PJ PİCḡPsC†PµCÍC-
PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrPḡPµPSCH PrCřPḡPµ C†P°CÍC,Ps
CÍPİPsCÍC,PµCḡC-PİP°P»PsCÍCḡ PİPsPİC-CḡC€PµPSPSCḡ CÍPëPjPİC,PsPjP°C,PëPePë
C...PIPsCḡPsP±Pë PµP°CḡPeC-PSCÍPsPSP° C,P° PİP°P»CḡC†PëPSP°C†C-PNë,
C†P°CÍC,C-C€Pµ, PSC-Pḡ PİCḡPë PİCḡPëPNëPsPjC- PİP»P°C†PµP±Ps (PrPëPI. C,P°PePsPḡ
CḡPsP·PrC-P» B«PµPsP±C-C†PSC- CḡPµP°PeC†C-C—B»); PİCḡPë P»C-PeCřPIP°PSPSC-
PİCÍPëC...PsC,PëC†PSPëC... CÍPëPjPİC,PsPjC-PI C,PµCḡP°PİC-Cḡ
PsP»P°PSP·P°PİC-PSPsPj PSPµ P±CřP»P° P±C-P»CHC€ PµC,,PµPeC,PëPIPSPsCḡ
PİPsCḡC-PIPSCḡPSPs P·C- P·P°CÍC,PsCÍCřPIP°PSPSCḡPj PİP»P°C†PµP±Ps. PJ C†PëC...
PrPsCÍP»C-PrPḡPµPSPSCḡC... PİPëPjP°PİP°P»PsCÍCḡ, C°PsP± CÍC,P°PS
PİP°C†C-C''PSC,C-PI P±CřPI CÍC,P°P±C-P»CHPSPëPNë, PePsP»Pë PİPsPSPë
PİCḡPëPNëPjP°P»Pë PSP°PNëPjPµPSC€Cř PµC,,PµPeC,PëPIPSCř PrPsP·Cř
P°PSC,PëPİP°CḡPeC-PSCÍPsPSC-C†PSPëC... P»C-PeP°CḡCÍCHPePëC... P·P°CÍPsP±C-PI
(P°PiPsPSC-CÍC,C-PI PrPsPİP°PjC-PSCř), P° C,P°PePsPḡ PİCḡPëPNëPjP°P»Pë C,C-
CÍP°PjC- P°PSC,PëPİP°CḡPeC-PSCÍPsPSC-C†PSC- P»C-PeP°CḡCÍCHPeC- P·P°CÍPsP±Pë
PİCḡPsC,CḡPiPsPj CřCÍCHPsPiPs PrPsCÍP»C-PrPḡPµPSPSCḡ. PḡPµCḡP°PİC-Cḡ
PsP»P°PSP·P°PİC-PSPsPj P±CřP»Ps CḡPsP·PİPsC†P°C,Ps P· PrPsP·Pë 2,5 PjPi PSP°
PrPsP±Cř, CḡPeCř P·P±C-P»CHC€CřPIP°P»Pë C€P»CḡC...PsPj C,PëC,CḡCřPIP°PSPSCḡ
PrPs PjP°PeCÍPëPjP°P»CHPSPsPiPs PİPsPeP°P·PSPëPeP° 15 PjPi PSP° PrPsP±Cř.

PkPµPNëCḡPsP»PµPİC,PëC†PSPëPNë P·P»PsCḡPeC-CÍPSPëPNë CÍPëPSPrCḡPsPj (PkP—PḢ)

PkP—PḢ вḡ C†Pµ PİPsC,PµPSC†C-PNëPSPs P»PµC,P°P»CHPSPëPNë
CÍPëPjPİC,PsPjPsPePsPjPİP»PµPeCÍ, PİPsPIBḡ™ CḡP·P°PSPëPNë P· PİCḡPëPNëPsPjPsPj
P°PSC,PëPİCÍPëC...PsC,PëC†PSPëC... PİCḡPµPİP°CḡP°C,C-PI. P C-PrPePs
PİPsPIC-PrPsPjP»CḡP»PsCÍCḡ PİCḡPs PİPëPİP°PrPePë PkP—PḢ PİC-Pr C†P°CÍ
P·P°CÍC,PsCÍCřPIP°PSPSCḡ PsP»P°PSP·P°PİC-PSCř. PḡP»C-PSC-C†PSPëPjPë
PİCḡPsCḡPIP°PjPë PkP—PḢ C'' PİC-PİPµCḡPİC-CḡPµPeCÍC-Cḡ, PjBḡ™ CḡP·PsPIP°
CḡPëPİC-PrPSC-CÍC,CH, PIC,CḡP°C,P° CÍPIC-PrPsPjPsCÍC,C- C,P° CÍPëPjPİC,PsPjPë
CÍPµCḡC†PµPIPsC— PSPµCÍC,P°P±C-P»CHPSPsCÍC,C- (PSPµCḡPµPİCřP»CḡCḡPSC-
PİCřP»CHCÍ P°P±Ps P·PjC-PSP° P°CḡC,PµCḡC-P°P»CHPSPsPiPs C,PëCÍPeCř,
C,P°C...C-PeP°CḡPrC-Cḡ, PİC-PrPIPëC°PµPSPµ PİPsC,PsPIPëPrC-P»PµPSPSCḡ C,P°
CÍPµCḡC†PµPIP° P°CḡPëC,PjC-Cḡ). P''PsPrP°C,PePsPIC- PsP·PSP°PePë PjPsPḡCřC,CH
PIPeP»CḡC†P°C,Pë PİC-PrPIPëC°PµPSPëPNë CḡC-PIPµPSCH
PeCḡPµP°C,PëPSC-PSC,,PsCÍC,,PsPeC-PSP°P·Pë, PjC-PsPiP»PsP±C-PSCřCḡC-Cḡ

PJ PīP»P°C†PμP±PsPePsPSC,CḡPsP»CHbPsPIP°PSPsPjCr PeP»C-PSC-C‡PSPsPjCr
PrPsCÍP»C-PrP¶PμPSPSC- Cr PīP°C†C-C”PSC,C-PI, CḡPeC- P»C-PeCrPIP°P»PëCÍCḡ
PsP»P°PSP·P°PīC-PSPsPj, CÍPīPsCÍC,PμCḡC-PiP°P»PëCÍCḡ PSPμP±P°P¶P°PSC-
P·PjC-PSPë Cr PePsPSC†PμPSC,CḡP°C†C-C— P»C-PīC-PrC-PI (PrPëPI. CḡPsP·PrC-P»
B«PμPsP±C-C‡PSC- CḡPμP°PeC†C-C—B»). PJ CḡP°P·C- PIPëCḡPIP»PμPSPSCḡ P·PjC-PS
Cr PePsPSC†PμPSC,CḡP°C†C-C— P»C-PīC-PrC-PI PSPμPsP±C...C-PrPSPs
PīCḡPsPIPsPrPëC,Pë PIC-PrPīPsPIC-PrPSPμ P»C-PeCrPIP°PSPSCḡ, P·PsPeCḡPμPjP° Cr

PiP°C†C-C"°PSC,C-PI P· PiPsCḡCfC€PμPSPSCḡPjPë PsP±PjC-PSCr P»C-PiC-PrC-PI C,P°
Cf PiP°C†C-C"°PSC,C-PI C-P· C,,P°PeC,PsCḡP°PjPë CḡPëP·PëPeCf CḡPsP·PIPëC,PeCf
C,P°PePëC... PiPsCḡCfC€PμPSCḡ. PμP°C†C-C"°PSC,P°Pj, CḡPeC-
P·P°CfC,PsCfPsPICfCḡC,CH P°PSC,PëPiCfPëC...PsC,PëC±PSC- P»C-PeP°CḡCfCḡPeC-
P·P°CfPsP±Pë, PI C,PsPjCf C±PëCfP»C- P»C-PeP°CḡCfCḡPePëPNë P·P°CfC-P±
P—PsP»P°C,,CḡPμPS PαP°CfC,, PSPμPsP±C...C-PrPSPs CḡPμPiCfP»CḡCḡPSPs
PePsPSC,CḡPsP»CḡPIP°C,Pë CḡC-PIPμPSCḡ P»C-PiC-PrC-PI PIC-PrPiPsPIC-PrPSPs
PrPs P·P°C,PIPμCḡPrP¶PμPSPëC... CḡPμPePsPjPμPSPrP°C†C-PNë, C°°Ps
CfC,PsCfCfCḡC,CHCfCḡ P°PSC,PëPiCfPëC...PsC,PëC±PSPsC— C,PμCḡP°PiC-C—,
PSP°PiCḡPëPeP»P°Pr PSP° PiPsC±P°C,PeCf P»C-PeCfPIP°PSPSCḡ, C±PμCḡPμP· 12
C,PëP¶PSC-PI, P° C,P°PePsP¶ Cf PiPsPrP°P»CHC€PsPjCf PePsP¶PSC- 5 CḡPsPeC-PI.

PḡPSC,PëC...PsP»C-PSPμCḡPiC-C±PSP° P°PeC,PëPIPSC-CfC,CH

PμPsPiCḡPë PIPëCḡPIP»PμPSPSCḡ P°PSC,PëC...PsP»C-PSPμCḡPiC-C±PSPsC—
P°PeC,PëPIPSPsCfC,C- PsP»P°PSP·P°PiC-PSCr *in vitro*, Cf PiCḡPsC†PμCfC-
PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PμPSCḡ PrPsPIPμPrPμPSPs PSPëP·CHPeCf
C±P°CfC,PsC,Cf CḡPsP·PIPëC,PeCf PiPsPiBḡ™ CḡP·P°PSPëC... P· PSPμCḡ
P°PSC,PëC...PsP»C-PSPμCḡPiC-C±PSPëC... CḡPIPëC°. PhPrPSP°Pe C±PμCḡPμP·
PsP±PjPμP¶PμPSPSCḡ PeP»C-PSC-C±PSPsPiPs PrPsCfPIC-PrCf C°°PsPrPs
P·P°CfC,PsCfCfPIP°PSPSCḡ PsP»P°PSP·P°PiC-PSCr PiP°C†C-C"°PSC,P°Pj P·C-
CfCfPiCfC,PSC-PjPë P·P°C...PIPSCḡCḡPIP°PSPSCḡPjPë CfP»C-Pr
PrPsC,CḡPëPjCfPIP°C,PëCfCḡ PsP±PμCḡPμP¶PSPsCfC,C- PiCḡPë
PiCḡPëP·PSP°C±PμPSPSC- PiCḡPμPiP°CḡP°C,Cf PiP°C†C-C"°PSC,P°Pj C-P·
PeP»C-PSC-C±PSPs P·PSP°C±CfC°°PsCḡ PiC-PiPμCḡC,CḡPsC,,C-C"ḡC
PiCḡPsCfC,P°C,Pë, PiP°CḡP°P»C-C,PëC±PSPsCḡ PePëC€PePsPIPsCḡ
PSPμPiCḡPsC...C-PrPSC-CfC,Cḡ P°P±Ps PiPsPrC-P±PSPëPjPë
P·P°C...PIPsCḡCḡPIP°PSPSCḡPjPë.

PμPsPeP°P·PSPëPePë C,,C±PSPeC†C-C— PiPμC±C-PSPePë

PμCḡPë P·P°CfC,PsCfCfPIP°PSPSC- PsP»P°PSP·P°PiC-PSCr C±P°CfC,Ps
CfPiPsCfC,PμCḡC-PiP°PICfCḡ C,CḡP°PSP·PëC,PsCḡPSPëPNë
P°CfPëPjPiC,PsPjP°C,PëC±PSPëPNë PiC-PrPNëPsPj CḡC-PIPSCḡ PiPμC±C-PSPePsPIPëC...
C,CḡP°PSCfP°PjC-PSP°P· P°P»P°PSC-PSP°PjC-PSPsC,CḡP°PSCfC,,PμCḡP°P·Pë
(PḡP»PḡPḡ) C,P° P°CfPiP°CḡC,P°C,P°PjC-PSPsC,CḡP°PSCfC,,PμCḡP°P·Pë (PḡCfPḡPḡ),
PsCfPsP±P»PëPIPs PSP° PiPsC±P°C,PeCf P»C-PeCfPIP°PSPSCḡ. PkPμPsP±C...C-PrPSPs
PrPsC,CḡPëPjCfPIP°C,PëCfCḡ PsP±PμCḡPμP¶PSPsCfC,C- C,P°
PsCḡPiP°PSC-P·CfPIP°C,Pë PiPsPrP°P»CHC€Pμ CfPiPsCfC,PμCḡPμP¶PμPSPSCḡ P·P°
PiP°C†C-C"°PSC,P°PjPë P· PiC-PrPIPëC°°PμPSPëPj CḡC-PIPSPμPj PḡP»PḡPḡ C,P°/P°P±Ps
PḡCfPḡPḡ, PiP°C†C-C"°PSC,P°PjPë P· PsP·PSP°PeP°PjPë C,P° CfPëPjPiC,PsPjP°PjPë
PiPsCḡCfC€PμPSPSCḡ C,,CfPSPeC†C-C— PiPμC±C-PSPePë. PμP°C†C-C"°PSC,P°Pj C-P·
PiC-PrPIPëC°°PμPSPëPj CḡC-PIPSPμPj PḡP»PḡPḡ C,P°/P°P±Ps PḡCfPḡPḡ,
PsP·PSP°PeP°PjPë C,P° CfPëPjPiC,PsPjP°PjPë PiPsCḡCfC€PμPSPSCḡ
PrC-CḡP»CHPSPsCfC,C- PiPμC±C-PSPePë, CfC,P°PSPsPj, PiPsPiBḡ™ CḡP·P°PSPëPj P·
PiPμC±C-PSPePsPIPsCḡ PSPμPrPsCfC,P°C,PSC-CfC,Cḡ, P° C,P°PePsP¶
PiP°C†C-C"°PSC,P°Pj, CḡPeC- PiCḡPëPNëPjP°CḡC,CH PiPsC,PμPSC†C-PNëPSPs
PiPμPiP°C,PsC,PsPeCfPëC±PSC- PiCḡPμPiP°CḡP°C,Pë, PsP»P°PSP·P°PiC-PS CfP»C-Pr

$P \gg C - \text{PeCrPIP}^{\circ}P \gg \text{PëCfCf} \text{ PsP} \gg P^{\circ} \text{PSP} \cdot P^{\circ} \text{P}^{\circ} \text{C} - \text{PSPsPj} \text{ (P} \propto \text{CfPpPrPpCfC} - \text{PeP}^{\circ} \text{ QT}$
 $\text{PePsCfPpPeC}^{\dagger} \text{C} - \text{Cf} \geq 500 \text{ PjC} - \text{P} \gg \text{C} - \text{CfPpPeCrPSPr} \text{ (PjCfPpPe)} \text{ Cr} \text{ P} \pm \text{CrPrCh} - \text{CfPePëPN}_{\infty}$
 $\text{C}^{\dagger} \text{P}^{\circ} \text{Cf}^{\circ} \text{P}^{\circ} \text{C} - \text{CfP} \gg \text{Cf} \text{ PiPsC}^{\dagger} \text{P}^{\circ} \text{C}, \text{PeCr} \text{ C}, \text{PpCfP}^{\circ} \text{P}^{\circ} \text{C} - \text{C} - \text{, Cr} \text{ PiP}^{\circ} \text{C}^{\dagger} \text{C} - \text{C}^{\circ} \text{PSC}, \text{C} - \text{PI} \text{ P} \cdot$
 $\text{P} \pm \text{P}^{\circ} \text{P} \cdot \text{PsPIPSCf} \text{ P} \gg \text{C} - \text{PSC} - \text{C}^{\circ} \text{Cf} \text{ QTcF} < 500 \text{ PjCfPpPe} \text{ PrPs} \text{ PiPsC}^{\dagger} \text{P}^{\circ} \text{C}, \text{PeCr}$
 $\text{C}, \text{PpCfP}^{\circ} \text{P}^{\circ} \text{C} - \text{C} - \text{), PIPëCfPIP} \gg \text{CfP} \gg \text{PsCfCf} \text{ PSPpC}^{\dagger} \text{P}^{\circ} \text{Cf}^{\circ} \text{C}, \text{Ps} (\geq 0,1 \% \text{ PrPs } 1 \%).$
 $\text{PpPsCfC} - \text{PIPSCfPSPs} \text{ P} \cdot \text{PiP} \gg \text{P}^{\circ} \text{C}^{\dagger} \text{PpP} \pm \text{Ps} \text{ PSPp} \text{ PIPëCfPIP} \gg \text{PpPSPs} \text{ P} \cdot \text{PSP}^{\circ} \text{C}^{\dagger} \text{PSPsC} -$
 $\text{CfC} - \text{P} \cdot \text{PSPëC}^{\dagger} \text{C} - \text{Cr} \text{ C}^{\dagger} \text{P}^{\circ} \text{Cf}^{\circ} \text{C}, \text{PsC}, \text{C} - \text{P}^{\circ} \text{Cf}^{\circ} \text{PsC}^{\dagger} \text{C} - \text{PN}_{\infty} \text{PsPIP}^{\circ} \text{PSPëC} \dots \text{PeP}^{\circ} \text{CfPrC} - \text{P}^{\circ} \text{P} \gg \text{ChPSPëC} \dots$
 $\text{PiPsP} \pm \text{C} - \text{C}^{\dagger} \text{PSPëC} \dots \text{CfPpP}^{\circ} \text{PeC}^{\dagger} \text{C} - \text{PN}_{\infty} \text{PhPrPSP}^{\circ} \text{Pe} \text{ CfP} \gg \text{C} - \text{Pr} \text{ P} \pm \text{CrC}, \text{Pë}$
 $\text{PsP} \pm \text{PpCfPpP} \text{ PIPSPëPjPë} \text{ Cr} \text{ CfP}^{\circ} \text{P} \cdot \text{C} - \text{PiCfPëP} \cdot \text{PSP}^{\circ} \text{C}^{\dagger} \text{PpPSPSCf} \text{ PsP} \gg \text{P}^{\circ} \text{PSP} \cdot \text{P}^{\circ} \text{P}^{\circ} \text{C} - \text{PSCr}$
 $\text{PsPrPSPsC}^{\dagger} \text{P}^{\circ} \text{Cf}^{\circ} \text{PSPs} \text{ P} \cdot \text{P} \gg \text{C} - \text{PeP}^{\circ} \text{CfCfChPePëPjPë} \text{ P} \cdot \text{P}^{\circ} \text{Cf}^{\circ} \text{PsP} \pm \text{P}^{\circ} \text{PjPë}, \text{CfPeC} -$
 $\text{P} \cdot \text{P} \pm \text{C} - \text{P} \gg \text{ChC} \propto \text{CrCfC}, \text{Ch} \text{ C} - \text{PSC}, \text{PpCfPIP}^{\circ} \text{P} \gg \text{QTCf}^{\circ}, \text{PsCfPsP} \pm \text{P} \gg \text{PëPIPs} \text{ Cr}$
 $\text{PiP}^{\circ} \text{C}^{\dagger} \text{C} - \text{C}^{\circ} \text{PSC}, \text{C} - \text{PI} \text{ P} \gg \text{C} - \text{C}, \text{PSCfPsPiPs} \text{ PIC} - \text{PeCr}^{\circ}, \text{PiP}^{\circ} \text{C}^{\dagger} \text{C} - \text{C}^{\circ} \text{PSC}, \text{C} - \text{PI} \text{ C} - \text{P} \cdot$
 $\text{PICfPsPrP} \text{ PIPSPëPj} \text{ CfPëPSPrCfPsPjPsPj} \text{ QT}, \text{P} \cdot \text{P}^{\circ} \text{Cf}^{\circ} \text{C}, \text{C} - \text{PN}_{\infty} \text{PSPsCf} \text{ CfPpCfC}^{\dagger} \text{PpPIPsCf}$
 $\text{PSPpPrPsCf}^{\circ} \text{C}, \text{P}^{\circ} \text{C}, \text{PSC} - \text{Cf}^{\circ} \text{C}, \text{Cf}, \text{CfPpCfC}^{\dagger} \text{PpPIPsCf} \text{ PiC} - \text{PiPuCfC}, \text{CfPsC}, \text{C} - \text{C}^{\circ} \text{Cf},$

PiC-PiPsPeP°P»C-C"PjC-C"Ch P°P±Ps PiC-PiPsPjP°PiPSPμP·PμPjC-C"Ch.

PÿCḡPsPjP±PsPμPjP±PsP»C-Cḡ

PkPμC†P°CfC,Ps PiPsPIC-PrPsPjP»CḡP»PsCfCḡ PiCḡPs C,PëPjC†P°CfPsPIPëPNë
P·PIBḡ™ CḡP·PsPe PjC-Pḡ P»C-PeCfPIP°PSPSCḡPj PsP»P°PSP·P°PiC-PSPsPj C,P°
PIPëPiP°PrPeP°PjPë CḡPsP·PIPëC,PeCf PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C— (≥ 0,1 % Bḡ" < 1 %). PḡCḡPëC†PëPSPSPs-
PSP°CfP»C-PrPePsPIPsPiPs P·PIBḡ™ CḡP·PeCf PjC-Pḡ P»C-PeCfPIP°PSPSCḡPj
PsP»P°PSP·P°PiC-PSPsPj C,P° CḡPsP·PIPëC,PePsPj PIPμPSPsP·PSPsC—
C,CḡPsPjP±PsPμPjP±PsP»C-C— PSPμ PICfC,P°PSPsPIP»PμPSPs. PhPrPSP°Pe,
P±PμCḡCfC†Pë PrPs CfPIP°PiPë C,Pμ, C%Ps Cf PiP°C†C-C"PSC,C-PI C-P·
C€PëP·PsC,,CḡPμPSC-C"Ch C†P°CfC,Ps CḡPsP·PIPëPIP°C"C,ChCfCḡ
CfC...PëP»ChPSC-CfC,Ch PrPs C,CḡPsPjP±PsPμPjP±PsP»C-C—,
PSPμPsP±C...C-PrPSPs PICḡP°C...PsPICfPIP°C,Pë CfCfC- PjPsPḡP»PëPIC-
C,,P°PeC,PsCḡPë CḡPëP·PëPeCf, PSP°PiCḡPëPeP»P°Pr C-PjPjPsP±C-P»C-P·P°C†C-Ch
PiP°C†C-C"PSC,P°, C,P° PIPḡPëPIP°C,Pë PICfC-C... PSPμPsP±C...C-PrPSPëC...
PiPsPiPμCḡPμPrPḡCfPIP°P»ChPSPëC... P·P°C...PsPrC-PI.

P—P°PiP°P»ChPSP° P°PeC,PëPIPSC-CfC,Ch PiPkPÿ

P'CḡP°C...PsPICfChC†Pë PiPμCḡPμPIP°PḡPSPëPNë PIPiP»PëPI PsP»P°PSP·P°PiC-PSCf
PSP° PiPkPÿ, PSPμPsP±C...C-PrPSPs PiCḡPsPIPsPrPëC,Pë PrPsPrP°C,PePsPIC-
P·P°CfC,PμCḡPμPḡPSC- P·P°C...PsPrPë PiCḡPë PiCḡPëPNëPsPjC- PsP»P°PSP·P°PiC-PSCf
CḡP°P·PsPj P· C-PSC€PëPjPë PiCḡPμPiP°CḡP°C,P°PjPë C†PμPSC,CḡP°P»ChPSPsC—
PrC-C—, PIPeP»ChC†P°ChC†Pë PIPḡPëPIP°PSPSCḡ P°P»PePsPiPsP»Ch. PḡCḡPë
PrPsCfP»C-PrPḡPμPSPSCḡC... *in vitro* P· P°PSC,P°PiPsPSC-CfC,P°PjPë PrPsPiP°PjC-PSCf
PIPëCḡPIP»PμPSPs, C%Ps PsP»P°PSP·P°PiC-PS PjPsPḡPμ P°PSC,P°PiPsPSC-CfC,PëC†PSPs
PIPiP»PëPIP°C,Pë PSP° PμC,,PμPeC,Pë PiCḡCḡPjPëC... C,P° PSPμPiCḡCḡPjPëC...
P°PiPsPSC-CfC,C-PI PrPsPiP°PjC-PSCf.

PkP°PiP°PrPë CfCâPrPsPj

PhP»P°PSP·P°PiC-PS PSPμPsP±C...C-PrPSPs PsP±PμCḡPμPḡPSPs P·P°CfC,PsCfPsPICfPIP°C,Pë
PiP°C†C-C"PSC,P°Pj P· PμPiC-P»PμPiC,PëC†PSPëPjPë PSP°PiP°PrP°PjPë PI P°PSP°PjPSPμP·C-
P°P±Ps P· C,,P°PeC,PsCḡP°PjPë, C%Ps P·PSPëPḡCfChC,Ch CfCfPrPsPjPSPëPNë
PiPsCḡC-Pi. PkPμC†P°CfC,Ps PiPsPIC-PrPsPjP»CḡP»PsCfCḡ PiCḡPs PIPëPiP°PrPePë
PμPiC-P»PμPiC,PëC†PSPëC... PSP°PiP°PrC-PI PiCḡPë P»C-PeCfPIP°PSPSC-
PsP»P°PSP·P°PiC-PSPsPj. Pj P±C-P»ChC€PsCfC,C- C†PëC... PIPëPiP°PrPeC-PI
PiP°C†C-C"PSC,Pë PjP°P»Pë PI P°PSP°PjPSPμP·C- PμPiC-P»PμPiC,PëC†PSC- PSP°PiP°PrPë
P°P±Ps CḡPëP·PëPe C—C... PIPëPSPëPePSPμPSPSCḡ P±CfPI PiC-PrPIPëC%PμPSPëPNë.

PμC-P·PSCḡ PrPëCfPeC-PSPμP·C-Cḡ

Pj PiCḡPsC†PμCfC- PiPsCḡC-PIPSCḡP»ChPSPëC... PeP»C-PSC-C†PSPëC...
PrPsCfP»C-PrPḡPμPSCḡ C,CḡPëPIP°P»C-CfC,Ch 1 CḡC-Pe P°P±Ps PjPμPSC€Pμ PiCḡPë
PiCḡPëPNëPsPjC- PsP»P°PSP·P°PiC-PSCf CfPiPsCfC,PμCḡC-PiP°P»P°CfCḡ
CfC,P°C,PëCfC,PëC†PSPs P·PSP°C†CfC%Ps PSPëPḡC†P° C†P°CfC,PsC,P°
PIPëPSPëPePSPμPSPSCḡ PrPëCfPeC-PSPμP·C-C—, CfPiCḡPëC†PëPSPμPSPsC—

P»C-PeCfPIP°PSPSCIJ. PŞPµCŞPµP· P·CŞPsCfC,P°CŞC±PëPNë CŞPëP·PëPe
CŞPsP·PIPëC,PeCf PiC-P·PSCŞPsC— PrPëCfPeC-PSPµP·C-C— PiCŞPë
C,CŞPëPIP°P»PsPjCf PiCŞPëPNëPsPjC- P°PSC,PëPiCfPëC...PsC,PëC±PSPëC...
PiCŞPµPiP°CŞP°C,C-PI PSPµPsP±C...C-PrPSPµ CfP·PiPsPrP¶PµPSPµ P·PSPëP¶PµPSPSCIJ
PrPsP·Pë P°P±Ps PiPsPIPS° PIC-PrPjC-PSP° PiCŞPµPiP°CŞP°C,Cf PiCŞPë PiPsCIJPIC- Cf
PiP°C†C-C”PSC,P° PsP·PSP°Pe C±Pë CfPëPjPiC,PsPjC-PI PiC-P·PSCŞPsC—
PrPëCfPeC-PSPµP·C-C—. P— C±P°CfPsPj C†C- CfPëPjPiC,PsPjPë PjPsP¶CfC,CH
PiPsPiC-CŞCëCfPIP°C,PëCfCH P°P±Ps PSP°PIC-C,CH P·BŞ™ CIPIP»CIJC,PëCfCI
PiC-CfP»CI PiCŞPëPiPëPSPµPSPSCIJ P»C-PeCfPIP°PSPSCIJ.

PhCŞC,PsCfC,P°C,PëC±PSP° PiC-PiPsC,PµPSP·C-CIJ

PkPµC±P°CfC,Ps PiPsPIC-PrPsPjP»CIJ»PsCfCIJ PiCŞPs PIPëPiP°PrPePë
PsCŞC,PsCfC,P°C,PëC±PSPsC— PiC-PiPsC,PµPSP·C-C— Cf PiP°C†C-C”PSC,C-PI
P»C-C,PSCŞPsPiPs PIC-PeCf PI PiCŞPsC†PµCfC- PeP»C-PSC-C±PSPëC...
PrPsCfP»C-PrP¶PµPSCŞ. PµC-Pr C±P°Cf P·P°CfC,PsCfCfPIP°PSPSCIJ PsP»P°PSP·P°PiC-PSCf
CŞPµPePsPjPµPSPPrCfC”C,CHCfCIJ PiPµCŞC-PsPrPëC±PSPµ PIPëPjC-CŞCHPIP°PSPSCIJ
P°CŞC,PµCŞC-P°P»CHPSPsPiPs C,PëCfPeCf PiP°C†C-C”PSC,P°Pj PIC-PePsPj PIC-Pr 65
CŞPsPeC-PI.

P P°PiC,PsPIP° CfPµCŞC†PµPIP° CfPjPµCŞC,CH

PJ PiPsCfC,PjP°CŞPePµC,PëPSPiPsPIPëC... P·PIC-C,P°C... PiPsPIC-PrPsPjP»CIJ»PsCfCIJ
PiCŞPs PIPëPiP°PrPePë CŞP°PiC,PsPIPsC— CfPµCŞC†PµPIPsC— CfPjPµCŞC,C-
PiP°C†C-C”PSC,C-PI, CIJPeC- PiCŞPëPNëPjP°P»Pë PsP»P°PSP·P°PiC-PS.
P’C-PrPiPsPIC-PrPSPs PrPs CŞPµC,CŞPsCfPiPµPeC,PëPIPSsPiPs
PsP±CfPµCŞPIP°C†C-PNëPSPsPiPs PePsPiPsCŞC,PSPsPiPs PrPsCfP»C-PrP¶PµPSPSCIJ
CŞPëP·PëPe CŞP°PiC,PsPIPsC— CfPµCŞC†PµPIPsC— CfPjPµCŞC,C- Cf
PiP°C†C-C”PSC,C-PI, CIJPeC- P·P°CfC,PsCfPsPICfPIP°P»Pë PsP»P°PSP·P°PiC-PS,
PiC-PrPIPëC%oCfPIP°PICfCIJ PjP°PNëP¶Pµ PIPrPIC-C±C- PiPsCŞC-PIPSCIJPSPs P·
PiP°C†C-C”PSC,P°PjPë, CIJPeC- PSPµ P·P°CfC,PsCfPsPICfPIP°P»Pë
P°PSC,PëPiCfPëC...PsC,PëPePë. P PëP·PëPe PiCŞPë P·P°CfC,PsCfCfPIP°PSPSC-
PsP»P°PSP·P°PiC-PSCf PIC-PrPiPsPIC-PrP°C” C,P°PePsPjCf PiCŞPë
P·P°CfC,PsCfCfPIP°PSPSC- P°C,PëPiPsPIPëC... P°PSC,PëPiCfPëC...PsC,PëC±PSPëC...
P»C-PeP°CŞCfCHPePëC... P·P°CfPsP±C-PI, C%oPs P±CfP»Pë PIPeP»CHC±PµPSC- PrPs
PsP±BŞ™ C”PrPSP°PSPsPiPs P°PSP°P»C-P·Cf.

P”C-C,Pë C- PiC-PrP»C-C,PePë

PhP»P°PSP·P°PiC-PS PSPµ CŞPµPePsPjPµPSPPrPsPIP°PSPëPNë PrP»CIJ P»C-PeCfPIP°PSPSCIJ
PrC-C,PµPNë C,P° PiC-PrP»C-C,PeC-PI. PJ PiCŞPsC†PµCfC- PrPsCfP»C-PrP¶PµPSPSCIJ
PiP°C†C-C”PSC,C-PI PIC-PePsPj 13-17 CŞPsPeC-PI P·P°C,,C-PeCfPsPIP°PSPs CŞC-P·PSC-
PiPsP±C-C±PSC- CŞPµP°PeC†C-C—: P·P±C-P»CHCëPµPSPSCIJ PjP°CfPë C,C-P»P°, P·PjC-PSCf
PjPµC,P°P±PsP»C-C±PSPëC... PiP°CŞP°PjPµC,CŞC-PI C,P° P·P±C-P»CHCëPµPSPSCIJ
CŞC-PIPSCIJ PiCŞPsP»P°PeC,PëPSCf. P PµP·CfP»CHC,P°C,Pë, C%oPs P±CfP»Pë
PiPsPiBŞ™ CIJ·P°PSC- P· C†PëPjPë PiPsP±C-C±PSPëPjPë PrC-CIJPjPë, PSPµ
PrPsCfP»C-PrP¶CfPIP°P»PëCfCH C- P·P°P»PëCëP°CŞC,CHCfCIJ PSPµPIC-PrPsPjPëPjPë
(PrPëPI. CŞPsP·PrC-P»Pë B«PαP°CŞPjP°PePsP»PsPiC-C±PSC- PIP»P°CfC,PëPIPsCfC,C-B» C,P°
B«PµPsP±C-C±PSC- CŞPµP°PeC†C-C-B»).

$\text{P}_{\mu}\text{C}\bar{\text{H}}\text{P}\ddot{\text{e}} \text{ PrPsC}\bar{\text{r}}\text{P}\rangle\text{C-PrP}\|\text{P}_{\mu}\text{PSPSC- P}\cdot\text{PrPsC}\bar{\text{H}}\text{PsPIP}\ddot{\text{e}}\text{C}\dots \text{P}\|\text{C-PSPsPe, ClPeC- PiPsPrC}\bar{\text{r}}\text{PIP}^{\circ}\text{P}\rangle\ddot{\text{P}}\ddot{\text{e}}$
 $\text{PiC}\bar{\text{H}}\text{C}\bar{\text{r}}\text{PrPrC}\bar{\text{H}}, \text{PsP}\rangle\text{P}^{\circ}\text{PSP}\cdot\text{P}^{\circ}\text{PiC-PS P}\pm\text{C}\bar{\text{r}}\text{P}\rangle\text{Ps PIP}\ddot{\text{e}}\text{ClPIP}\rangle\text{P}_{\mu}\text{PSPs C}\bar{\text{r}} \text{PiC}\bar{\text{H}}\text{C}\bar{\text{r}}\text{PrPSPsPjC}\bar{\text{r}}$
 $\text{PjPsP}\rangle\text{PsC}\bar{\text{t}}\text{C-}. \text{P}\ddot{\text{Y}}\text{P}_{\mu}\text{C}\bar{\text{H}}\text{P}_{\mu}\text{PrPSC}\bar{\text{t}} \text{PrPsP}\cdot\text{P}^{\circ} \text{PrP}\rangle\text{Cl PSP}_{\mu}\text{PjPsPIP}\rangle\text{ClC,}\ddot{\text{P}}\ddot{\text{e}} (\text{PjPi/PePi}) \text{P}\pm\text{P}_{\mu}\text{P}\cdot$
 $\text{C}\bar{\text{H}}\text{P}\ddot{\text{e}}\text{P}\cdot\ddot{\text{P}}\text{ePeC}\bar{\text{r}} \text{PrP}\rangle\text{Cl PSCH}\bar{\text{H}}\text{PsPiPs PsC}\bar{\text{t}}\text{C-PSCH}\bar{\text{H}}\text{PIP}^{\circ}\text{P}\rangle\text{P}^{\circ}\text{C}\bar{\text{t}}\text{Cl ClPe } 1,8 \%$

PjP°C, PμCḡPēPSCÍCHPePsC— PrPsP·Pē (PjPi/PePi). PμP°C†C-C''PSC, PeP°Pj PSPμ
CḡPμPePsPjPμPSPPrCfC''C, CHCÍCḡ PiPsPrCfPIP°C, Pē PSPμPjPsPIP»CḡC, PiCḡCfPrPrCḡ,
CḡPeC‰Ps PIPsPSPē PiCḡPēPNPjP°CḡC, CH PsP»P°PSP·P°PīC-PS.

*P—PrP°C, PSC—CÍC, CH PIPiP»PēPIP°C, Pē PSP° CēPIPēPrPeC—CÍC, CH CḡPμP°PeC†C— PiCḡPē
PePμCḡCáPIP°PSPSC— P°PIC, PsC, CḡP°PSCÍPiPsCḡC, PsPj P°P±Ps C—PSCēPēPjPē
PjPμC...P°PSC—P·PjP°PjPē.*

P''PSCÍP»C—PrP¶PμPSCḡ PIPiP»PēPICf PsP»P°PSP·P°PīC—PSCf PSP° CēPIPēPrPeC—CÍC, CH
CḡPμP°PeC†C— PiCḡPē PePμCḡCfPIP°PSPSC— P°PIC, PsC, CḡP°PSCÍPiPsCḡC, PsPj P°P±Ps
CḡPsP±PsC, C— P· C—PSCēPēPjPē PjPμC...P°PSC—P·PjP°PjPē PSPμ PiCḡPsPIPsPrPēP»Pē.
PhCÍPeC—P»CHPePē PsP»P°PSP·P°PīC—PS PjPsP¶Pμ CÍPiCḡPēC†PēPSPēC, Pē
CÍPsPSP»PēPIC—CÍC, CH C, P° P·P°PīP°PjPsCḡPsC†PμPSPSCḡ, PiP°C†C—C''PSC, C—PI CÍP»C—Pr
PiPsPiPμCḡPμPrPēC, Pē PiCḡPs PSPμP±PμP·PiPμPeCf, PiPsPIBḡ™ CḡP·P°PSCf P·
PμPeCÍPiP»CfP°C, P°C†C—C''Cḡ PjPμC...P°PSC—P·PjC—PI, Cf C, .C†.
P°PIC, PsC, CḡP°PSCÍPiPsCḡC, PSPēC... P·P°CÍPsP±C—PI.

PŸPiPsCÍC—P± P·P°CÍC, PsCÍCáPIP°PSPSCḡ C, P° PrPsP·Pē.

P''PsCḡPsCÍP»C—

*PēPēP·PsC,, CḡPμPSC—Cḡ. P PμPePsPjPμPSPPrPsPIP°PSP° PiPsC†P°C, PePsPIP° PrPsP·P°
PsP»P°PSP·P°PīC—PSCf CÍC, P°PSPsPIPēC, CH 10 PjPi 1 CḡP°P· PSP° PrPsP±Cf.*

*PḡP°PSC—P°PeP°P»CHPSC— PμPiC—P·PsPrPē. P PμPePsPjPμPSPPrPsPIP°PSP° PiPsC†P°C, PePsPIP°
PrPsP·P° PsP»P°PSP·P°PīC—PSCf CḡPe PjPsPSPsC, PμCḡP°PiC—C— CÍC, P°PSPsPIPēC, CH
B B B B 15 PjPi PSP° PrPsP±Cf P°P±Ps 10 PjPi PSP° PrPsP±Cf PiCḡPē
PePsPjP±C—PSPsPIP°PSPsPjCf P»C—PeCfPIP°PSPSC—.*

*PμCḡPsC,, C—P»P°PeC, PēPeP° PiPsPIC, PsCḡPSPēC... PSP°PiP°PrC—PI Cá PiP°C†C—C''PSC, C—PI P·
P±C—PiPsP»CḡCḡPSPēPjPē CḡPsP·P»P°PrP°PjPē. P PμPePsPjPμPSPPrPsPIP°PSP°
PiPsC†P°C, PePsPIP° PrPsP·P° CÍC, P°PSPsPIPēC, CH 10 PjPi PSP° PrPsP±Cf. PμP°C†C—C''PSC, Pē P·
P±C—PiPsP»CḡCḡPSPēPjPē CḡPsP·P»P°PrP°PjPē, CḡPeC— PsC, CḡPēPjCfPIP°P»Pē
PsP»P°PSP·P°PīC—PS PrP»Cḡ P»C—PeCfPIP°PSPSCḡ PjP°PSC—P°PeP°P»CHPSPēC...
PμPiC—P·PsPrC—PI, PiCḡPsPrPsPIP¶CfCḡC, CH PsC, CḡPēPjCfPIP°C, Pē PsP»P°PSP·P°PīC—PS Cf
C, PsPjCf P¶ PrPsP·CfPIP°PSPSC— C— PrP»Cḡ PiCḡPsC,, C—P»P°PeC, PēPePē PiPsPIC, PsCḡPSPēC...
PSP°PiP°PrC—PI. P—P° CfPjPsPIPē CḡPsP·PIPēC, PeCf PSPsPIPsPiPs
PjP°PSC—P°PeP°P»CHPSPsPiPs, PrPμPiCḡPμCÍPēPIPSsPiPs P°P±Ps P·PjC—CēP°PSPsPiPs
PμPiC—P·PsPrCf P»C—PeCfPIP°PSPSCḡ PSPμPsP±C...C—PrPSPs PiCḡPsPrPsPIP¶CfPIP°C, Pē (Cf
CḡP°P·C— PSPμPsP±C...C—PrPSPsCÍC, C— PsPiC, PēPjC—P·CfPIP°PICēPē PrPsP·Cf) CḡP°P·PsPj C—P·
PiC—PrC, CḡPēPjCfCḡC†PsCḡ C, PμCḡP°PiC—C''Cḡ PrP»Cḡ P»C—PeCfPIP°PSPSCḡ
CÍPēPjPiC, PsPjC—PI PiPsCḡCfCēPμPSPSCḡ PSP°CÍC, CḡPsCḡ, CḡPeC‰Ps C'' PeP»C—PSC—C†PSP°
PSPμPsP±C...C—PrPSC—CÍC, CH.*

*P>C—PeCáPIP°PSPSCḡ CēPēP·PsC,, CḡPμPSC—C—, PjP°PSC—P°PeP°P»CHPSPēC... PμPiC—P·PsPrC—PI
C, P° PiPsPiPμCḡPμPrP¶PμPSPSCḡ CḡPμC†PēPrPēPIC—PI P±C—PiPsP»CḡCḡPSPsPiPs
CḡPsP·P»P°PrCá. P©PsPrPμPSPSCf PrPsP·Cf CÍP»C—Pr PIPēP·PSP°C†P°C, Pē PSP°
PiC—PrCÍC, P°PIC— PeP»C—PSC—C†PSPsPiPs CÍC, P°C, CfCÍCf PI PrC—P°PiP°P·PsPSC— PIC—Pr 5 PrPs
B B B B B 20 PjPi PSP° PrPsP±Cf. P—P±C—P»CHCēPμPSPSCḡ CḡPμPePsPjPμPSPPrPsPIP°PSPsC—*

PiPsC†P°C,PePsPIPsC— PrPsP·Pë PiCḡPsPIPsPrPëC,Pë P· C-PSC,PμCḡPIP°P»P°PjPë PSPμ
PjPμPSC€Pμ 24 PiPsPrPëPS P»PëC€Pμ PiC-CḡP»Cḡ PeP»C-PSC-C†PSPsPiPs
PsP±CḡC,PμPḡPμPSPSCḡ. PhP»P°PSP·P°PiC-PS PiPsC,CḡC-P±PSPs P·P°CḡC,PsCḡPsPICḡPIP°C,Pë
PSPμP·P°P»PμPḡPSPs PIC-Pr PIPḡPëPIP°PSPSCḡ C—PḡC-, PsCḡPeC-P»CHPePë C—PḡP° PSPμ
PIPiP»PëPIP°C” PSP° P°P±CḡPsCḡP±C†C-Cḡ PiCḡPμPiP°CḡP°C,Cḡ. PμCḡPë PIC-PrPjC-PSC-
PiCḡPμPiP°CḡP°C,Cḡ P·P°PIPμCḡC€PμPSPSCḡ C,PμCḡP°PiC-C— PiPsC,CḡC-P±PSPs
PiCḡPsPIPsPrPëC,Pë PiPsCḡC,CḡPiPsPIPs.

PŷP°P±P»PμC,PeCḡ, C%oPs PrPëCḡPiPμCḡPiCḡC”C,CHCḡCḡ PI CḡPsC,PsPIC-PNë
PiPsCḡPsPḡPSPëPSC-, PSPμPsP±C...C-PrPSPs PiPsPjC-CḡC,PëC,Pë Cḡ CḡPsC,, PrPμ PIPsPSP°
C€PIPëPrPePs CḡPsP·PiP°PrP°C”C,CHCḡCḡ. PhCḡPeC-P»CHPePë C,P°P±P»PμC,PeP°, C%oPs
PrPëCḡPiPμCḡPiCḡC”C,CHCḡCḡ PI CḡPsC,PsPIC-PNë PiPsCḡPsPḡPSPëPSC-, PeCḡPëC...PeP°,
C—C— CḡP»C-Pr PiCḡPëPNëPjP°C,Pë PIC-PrCḡP°P·Cḡ PiC-CḡP»Cḡ PIC-PrPeCḡPëC,C,Cḡ
P±P»C-CḡC,PμCḡP°. PhP»CHC,PμCḡPSP°C,PëPIPSs, P±PμP·PiPsCḡPμCḡPμPrPSCḡPs
PiPμCḡPμPr P·P°CḡC,PsCḡCḡPIP°PSPSCḡPj C,P°P±P»PμC,PeP° PjPsPḡPμ P±CḡC,Pë
CḡPsP·C†PëPSPμPSP° Cḡ PiPsPIPsC-PNë CḡPeP»CḡPSC†C- PIPsPrPë P°P±Ps C-PSC€PsPiPs
PSP°PiPsCḡ (P°PiPμP»CHCḡPëPSPsPIPëPNë CḡC-Pe, CḡP±P»CḡC†PSPëPNë CḡC-Pe, PjPsP»PsPePs
P°P±Ps PeP°PIP°).

PhCḡPsP±P»PëPIC- PiCḡCḡPiPë PiP°C†C-C”PSC,C-PI

PμP°C†C-C”PSC,Pë P»C-C,PSCḡPsPiPs PIC-PeCḡ

PμCḡPëP·PSP°C†PμPSPSCḡ PjPμPSC€PsC— PiPsC†P°C,PePsPIPsC— PrPsP·Pë (5 PjPi PSP°
PrPsP±Cḡ) P·P°P·PIPëC†P°PNë PSPμ PiPsC,CḡC-P±PSPμ. PḡPμPsP±C...C-PrPSC-CḡC,CH
PiCḡPëP·PSP°C†PμPSPSCḡ PjPμPSC€PsC— PiPsC†P°C,PePsPIPsC— PrPsP·Pë
PiPsC,CḡC-P±PSPs CḡPsP·PiP»CḡPrP°C,Pë PrP»Cḡ PiP°C†C-C”PSC,C-PI PIC-PePsPj
PIC-Pr 65 CḡPsPeC-PI PiCḡPë PSP°CḡPIPSsCḡC,C- PeP»C-PSC-C†PSPëC...
PiPsPeP°P·P°PSCḡ (PrPëPI. CḡPsP·PrC-P» B«PhCḡPsP±P»PëPIPsCḡC,C-
P·P°CḡC,PsCḡCḡPIP°PSPSCḡB»).

*PμP°C†C-C”PSC,Pë P· PSPëCḡPePsPIPsCḡ C,P°/P°P±Ps PiPμC†C-PSPePsPIPsCḡ
PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ*

PḡPμPSC€Cḡ PiPsC†P°C,PePsPICḡ PrPsP·Cḡ (5 PjPi PSP° PrPsP±Cḡ) PjPsPḡPSP°
PiCḡPëP·PSP°C†P°C,Pë C,P°PePëPj PiP°C†C-C”PSC,P°Pj. Pj CḡP°P·C-
PSP°CḡPIPSsCḡC,C- PiPsPjC-CḡPSPsC— PiPμC†C-PSPePsPIPsC—
PSPμPrPsCḡC,P°C,PSPsCḡC,C- (C†PëCḡPsP·, PeP»P°CḡPë PSPμPrPsCḡC,P°C,PSPsCḡC,C-
Ph P°P±Ps P’ P·P° C€PeP°P»PsCḡ PḡP°PNëP»PrP° PμBḡ™ Cḡ) PiPsC†P°C,PePsPIP° PrPsP·P°
PiPsPIPëPSPSP° CḡC,P°PSPsPIPëC,Pë 5 PjPi, PiC-PrPIPëC%oCḡPIP°C,Pë PrPsP·Cḡ
PSPμPsP±C...C-PrPSPs P· PsP±PμCḡPμPḡPSC-CḡC,Cḡ.

PŸC,P°C,CH

PḡPsCḡPμPeC†C-Cḡ PrPsP·Pë P·P°P»PμPḡPSPs PIC-Pr CḡC,P°C,C- PiP°C†C-C”PSC,P°
PSPμ PiPsC,CḡC-P±PSP°.

PμP°C†C-C”PSC,Pë, CḡPeC- PiP°P»CḡC,CH

PμPsC†P°C,PePsPIP° PrPsP·P° C,P° PePsP»PëPIP°PSPSCḡ PrPsP·Pë PSPμ PiPsPIPëPSPSC-
P·PjC-PSCḡPIP°C,PëCḡCḡ CḡCḡC,PëPSPSPëPj C†PëPSPsPj P·P°P»PμPḡPSPs PIC-Pr

PSP°CΠIPSPsCfC,C-/PIC-PrCfCfC,PSPsCfC,C- P·PIPëC‡PePë PrPs PïP°P»C-PSPSCΠ.
PḥPμC,P°P±PsP»C-P·Pj PsP»P°PSP·P°PïC-PSCr PjPsP¶Pμ P±CfC,Pë
C-PSPrCfPePsPIP°PSPëPNë PïP°P»C-PSPSCΠPj C,CḥC,CḥPSCr.
P PμPePsPjPμPSPrCfC”C,CḥCfCΠ PjPsPSC-C,PSCḥPëPSPi PeP»C-PSC-C‡PSPsPiPs
CfC,P°PSCr, Cḥ CḥP°P·C- PSPμPsP±C...C-PrPSPsCfC,C- Bḥ” CḥPsP·PiP»CΠPr
P·P±C-P»CḥC€PμPSPSCΠ PrPsP·Pë PsP»P°PSP·P°PïC-PSCr (PrPëPI. CḥPsP·PrC-P»
B«P’P·P°C”PjPsPrC-CΠ P· C-PSC€PëPjPë P»C-PeP°CḥCfCḥPePëPjPë P·P°CfPsP±P°PjPë
C,P° C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PNëB»). PïPeC%Ps PSP°CΠIPSPëPNë
P±C-P»CḥC€Pμ PSC-P¶ PsPrPëPS C,,P°PeC,PSCḥ, CΠPePëPNë PjPsP¶Pμ
PIPïP»PëPSCrC,Pë PSP° CfPïPsPIC-P»CḥPSPμPSPSCΠ PjPμC,P°P±PsP»C-P·PjCf
(P¶C-PSPsC‡P° CfC,P°C,Cḥ, PiPsC...PëP»PëPNë PIC-Pe, PIC-PrCfCfC,PSC-CfC,Cḥ
P·PIPëC‡PePë PrPs PïP°P»C-PSPSCΠ), CfP»C-Pr CḥPsP·PiP»CΠPrP°C,Pë PjPsP¶P»PëPIPμ
P·PSPëP¶PμPSPSCΠ PiPsC‡P°C,PePsPIPSC— PrPsP·Pë. PḥC-PrPIPëC%PμPSPSCΠ
PrPsP·Pë PïCḥPë PïPsPeP°P·P°PSPSCΠC... PrPs C‡CḥPsPiPs CfP»C-Pr
PïCḥPsPIPsPrPëC,Pë PePsPSCfPμCḥPIP°C,PëPIPSPs. Pj PIPëPïP°PrPeP°C..., PePsP»Pë
PïC-PrPIPëC%PμPSPSCΠ PrPsP·Pë PSP° 2,5 PjPi PIPIP°P¶P°C”C,CḥCfCΠ
PSPμPsP±C...C-PrPSPëPj, CfP»C-Pr PIPëPePsCḥPëCfC,PSPICfPIP°C,Pë C-PSC€C-
P»C-PeP°CḥCfCḥPeC- C,,PSCḥPjPë PsP»P°PSP·P°PïC-PSCr, CΠPeC-
PrPsP·PIPSP»CΠCḥC,Cḥ PrPsP·CfPIP°C,Pë 2,5 PjPi.

P”C-C,Pë

PḥP»P°PSP·P°PïC-PS PSPμ CḥPμPePsPjPμPSPrCfC”C,CḥCfCΠ
P·P°CfC,PSCfPsPICfPIP°C,Pë PrC-C,CΠPj PIC-PePsPj PrPs 18 CḥPsPeC-PI, PsCfPeC-P»CḥPePë
PSPμPjP°C” PrPsCfC,P°C,PSC-C... PrP°PSPëC... C%PsPrPs P±PμP·PïPμPePë C,P°
PμC,,PμPeC,PëPIPSPsCfC,C- PNëPsPiPs P·P°CfC,PSCfCfPIP°PSPSCΠ.

PμPμCḥPμPrPsP·CžPIP°PSPSCΠ.

P”CfP¶Pμ PiPsC€PëCḥPμPSPëPjPë CfPëPjPiC,PsPjP°PjPë PïPμCḥPμPrPsP·CfPIP°PSPSCΠ
(>10 %) C” C,P°C...C-PeP°CḥPrC-CΠ, P°P¶PëC,P°C‡C-CΠ/P°PiCḥPμCfPëPIPSC-CfC,Cḥ,
PrPëP·P°CḥC,CḥC-CΠ, CḥC-P·PSC- PμPeCfC,CḥP°PïC-CḥP°PjC-PrPSC-
CfPëPjPiC,PsPjPë C,P° P·PSPëP¶PμPSPëPNë CḥC-PIPμPSCḥ CfPIC-PrPsPjPsCfC,C-,
C%Ps PIP°CḥC-CḥC”C,CḥCfCΠ PIC-Pr CfPμPrP°C‡C-C— PrPs PePsPjPë.

P‡PSC€PëPjPë P·PSP°C‡PSPëPjPë CfCfPeP»P°PrPSPμPSPSCΠPjPë
PïPμCḥPμPrPsP·CfPIP°PSPSCΠ C” PrPμP»C-CḥC-PNë, CfCfPrPsPjPë, PePsPjP°,
PjPsP¶P»PëPIC-CfC,Cḥ PSPμPNëCḥPsP»PμPiC,PëC‡PSPsPiPs P·P»PsCΠPeC-CfPSPsPiPs
CfPëPSPrCḥPsPjCf, PïCḥPëPiPSC-C‡PμPSPSCΠ PrPëC...P°PSPSCΠ,
P°CfPiC-CḥP°C‡C-CΠ, P°CḥC,PμCḥC-P°P»CḥPSP° PiC-PïPμCḥC,PμPSP·C-CΠ P°P±Ps
PiC-PiPsC,PμPSP·C-CΠ, CfPμCḥC‡PμPIP° P°CḥPëC,PjC-CΠ (< 2 % PIPëPïP°PrPeC-PI
PïPμCḥPμPrPsP·CfPIP°PSPSCΠ) C,P° PeP°CḥPrC-PsPiCfP»CḥPjPsPSP°P»CḥPSPëPNë
C€PsPe. P>PμC,P°P»CḥPSC- PSP°CfP»C-PrPePë PIC-PrP·PSP°C‡P°P»PëCfCΠ PïCḥPë
PiPsCfC,CḥPsPjCf PïPμCḥPμPrPsP·CfPIP°PSPSC- PSP° CḥC-PIPSC- PrPs 450 PjPi,
P°P»Pμ P±CfP»Pë PNë PIPëPïP°PrPePë PIPëP¶PëPIP°PSPSCΠ PïC-CfP»CΠ

PiPsCfC, CḡPsPiPs PīPμCḡPμPrPsP·CfPIP°PSPSClI PīC-CfP»Cḡ PīCḡPēPNḡPsPjCf B 2 Pi PsP»P°PSP·P°PīC-PSCf PīPμCḡPsCḡP°P»CHbPSPs.

P>C-PeCzPIP°PSPSClI

PŸPīPμC†PēC,,C-C†PSPsPiPs P°PSC,PēPrPsC,Cf PSPμPjP°C". PkPμ CḡPμPePsPjPμPSPrCfCḡC,CHbCfCḡ PīCḡPμPīP°CḡP°C,Pē, C%Ps CfPīCḡPēC†PēPSClIChC,CHb P±P»CḡPIP°PSPSClI. P PμPePsPjPμPSPrPsPIP°PSPs CfC,P°PSPrP°CḡC,PSC- PīCḡPsC†PμPrCfCḡPē PīCḡPē PīPμCḡPμPrPsP·CfPIP°PSPSC- (PSP°PīCḡPēPeP»P°Pr, PīCḡPsPjPēPIP°PSPSClI CēP»CfPSPeP°, PīCḡPēPNḡPsPj P°PeC,PēIPsPIP°PSPsPiPs PICfPiC-P»P»Cḡ). P"PsPIPμPrPμPSPs, C%Ps CfCfPīCfC,PSC-PNḡ PīCḡPēPNḡPsPj P°PeC,PēIPsPIP°PSPsPiPs PICfPiC-P»P»Cḡ P·PjPμPSCēCfC" P±C-PsPrPsCfC,CfPīPSC-CfC,CHb PsP»P°PSP·P°PīC-PSCf PīCḡPē PīPμCḡPsCḡP°P»CHbPSPsPjCf PīCḡPēPNḡPsPjC- PSP° 50-60 %.

P'C-PrPīPsPIC-PrPSPs PrPs PeP»C-PSC-C†PSPēC... PīCḡPsCḡPIC-PI CfP»C-Pr PSP°P»P°PiPsPrPēC,Pē CfPēPjPīC,PsPjP°C,PēC†PSPμ P»C-PeCfPIP°PSPSClI C,P° PjPsPSC-C,PsCḡPēPSPi P¶PēC,C,C"PIPs PIP°P¶P»PēPIPēC... C,,CfPSPeC†C-PNḡ, PIPEP»CḡC†P°CḡC†Pē P»C-PeCfPIP°PSPSClI P°CḡC,PμCḡC-P°P»CHbPSPsC— PiC-PīPsC,PμPSP·C-C— C,P° C†PēCḡPeCfP»CḡC,PsCḡPSPsC— PSPμPrPsCfC,P°C,PSPsCfC,C-, P° C,P°PePsP¶ PīC-PrC,CḡPēPjP°PSPSClI PrPēC...P°PSPSClI. PkPμ P·P°CfC,PsCfPsPICfPIP°C,Pē P°PrCḡPμPSP°P»C-PS, PrPsPīP°PjC-PS C,P° C-PSCēC- CfPēPjPīP°C,PsPjC-PjPμC,PēPePē P· PrC-C"Ch, C...P°CḡP°PeC,PμCḡPSPsCh PrP»Cḡ P±PμC,P°-P°PiPsPSC-CfC,C-PI, PsCfPeC-P»CHbPePē P±PμC,P°-CfC,PēPjCfP»CḡC†C-Cḡ PjPsP¶Pμ PīPsPiC-CḡCēPēC,Pē PīCḡPsCḡPIPē PiC-PīPsC,PsPSC-C—. P"P»Cḡ PIPēCḡPIP»PμPSPSClI PjPsP¶P»PēIPsC— P°CḡPēC,PjC-C— PSPμPsP±C...C-PrPSPēPNḡ PjPsPSC-C,PsCḡPēPSPi CfPμCḡC†PμPIPs- CfCfPrPēPSPSPsC— CfPēCfC,PμPjPē. P PμC,PμP»CHbPSPēPNḡ PjPμPrPēC†PSPēPNḡ PSP°PiP»CḡPr C,P° PjPsPSC-C,PsCḡPēPSPi PīPsPIPēPSPμPS C,CḡPēPIP°C,Pē PrPs PīPsPIPSPsPiPs PsPrCfP¶P°PSPSClI PīP°C†C-C"PSC,P°.

PμPsP±C-C†PSC- CḡPμP°PeC†C-C—.

PkP°PNḡC†P°CfC,C-CēC- PīPsP±C-C†PSC- CḡPμP°PeC†C-C— (CfPīPsCfC,PμCḡC-PiP°P»PēCfCḡ Cf ≥ 1 % PīP°C†C-C"PSC,C-PI), PīPsPIbḡ™ CḡP·P°PSC- P·C- P·P°CfC,PsCfCfPIP°PSPSClI Pj PsP»P°PSP·P°PīC-PSCf PI PīCḡPsC†PμCfC- PeP»C-PSC-C†PSPēC... PrPsCfP»C-PrP¶PμPSCḡ: CfPsPSP»PēPIC-CfC,CHb, P·P±C-P»CHbCēPμPSPSClI PjP°CfPē C,C-P»P°, PμPsP·PēPSPsC,,C-P»C-Cḡ, PīC-PrPIPēC%PμPSPSClI CḡC-PIPSClI PīCḡPsP»P°PeC,PēPSCf, C...PsP»PμCfC,PμCḡPsP»Cf (C...PsP»PμCfC,PμCḡPēPSCf), PiP»CḡPePsP·Pē C,P° C,CḡPēPiP»C-C†PμCḡPēPrC-PI Cf PeCḡPsPIC-, PiP»CḡPePsP·CfCḡC-Cḡ, PīC-PrPIPēC%PμPSPSClI P°PīPμC,PēC,Cf, P·P°PiP°PjPsCḡPsC†PμPSPSClI, P°PeP°C,PēP·C-Cḡ, PīP°CḡPeC-PSCfPsPSC-P·Pj, P»PμPNḡPePsPīPμPSC-Cḡ, PSPμPNḡC,CḡPsPīPμPSC-Cḡ, PrPēCfPeC-PSPμP·C-Cḡ, PsCḡC,PsCfC,P°C,PēC†PSP° PiC-PīPsC,PμPSP·C-Cḡ, P°PSC,PēC...PsP»C-PSPμCḡPiC-C†PSC- PμC,,PμPeC,Pē, C,CḡP°PSP·PēC,PsCḡPSPμ P°CfPēPjPiC,PsPjP°C,PēC†PSPμ PīC-PrPIPēC%PμPSPSClI PīPμC†C-PSPePsPIPēC... C,CḡP°PSCfP°PjC-PSP°P, PIPēCfPēPīP°PSPSClI, P°CfC,PμPSC-Cḡ, PīC-PrPIPēC%PμPSP° PIC,PsPjP»CḡPIP°PSC-CfC,CHb, PiC-PīPμCḡC,PμCḡPjC-Cḡ, P°CḡC,CḡP°P»PiC-Cḡ, PīC-PrPIPēC%PμPSPSClI CḡC-PIPSClI P°P»PeP°P»C-PSC,,PsCfC,,P°C,P°P·Pē,

P— P±PsPeCf CГPеPμP»PμC,PSPs-PjбГ™ CГP-PsPIPsC— C,P° CГPиPsP»CfC±PSPsC— CГPеCГC,PμPj PbГГC,CГP°P»PiC-CГ ⁹	P P°P±PrPsPjC-PsP»C-P. ¹¹
P— P±PsPeCf PSPеCГPsPe C,P° CГPμC±PsPIPеPrC-P»CHbPSPsC— CГPеCГC,PμPjPе PкPμC,CГPеPjP°PSPSCГ CГPμC±C-, P-P°C,CГPеPjPеP° CГPμC±C-, CfC,CГCfPrPSPμPSPμ CГPμC±PsPIPеPiCfCГPеP°PSPSCГ ¹¹	
P°P°PiC-C,PSC-CГC,CHb, PiC-CГP»CГCГPsPrPsPIPеPNе C,P° PiPμCГPеPSP°C,P°P»CHbPSPеPNе PiPμCГC-PsPr	PŸPеPSPPrCГPsPj PIC-PrPjC-PSPе Cf PSPsPIPsPSP°CГPsPr- P¶PμPSPеC...
P— P±PsPeCf CГPμPiCГPsPrCfPeC,PеPIPSPsC— CГPеCГC,PμPjPе C,P° PjPsP»PsC±PSPеC... P-P°P»PsP- P•CГPμPeC,PеP»CHbPSP° PrPеCГC,,CfPSPeCГC-CГ Cf C±PsP»PsPIC-PeC-PI, P-PSPеP¶PμPSPSCГ P»C-P±C-PrPs Cf P¶C-PSPsPe C,P° C±PsP»PsPIC-PeC-PI	PμCГC-P°PiC-P-Pj ¹² PbPjPμPSPsCГPμCГ, P-P±C-P»CHbCеPμPSPSCГ PiCГCfPrPμPNе, PiP°P»P°PeC,PsCГPμCГ Cf P¶C-PSPsPe, PiC-PSPμPePsPjP°CГC,C-CГ/ P-P±C-P»CHbCеPμPSPSCГ PiCГCfPrPμPNе Cf C±PsP»PsPIC-PeC-PI
P—P°PiP°P»CHbPSC- CГPsP-P»P°PrPе C,P° PsCГPsP±P»PеPIPsCГC,C- P-P°CГC,PсCГCfPIP°PSPSCГ PbCГC,PμPSC-CГ, PiC-PrPIPеC%PμPSP° PIC,PsPjP»CГPIP°PSC-CГC,CHb, PSP°P±CГCГPePе, PiC-CГPμPeCГC-CГ ¹⁰	
P°C-P°PiPSPsCГC,PеC±PSC- PrPsCГP»C-PrP¶PμPSPSCГ PμC-PrPIPеC%PμPSPSCГ PμC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ PePsPSCfPμPSC,CГP°CГC-C—P°P»PeP°P»C-PS- C,,PsCГC,,P°C,P°P-Pе ¹⁰ , PiCГPsP»P°PeC,PеPSCf Cf PiP°P°PjC- PeCГPsPIC- ⁸	PμC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ P-P°PiP°P»CHbPSPsPiPs P±C-P»C-CГCfP±C-PSCf
PeCГPμP°C,PеPSC,,PsCГC,,PsPeC-PSP°-P-Pе ¹¹ , PiC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ PiP°PjPjP°PiP»CfC,P°PjC-P»- C,CГP°PSCГC,PμCГP°P-Pе ¹⁰ , PiC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ CГPμC±PsPIPsC— PePеCГP»PsC,Pе ¹⁰	

¹ PлbP»C-PSC-C±PSPs P·PSP°C±CfC%Pμ P·P±C-P»CHbCеPμPSPSCГ PjP°CГPе C,C-P»P° CГPiPsCГC,PμCГC-PiP°P»PsCГCГ PI CrCГC-C... PeP°C,PμPiPsCГC-PNе PiP°CГC-C”PSC,C-PI P·P° P†PлbPŸ (C-PSPPrPμPeCГ PjP°CГPе C,C-P»P°). PμC-CГP»CГ PePsCГPsC,PePsC±P°CГPSPsPiPs P»C-PeCfPIP°PSPSCГ (CГPμCГPμPrPSCГ C,CГPеPIP°P»C-CГC,CHb CГC,P°PSPsPIPеP»P° 47 PrPSC-PI) P·P±C-P»CHbCеPμPSPSCГ PjP°CГPе C,C-P»P° PSP° ≥ 7 % CГPiPsCГC,PμCГC-PiP°P»PsCГCГ PrCfP¶Pμ C±P°CГC,Ps (22,2 % PIPеPiP°PrPeC-PI), PSP° ≥ 15 % CГPiPsCГC,PμCГC-PiP°P»PsCГCГ C±P°CГC,Ps (4,2 % PIPеPiP°PrPeC-PI), PSP° ≥ 25 % CГPiPsCГC,PμCГC-PiP°P»PsCГCГ PSPμC±P°CГC,Ps (0,8 % PIPеPiP°PrPeC-PI). Pj PiP°CГC-C”PSC,C-PI, CГPeC- PsC,CГPеPjCfPIP°P»Pе C,CГPеPIP°P»Cf C,PμCГP°PiC-CT (PiCГPеPSP°PNеPjPSC- PiCГPsC,CГPiPsPj 48 C,PеP¶PSC-PI), P·P±C-P»CHbCеPμPSPSCГ PjP°CГPе C,C-P»P° PSP° ≥ 7 %, ≥ 15 %, ≥ 25 % CГPiPsCГC,PμCГC-PiP°P»PsCГCГ PrCfP¶Pμ C±P°CГC,Ps (Cf 64,4 %, 31,7 %, 12,3 % PIPеPiP°PrPeC-PI PIC-PrPiPsPIC-PrPSPs).

² PŸPμCГPμPrPSC- PiC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ P»C-PiC-PrC-PI PSP°C,C%Pμ (P·P°PiP°P»CHbPSPеPNе C...PsP»PμCГC,PμCГPsP», P·PμPкP© C- C,CГPеPiP»C-C†PμCГPеPrPе) P±CfP»Pе P±C-P»CHbCе P·PSP°C±PSC- Cr PiP°CГC-C”PSC,C-PI, Cr CГPePеC... PrPs PiPsC±P°C,PeCf P»C-PeCfPIP°PSPSCГ PSPμ CГPiPsCГC,PμCГC-PiP°P»PsCГCГ P»C-PiC-PrPSPsC— PrPеCГCГPμPiCfP»CГCГC-C—.

³ PŸPiPsCГC,PμCГC-PiP°P»PsCГCГ Cr PiP°CГC-C”PSC,C-PI P· PSPsCГPjP°P»CHbPSPеPj PiPsC±P°C,PePsPIPеPj CГC-PIPSPμPj PSP°C,C%Pμ (< 5,17 PjPjPsP»CHb/P»), CГPePеPNе PiC-PrPIPеC%CrPIP°PICГCГ PrPs PIPеCГPsPePsPiPs (≥ 6,2 PjPjPsP»CHb/P»). P”CfP¶Pμ C±P°CГC,Ps PiPsPIC-PrPsPjP»CГP»PsCГCГ PiCГPs CГC-P·PePμ PiC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ P·P°PiP°P»CHbPSPsPiPs C...PsP»PμCГC,PμCГPsP»Cf PSP°C,C%Pμ P· PiPsC±P°C,PePsPIPsPiPs CГC-PIPSCГ (≥ 5,17 - < 6,2 PjPjPsP»CHb/P») PrPs PIPеCГPsPePsPiPs CГC-PIPSCГ B B B B B B B B B B B B B B (≥ 6,2 PjPjPsP»CHb/P»).

⁴ PŸPiPsCГC,PμCГC-PiP°P»PsCГCГ Cr PiP°CГC-C”PSC,C-PI P· PSPsCГPjP°P»CHbPSPеPj PiPsC±P°C,PePsPIPеPj CГC-PIPSPμPj PSP°C,C%Pμ (< 5,56 PjPjPsP»CHb/P»), CГPePеPNе PiC-PrPIPеC%CrPIP°PICГCГ PrPs PIPеCГPsPePsPiPs (≥ 7 PjPjPsP»CHb/P»). P”CfP¶Pμ C±P°CГC,Ps PiPsPIC-PrPsPjP»CГP»PsCГCГ PiCГPs CГC-P·PePμ PiC-PrPIPеC%PμPSPSCГ CГC-PIPSCГ PiP»CTPePsP·Pе PSP°C,C%Pμ P· PiPsC±P°C,PePsPIPsPiPs CГC-PIPSCГ (≥ 5,56 - < 7

PjPjPsP»CH/P») PrPs PIPëCÍPsPePsPiPs CĤC-PIPSCĬ (≥ 7 PjPjPsP»CH/P»).

⁵ PŸPİPsCÍC,PμCĤC-PİP°P»PsCÍCĬ Cr PİP°C†C-C”PSC,C-PI P· PSPsCĤPjP°P»CHPSPëPj PİPsC†P°C,PePsPIPëPj CĤC-PIPSPμPj PSP°C,C%Ps (< 1,69 PjPjPsP»CH/P»), CĬPePëPNë PİC-PrPIPëC%CrPIP°PICÍCĬ PrPs PIPëCÍPsPePsPiPs (≥ 2,26 PjPjPsP»CH/P»). P”CrP¶Pμ C†P°CÍC,Ps PİPsPIC-PrPsPjP»CĬP»PsCÍCĬ PİCĤPs CĤC-P·PePμ PİC-PrPIPëC%PμPSPSCĬ CĤC-PIPSCĬ C,CĤPëPİP»C-C†PμCĤPëPrC-PI PSP°C,C%Ps P· PİPsC†P°C,PePsPIPëPiPs CĤC-PIPSCĬ (≥ 1,69 - < 2,26 PjPjPsP»CH/P») PrPs PIPëCÍPsPePsPiPs CĤC-PIPSCĬ (≥ 2,26 PjPjPsP»CH/P»).

⁶ PμC-Pr C†P°CÍ PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PμPSCH C†P°CÍC,PsC,P° PIPëPSPëPePSPμPSPSCĬ PİP°CĤPeC-PSCÍPsPSC-P·PjCr C- PrPëCÍC,PsPSC-C— Cr PİP°C†C-C”PSC,C-PI, CĬPeC- PsC,CĤPëPjCrPIP°P»Pë P»C-PeCrPIP°PSPSCĬ PsP»P°PSP·P°PİC-PSPsPj, P±CrP»P° PIPëC%P°, P°P»Pμ PeP»C-PSC-C†PSPs PSPμP·PSP°C†PSPs, PİPsCĤC-PIPSCĬPSPs P· PİCĤCrPİPsCĤ, C%Ps PsC,CĤPëPjCrPIP°P»P° PİP»P°C†PμP±Ps. PŞP°CÍC,PsC,P° PIPëPSPëPePSPμPSPSCĬ PİP°CĤPeC-PSCÍPsPSC-P·PjCr, P°PeP°C,PëP·C-C— C- PrPëCÍC,PsPSC-C— Cr PİP°C†C-C”PSC,C-PI, CĬPeC- PsC,CĤPëPjCrPIP°P»Pë P»C-PeCrPIP°PSPSCĬ PsP»P°PSP·P°PİC-PSPsPj, P±CrP»P° PSPëP¶C†P°, PSC-P¶ PİCĤPë P·P°CÍC,PsCÍCrPIP°PSPSC- C,PëC,CĤPsPIP°PSPëC... PrPsP· PİP°P»PsPİPμCĤPëPrPsP»Cr. PŞPμCĤPμP· PIC-PrCÍCrC,PSC-CÍC,CH C-PSC„PsCĤPjP°C†C-C— PİCĤPs PSP°CĬPIPSC-CÍC,CH PI P°PSP°PjPSPμP·C- PİPsCÍC,CĤPëC... P°P±Ps PİC-P·PSC-C... PμPeCÍC,CĤP°PİC-CĤP°PjC-PrP°P»CHPSPëC... CĤCrC...PsPIPëC... PİPsCĤCrC€PμPSCH PSPμ PjPsP¶PSP° PICÍC,P°PSPsPIPëC,Pë, C%Ps PsP»P°PSP·P°PİC-PS PjPμPSC€Pμ CÍPİCĤPëC†PëPSCĬC” PİC-P·PSCĤ PrPëCÍPeC-PSPμP·C-CĤ C,P°/P°P±Ps C-PSC€C- PİC-P·PSC- PμPeCÍC,CĤP°PİC-CĤP°PjC-PrP°P»CHPSC- CÍPëPSPrCĤPsPjPë.

⁷ PJ PIPëPİP°PrPeCr CĤC-P·PePsPiPs PİCĤPëPİPëPSPμPSPSCĬ C,PμCĤP°PİC-C— PsP»P°PSP·P°PİC-PSPsPj PİPsPIC-PrPsPjP»CĬP»PsCÍCĬ PİCĤPs PİPsCÍC,CĤC- CÍPëPjPİC,PsPjPë: PİC-PrPIPëC%PμPSPμ PİPsC,PsPIPëPrC-P»PμPSPSCĬ, P±PμP·CÍPsPSPSCĬ, C,CĤPμPjPsCĤ, PIC-PrC†CrC,C,CĬ CÍC,CĤP°C...Cr, PSCrPrPsC,Cr C- P±P»CHPIP°PSPSCĬ.

⁸ PJ PİCĤPsC†PμCÍC- PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PμPSCH (PrPs 12 C,PëP¶PSC-PI) PIPëP·PSP°C†PμPSPs, C%Ps PePsPSC†PμPSC,CĤP°C†C-CĬ PİCĤPsP»P°PeC,PëPSCr Cr PİP»P°P·PjC- PeCĤPsPIC- PİPμCĤPμPIPëC%CrPIP°P»P° PIPμCĤC...PSC-PNë P»C-PjC-C, PSPsCĤPjPë Cr 30 % PİP°C†C-C”PSC,C-PI, CĬPeC- P·P°CÍC,PsCÍPsPICrPIP°P»Pë PsP»P°PSP·P°PİC-PS, C,P° PI CĬPePëC... PePsPSC†PμPSC,CĤP°C†C-CĬ PİCĤPsP»P°PeC,PëPSCr PSP° PİPsC†P°C,PeCr PrPsCÍP»C-PrP¶PμPSPSCĬ PIC-PrPİPsPIC-PrP°P»P° PSPsCĤPjC-. PJ P±C-P»CHC€PsCÍC,C- PİP°C†C-C”PSC,C-PI C,P°PePμ PİC-PrPIPëC%PμPSPSCĬ P±CrP»Ps PİPsPjC-CĤPSPëPj C- P·P°P»PëC€P°P»PsCÍCĬ PI PjPμP¶P°C... P·PSP°C†PμPSCH, Cr PrPIP° CĤP°P·Pë PSPëP¶C†PëC... PIC-Pr PIPμCĤC...PSCHPsPiPs CĤC-PIPSCĬ PSPsCĤPjPë.

⁹ PμPsP±C-C†PSC- CĤPμP°PeC†C-C— PIPëP·PSP°C†PμPSPs PI CĤPμP·CrP»CHC,P°C,C- PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PμPSCH PI C-PSC,PμPİCĤPsPIP°PSC-PNë P±P°P·C- PrP°PSPëC... PsP»P°PSP·P°PİC-PSCr.

¹⁰ PhC†C-PSPeP° PIPëPjC-CĤCĬPSPëC... P·PSP°C†PμPSCH PIPëP·PSP°C†PμPSP° PI CĤPμP·CrP»CHC,P°C,C- PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PμPSCH PI C-PSC,PμPİCĤPsPIP°PSC-PNë P±P°P·C- PrP°PSPëC... PsP»P°PSP·P°PİC-PSCr.

¹¹ PμPsP±C-C†PSC- CĤPμP°PeC†C-C— PIPëP·PSP°C†PμPSPs P·C- CÍPİPsPSC,P°PSPSPëC... PİPsCÍC,PjP°CĤPePμC,PëPSPİPsPIPëC... P·PIC-C,C-PI P· PİPμCĤC-PsPrPëC†PSC-CÍC,CĤ, C%Ps PICÍC,P°PSPsPIP»PμPSP° PSP° PsCÍPSPsPIC- C-PSC,PμPİCĤPsPIP°PSPsC— P±P°P·Pë

PrP°PSPëC... PsP»P°PSP·P°PïC-PSCř.

¹² PµPsP±C-C±PSC- CĤPµP°PeC†C-C— PIPëP·PSP°C±PµPSPs P·C- CřPïPsPSC,P°PSPSPëC... PïPsCřC,PjP°CĤPePµC,PëPSPiPsPIPëC... P·PIC-C,C-PI P· PïPµCĤC-PsPrPëC±PSC-CřC,CĤ, C%Ps PsC†C-PSPµPSP° P· PIPëPePsCĤPëCřC,P°PSPSCĬPj PrPsPIC-CĤC±PsPiPs C-PSC,PµCĤPIP°P»Cř PI PIPµCĤC...PSCĤPsPjCř P»C-PjC-C,C- PSPsCĤPjPë (95 %) PSP° PsCřPSPsPIC- C-PSC,PµPiCĤPsPIP°PSPsC— P±P°P·Pë PrP°PSPëC... PsP»P°PSP·P°PïC-PSCř.

P'PïP»PëPI PïCĤPë PrPsPIPiPsC,CĤPëPIP°P»PsPjCž P·P°CřC,PsCřCžPIP°PSPSC- (PSPµ PjPµPSCëPµ 48 C,PëP¶PSC-PI)

P'C-PrCřPsC,PsPe PïP°C†C-C"PSC,C-PI, Cř CĬPePëC... PIC-PrP·PSP°C±P°P»PëCřCĬ PïPsP±C-C±PSC- CĤPµP°PeC†C-C— Cř PIPëPiP»CĬPrC- PeP»C-PSC-C±PSPs CřCřC,C,C"PïPsPiPs PïC-PrPIPëC%PµPSPSCĬ PjP°CřPë C,C-P»P°, P·PjC-PSPë CĤC-PIPSCĬ PiP»CĤPePsP·Pë, P·P°PiP°P»CĤPSPsPiPs C...PsP»PµCřC,PµCĤPëPSCř/P·PµPķP©/P·PµP'P© P°P±Ps C,CĤPëPiP»C-C†PµCĤPëPrC-PI, PïPsCřC,C-PN₂PSPs P·P±C-P»CĤCëCřPIP°PICřCĬ. Pj PrPsCĤPsCřP»PëC... PïP°C†C-C"PSC,C-PI, CĬPeC- P·P°PeC-PSC±PëP»Pë 9-12- PjC-CřCĬC±PSPëPN₂ PeCřCĤCř C,PµCĤP°PïC-C—, C,PµPjPï PïC-PrPIPëC%PµPSPSCĬ CĤC-PIPSCĬ PiP»CĤPePsP·Pë PI PeCĤPsPIC- PSP°C,C%Pµ CřPïPsPIC-P»CĤPSPëPICřCĬ PiCĤPëP±P»PëP·PSPs PïC-CřP»CĬ 6 PjC-CřCĬC†C-PI P»C-PeCřPIP°PSPSCĬ.

PµPsP±C-C±PSC- CĤPµP°PeC†C-C— PI PsPeCĤPµPjPëC... PïPsPïCžP»CĬC†C-CĬC...

Pj PïCĤPsC†PµCřC- PeP»C-PSC-C±PSPëC... PrPsCřP»C-PrP¶PµPSCĤ Cř PïP°C†C-C"PSC,C-PI P»C-C,PSCĤPsPiPs PIC-PeCř P· PrPµPjPµPSC†C-C"CĤ C,PµCĤP°PïC-CĬ PsP»P°PSP·P°PïC-PSPsPj P±CřP»P° PïPsPiBĤ™ CĬP·P°PSP° P· PïC-PrPIPëC%PµPSPëPj CĤC-PIPSPµPj P»PµC,P°P»CĤPSPëC... PIPëPïP°PrPeC-PI C,P° C†PµCĤPµP±CĤPsPIP°CřPeCřP»CĬCĤPSPëPjPë PïPsP±C-C±PSPëPjPë CĤPµP°PeC†C-CĬPjPë PïPsCĤC-PIPSCĬPSPs P· C,P°PePëPj Cř PiCĤCřPïC- PïP»P°C†PµP±Ps. P"CřP¶Pµ PïPsCëPëCĤPµPSPëPjPë PïPsP±C-C±PSPëPjPë CĤPµP°PeC†C-CĬPjPë, PïPsPiBĤ™ CĬP·P°PSPëPjPë P·C- P·P°CřC,PsCřCřPIP°PSPSCĬPj PsP»P°PSP·P°PïC-PSCř, Cř PrP°PSPsC— PiCĤCřPïPë PïP°C†C-C"PSC,C-PI P±CřP»Pë PïPsCĤCřCëPµPSPSCĬ C...PsPrPë C,P° PïP°PrC-PSPSCĬ. PşP°CřC,Ps CřPïPsCřC,PµCĤC-PiP°P»P°CřCĬ PïPSPµPIPjPsPSC-CĬ, PïC-PrPIPëC%PµPSPSCĬ C,PµPjPïPµCĤP°C,CřCĤPë C,C-P»P°, P»PµC,P°CĤPiC-CĬ, PµCĤPëC,PµPjP°, P·PsCĤPsPIC- PiP°P»CĤC†PëPSP°C†C-C— C,P° PSPµC,CĤPëPjP°PSPSCĬ CřPµC±C-.

Pj PïCĤPsC†PµCřC- PeP»C-PSC-C±PSPëC... PrPsCřP»C-PrP¶PµPSCĤ CřPµCĤPµPr PïP°C†C-C"PSC,C-PI C-P· PjPµPrPëPeP°PjPµPSC,PsP·PSPs C-PSPřCřPePsPIP°PSPëPj (P°PiPsPSC-CřC, PrPsPïP°PjC-PSCř) PïCřPëC...PsP·PsPj, PïPsPiBĤ™ CĬP·P°PSPëPj C-P· C...PIPsCĤPsP±PsCĤ PµP°CĤPeC-PSCřPsPSP°, PïPsPiC-CĤCëPµPSPSCĬ PïP°CĤPeC-PSCřPsPSC-PICřCĤPePsC— CřPëPjPiC,PsPjP°C,PëPePë C,P° PiP°P»CĤC†PëPSP°C†C-C— PIC-PrP·PSP°C±P°P»PsCřCĬ PrCřP¶Pµ C±P°CřC,Ps, C±P°CřC,C-CëPµ, PSC-P¶ Cř PiCĤCřPïC- PiP°P°C†PµP±Ps.

Pj PïCĤPsC†PµCřC- PsPrPSPsPiPs PeP»C-PSC-C±PSPsPiPs PrPsCřP»C-PrP¶PµPSPSCĬ Cř 4,1 % PïP°C†C-C"PSC,C-PI C-P· P±C-PïPsP»CĬCĤPSPsCĤ PjP°PSC-C"CĤ PI CĤPµP·CřP»CĤC,P°C,C- P·P°CřC,PsCřCřPIP°PSPSCĬ PsP»P°PSP·P°PïC-PSCř Cř PePsPjP±C-PSP°C†C-C— P· PIP°P»CĤPïCĤPsP°C,PsPj CřPïPsCřC,PµCĤC-PiP°P»P°CřCĬ PSPµPN₂C,CĤPsPïPµPSC-CĬ; PjPsP¶P»PëPiPsCĤ PïCĤPëC±PëPSPsCĤ PjPsP¶Pµ P±CřC,Pë PïC-PrPIPëC%PµPSPSCĬ CĤC-PIPSCĬ PIP°P»CĤPïCĤPsP°C,Cř Cř PïP°P°PjC- PeCĤPsPIC-. Pj CĤPµP·CřP»CĤC,P°C,C- P·P°CřC,PsCřCřPIP°PSPSCĬ PsP»P°PSP·P°PïC-PSCř P· P»C-C,C-C"Pj P°P±Ps PIP°P»CĤPïCĤPsP°C,PsPj Cř ≥ 10 % CřPïPsCřC,PµCĤC-PiP°P»PëCřCĬ C,CĤPµPjPsCĤ,

$C\dot{C}C\dot{C}C...C-C\dot{C}C,CH$ $C\dot{r}$ $C\dot{H}PsC,C-$, $P\dot{C}-PrPIP\ddot{C}\%P\mu PSPSC\dot{C}$ $P^{\circ}P\dot{P}\mu C,P\ddot{C},C\dot{r}$,
 $P\cdot P\pm C-P\gg CHC\epsilon P\mu PSPSC\dot{C}$ $PjP^{\circ}C\dot{r}P\ddot{e}$ $C,C-P\gg P^{\circ}$. $P\ddot{y}P^{\circ}PePsP\dot{P}$ $P\dot{P}PsPIC-PrPsPjP\gg C\dot{C}P\gg PsC\dot{C}C\dot{C}$
 $P\dot{C}C\dot{H}Ps$ $P\dot{P}PsC\dot{H}C\dot{r}C\epsilon P\mu PSPSC\dot{C}$ $PjPsPIP\gg P\mu PSPSC\dot{C}$. $P\mu C-Pr$ $C\ddot{P}^{\circ}C\dot{r}$ $C,P\mu C\dot{H}P^{\circ}P\dot{C}-C-$
 $PsP\gg P^{\circ}PSP\cdot P^{\circ}P\dot{C}-PSPsPj$ $C\dot{r}$ $PePsPjP\pm C-PSP^{\circ}C\dot{r}C-C-$ $P\cdot$ $P\gg C-C,C-C''Pj$ $P^{\circ}P\pm Ps$
 $PIP^{\circ}P\gg CHP\dot{C}HPsP^{\circ}C,PsPj$ $C\dot{r}P\dot{P}PsC\dot{r}C,P\mu C\dot{H}C-PiP^{\circ}P\gg PsC\dot{C}C\dot{C}$ $P\cdot P\pm C-P\gg CHC\epsilon P\mu PSPSC\dot{C}$ $PjP^{\circ}C\dot{r}P\ddot{e}$
 $C,C-P\gg P^{\circ} \geq 7\%$ $P\dot{r}P\ddot{H}P\ddot{y}$ $C\dot{r}$ $17,4\%$ $P\dot{P}P^{\circ}C\dot{r}C-C''PSC,C-PI$ $P\dot{C}-Pr$ $C\ddot{P}^{\circ}C\dot{r}$
 $C-PSC,P\mu PSC\dot{C}P\ddot{e}PIPSPsC-$ $C,P\mu C\dot{H}P^{\circ}P\dot{C}-C-$ ($PrPs$ 6 $C,P\ddot{e}P\dot{P}PSC-PI$). $P''PsPIP\dot{P}PsC,C\dot{H}P\ddot{e}PIP^{\circ}P\gg P\mu$
 $P\gg C-PeC\dot{r}PIP^{\circ}PSPSC\dot{C}$ $PsP\gg P^{\circ}PSP\cdot P^{\circ}P\dot{C}-PSPsPj$ ($PrPs$ 12 $C,P\ddot{e}P\dot{P}PSC-PI$) $PrP\gg C\dot{C}$
 $P\dot{P}PsP\dot{P}\mu C\dot{H}P\mu PrP\dot{P}P\mu PSPSC\dot{C}$ $C\dot{H}P\mu C\dot{r}P\ddot{e}PrP\ddot{e}PIC-PI$ $C\dot{r}$ $P\dot{P}P^{\circ}C\dot{r}C-C''PSC,C-PI$ $C-P\cdot$
 $P\pm C-P\dot{P}PsP\gg C\dot{C}C\dot{H}PSP\ddot{e}PjP\ddot{e}$ $C\dot{H}PsP\cdot P\gg P^{\circ}PrP^{\circ}PjP\ddot{e}$ $P\pm C\dot{r}P\gg Ps$ $P\dot{P}PsPIb\dot{H}^{\text{TM}}C\dot{C}P\cdot P^{\circ}PSPs$ $P\cdot$
 $P\dot{C}-PrPIP\ddot{C}\%P\mu PSPSC\dot{C}$ $PjP^{\circ}C\dot{r}P\ddot{e}$ $C,C-P\gg P^{\circ}$
 $\geq 7\%$ $P\dot{r}P\ddot{H}P\ddot{y}$ $C\dot{r}$ $39,9\%$ $P\dot{P}P^{\circ}C\dot{r}C-C''PSC,C-PI$.

$P''C-C,P\ddot{e}$

$P\dot{H}P\gg P^{\circ}PSP\cdot P^{\circ}P\dot{C}-PS$ $PSP\mu$ $P\dot{P}PsPeP^{\circ}P\cdot P^{\circ}PSP\ddot{e}PN\ddot{e}$ $PrP\gg C\dot{C}$ $P\gg C-PeC\dot{r}PIP^{\circ}PSPSC\dot{C}$ $PrC-C,P\mu PN\ddot{e}$
 C,P° $P\dot{C}-PrP\gg C-C,P\epsilon C-PI$ $PIC-PePsPj$ $PrPs$ 18 $C\dot{H}PsPeC-PI$. $P\dot{H}P\gg C-PSC-C\ddot{P}SP\ddot{e}C...$
 $PrPsC\dot{r}P\gg C-PrP\dot{P}P\mu PSCH$, $C\dot{C}P\epsilon C-$ $P\dot{P}PsC\dot{H}C-PIPSC\dot{H}PIP^{\circ}P\gg P\ddot{e}$ $P\pm$ $P\cdot P^{\circ}C\dot{r}C,PsC\dot{r}C\dot{r}PIP^{\circ}PSPSC\dot{C}$
 $PsP\gg P^{\circ}PSP\cdot P^{\circ}P\dot{C}-PSC\dot{r}$ $C\dot{r}$ $P\dot{C}-PrP\gg C-C,P\epsilon C-PI$ C,P° $PrPsC\dot{H}PsC\dot{r}P\gg P\ddot{e}C...$, $PSP\mu$
 $P\dot{C}C\dot{H}PsPIPSPPrP\ddot{e}P\gg P\ddot{e}$. $P\dot{H}PrPSP^{\circ}Pe$ $PrP^{\circ}PSC-$ $P\cdot$ $PrPsC\dot{r}P\gg C-PrP\dot{P}P\mu PSCH$ $P\cdot P^{\circ}$ $C\dot{r}C\ddot{P}^{\circ}C\dot{r}C,C-$
 $PrC-C,P\mu PN\ddot{e}$ $P\dot{P}PsC\dot{H}C-PIPSC\dot{H}PIP^{\circ}P\gg P\ddot{e}C\dot{C}C\dot{C}$ $P\cdot$ $C\dot{H}P\mu P\cdot C\dot{r}P\gg CHC,P^{\circ}C,P^{\circ}PjP\ddot{e}$
 $PrPsC\dot{r}P\gg C-PrP\dot{P}P\mu PSCH$ $P\cdot P^{\circ}$ $C\dot{r}C\ddot{P}^{\circ}C\dot{r}C,C-$ $PrPsC\dot{H}PsC\dot{r}P\gg P\ddot{e}C....$

$P\acute{K}P\ddot{e}P\dot{P}C\dot{P}\mu$ $P\dot{P}PsPrP^{\circ}PSPs$ $P\dot{P}PsP\pm C-C\ddot{P}PSC-$ $C\dot{H}P\mu P^{\circ}PeC\dot{r}C-C-$, $C\%Ps$
 $P\cdot C\dot{r}C\dot{r}C,C\dot{H}C-C\ddot{P}^{\circ}P\gg P\ddot{e}C\dot{r}CH$ $C\ddot{P}^{\circ}C\dot{r}C,C-C\epsilon P\mu$ $C\dot{r}$ $P\dot{C}-PrP\gg C-C,P\epsilon C-PI$ ($PIC-PePsPj$ $PIC-Pr$ $13-17$
 $C\dot{H}PsPeC-PI$), $PSC-P\dot{P}$ $C\dot{r}$ $PrPsC\dot{H}PsC\dot{r}P\gg P\ddot{e}C...$, $P^{\circ}P\pm Ps$ $P\dot{P}PsP\pm C-C\ddot{P}PSC-$ $C\dot{H}P\mu P^{\circ}PeC\dot{r}C-C-$,
 $C\%Ps$ $P\pm C\dot{r}P\gg P\ddot{e}$ $PIP\ddot{e}C\dot{C}PIP\gg P\mu PSC-$ $C,C-P\gg CHPeP\ddot{e}$ $P\dot{C}-Pr$ $C\ddot{P}^{\circ}C\dot{r}$
 $PePsC\dot{H}PsC,PePsC,C\dot{H}P\ddot{e}PIP^{\circ}P\gg P\ddot{e}C...$ $PeP\gg C-PSC-C\ddot{P}SP\ddot{e}C...$ $PrPsC\dot{r}P\gg C-PrP\dot{P}P\mu PSCH$ $C\dot{r}$
 $P\dot{C}-PrP\gg C-C,P\epsilon C-PI$. $P\dot{H}P\gg C-PSC-C\ddot{P}SPs$ $P\cdot PSP^{\circ}C\ddot{P}^{\circ}C\dot{r}C\%P\mu$ $P\cdot P\pm C-P\gg CHC\epsilon P\mu PSPSC\dot{C}$ $PjP^{\circ}C\dot{r}P\ddot{e}$
 $C,C-P\gg P^{\circ} (\geq 7\%)$ $C\ddot{P}^{\circ}C\dot{r}C,C-C\epsilon P\mu$ $C\dot{r}P\dot{P}PsC\dot{r}C,P\mu C\dot{H}C-PiP^{\circ}P\gg PsC\dot{r}CH$ $C\dot{r}$ $P\dot{C}-PrP\gg C-C,P\epsilon C-PI$,
 $P\dot{P}PsC\dot{H}C-PIPSC\dot{C}PSPs$ $P\cdot$ $PrPsC\dot{H}PsC\dot{r}P\gg P\ddot{e}PjP\ddot{e}$. $P\mu C-Pr$ $C\ddot{P}^{\circ}C\dot{r}$ $PrPsPIP\dot{P}PsC,C\dot{H}P\ddot{e}PIP^{\circ}P\gg PsPiPs$
 $P\gg C-PeC\dot{r}PIP^{\circ}PSPSC\dot{C}$ ($PSP\mu$ $PjP\mu PSC\epsilon P\mu$ 24 $C,P\ddot{e}P\dot{P}PSC-PI$) $PeP\gg C-PSC-C\ddot{P}SPs$
 $P\cdot PSP^{\circ}C\ddot{P}^{\circ}C\dot{r}C\%P\mu$ $P\cdot P\pm C-P\gg CHC\epsilon P\mu PSPSC\dot{C}$ $PjP^{\circ}C\dot{r}P\ddot{e}$ $C,C-P\gg P^{\circ}$ $P\pm C\dot{r}P\gg Ps$ $PIP\ddot{e}C\%P\ddot{e}Pj$, $PSC-P\dot{P}$
 $P\dot{C}-Pr$ $C\ddot{P}^{\circ}C\dot{r}$ $PePsC\dot{H}PsC,PePsC,C\dot{H}P\ddot{e}PIP^{\circ}P\gg PsPiPs$ $P\gg C-PeC\dot{r}PIP^{\circ}PSPSC\dot{C}$.

$P\dot{S}P^{\circ}C\dot{r}C,PsC,C\dot{r}$ $P\dot{P}PsP\pm C-C\ddot{P}SP\ddot{e}C...$ $C\dot{H}P\mu P^{\circ}PeC\dot{r}C-PN\ddot{e}$, $P\cdot P^{\circ}P\cdot PSP^{\circ}C\dot{P}\mu PSP\ddot{e}C...$ $PSP\ddot{e}P\dot{P}C\dot{P}\mu$
 $P\cdot P^{\circ}$ $P\cdot PjP\mu PSC\epsilon P\mu PSPSC\dot{C}$ Pj $C\ddot{P}^{\circ}C\dot{r}C,PsC,P\ddot{e}$ $P\dot{C}C\dot{H}PsC\dot{C}PIC-PI$, $PIP\ddot{e}P\cdot PSP^{\circ}C\ddot{P}^{\circ}C\dot{r}C,CH$
 $C,P^{\circ}PeP\ddot{e}Pj$ $C\ddot{P}^{\circ}PSPsPj$: $PrC\dot{r}P\dot{P}P\mu$ $C\ddot{P}^{\circ}C\dot{r}C,Ps (\geq 1/10)$, $C\ddot{P}^{\circ}C\dot{r}C,Ps (\geq 1/100)$ $PrPs < 1/10$).

$P-$ $P\pm PsPeC\dot{r}$ $PsP\pm PjC-PSC\dot{r}$ $C\dot{H}P\mu C\dot{P}PsPIP\ddot{e}PS$ C,P° $C,C\dot{H}P^{\circ}PIP\gg P\mu PSPSC\dot{C}$ $P''C\dot{r}P\dot{P}P\mu$ $C\ddot{P}^{\circ}C\dot{r}C,Ps$: $P\cdot P\pm C-P\gg CHC\epsilon P\mu PSPSC\dot{C}$ $PjP^{\circ}C\dot{r}P\ddot{e}$ $C,C-P\gg P^{\circ 13}$, $P\dot{C}-PrPIP\ddot{C}\%P\mu PSPSC\dot{C}$ $C\dot{H}C-PIPSC\dot{C}$ $C,C\dot{H}P\ddot{e}PiP\gg C-C\dot{P}\mu C\dot{H}P\ddot{e}PrC-PI^{14}$, $P\dot{C}-PrPIP\ddot{C}\%P\mu PSPSC\dot{C}$ $P^{\circ}P\dot{P}\mu C,P\ddot{C},C\dot{r}$. $P\dot{S}P^{\circ}C\dot{r}C,Ps$: $P\dot{C}-PrPIP\ddot{C}\%P\mu PSPSC\dot{C}$ $C\dot{H}C-PIPSC\dot{C}$ $C...PsP\gg P\mu C\dot{r}C,P\mu C\dot{H}P\ddot{e}PSC\dot{r}^{15}$.
$P-$ $P\pm PsPeC\dot{r}$ $PSP\mu C\dot{H}PIPSPiPsC-$ $C\dot{r}P\ddot{e}C\dot{r}C,P\mu PjP\ddot{e}$ $P''C\dot{r}P\dot{P}P\mu$ $C\ddot{P}^{\circ}C\dot{r}C,Ps$: $C\dot{r}P\mu PrP^{\circ}C\dot{r}C-C\dot{C}$ ($C\dot{r}$ $C,PsPjC\dot{r}$ $C\ddot{P}^{\circ}C\dot{r}P\gg C-$ $P\dot{C}-P\dot{P}\mu C\dot{H}C\dot{r}PsPjPSC-C\dot{C}$, $PjP\gg C\dot{C}PIC-C\dot{r}C,CH$, $C\dot{r}PsPSP\gg P\ddot{e}PIC-C\dot{r}C,CH$).
$P-$ $P\pm PsPeC\dot{r}$ $C\epsilon P\gg C\dot{r}PSPePsPIPSP-PeP\ddot{e}C\epsilon PePsPIPSPiPs$ $C,C\dot{H}P^{\circ}PeC,C\dot{r}$ $P\dot{S}P^{\circ}C\dot{r}C,Ps$: $C\dot{r}C\dot{r}C...C-C\dot{r}C,CH$ $C\dot{r}$ $C\dot{H}PsC,C-$.

P— P±PsPeCf PiPμPīP°C,PsP±C-P»C-P°CḡPSPSC— CīPēCīC,PμPjPē P”CfP¶Pμ C‡P°CīC,Ps: PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ PīPμC‡C-PSPePsPIPēC... C,CḡP°PSCīP°PjC-PSP°P· (PḡP»PḡPḡ C,P° PḡCīPḡPḡ;
P”C-P°PiPSPSCīC,PēC‡PSC- PrPsCīP»C-PrP¶PμPSPSCḡ P”CfP¶Pμ C‡P°CīC,Ps: P·PSPēP¶PμPSPSCḡ CḡC-PIPSCḡ P·P°PiP°P»CHPSPsPiPs P±C-P»C-CḡCfP±C-PSCī, PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ PiP°PjPjP°PiP»CīC,P°PjC-P»-C,CḡP°PSCīC,,PμCḡP°P·Pē, PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ PīCḡPsP»P°PeC,PēPSCī Cī PīP»P°P·PjC- PeCḡPsPIC-¹⁶.

¹³ PμC-CīP»Cḡ PePsCḡPsC,PePsC‡P°CīPSPsPiPs P»C-PeCfPIP°PSPSCḡ (CīPμCḡPμPrPSCḡ C,CḡPēPIP°P»C-CīC,CH CīC,P°PSPsPIPēP»P° 22 PrPSC-) P·P±C-P»CHCēPμPSPSCḡ PjP°CīPē C,C-P»P° PSP° ≥ 7% CīPīPsCīC,PμCḡC-PiP°P»PsCīCḡ PrCfP¶Pμ C‡P°CīC,Ps (40,6 % PIPēPīP°PrPeC-PI), PSP° ≥ 15 % CīPīPsCīC,PμCḡC-PiP°P»PsCīCḡ C‡P°CīC,Ps (7,1 % PIPēPīP°PrPeC-PI) C,P° PSP° B B B B B ≥ 25 % Cī 2,5 % PIPēPīP°PrPeC-PI. PμC-Pr C‡P°Cī PrPsPiPiPsC,CḡPēPIP°P»PsPiPs P»C-PeCfPIP°PSPSCḡ (PSPμ PjPμPSCēPμ 24 C,PēP¶PSC-PI) Cī 89,4 % PīP°C‡C-C”PSC,C-PI CīPīPsCīC,PμCḡC-PiP°P»PsCīCḡ P·P±C-P»CHCēPμPSPSCḡ PjP°CīPē C,C-P»P° PSP° ≥ 7 %, Cī 55,3 % Bḡ” PSP° ≥ 15 % C,P° Cī 29,1 % Bḡ” PSP° ≥ 25 %.

¹⁴ PḡPīPsCīC,PμCḡC-PiP°P»PsCīCḡ Cī PīP°C‡C-C”PSC,C-PI P· PSPsCḡPjP°P»CHPSPēPj PīPsC‡P°C,PePsPIPēPj CḡC-PIPSPμPj PSP°C,C%Pμ (< 1,016 PjPjPsP»CH/P»), CḡPePēPNē PīC-PrPIPēC%CfPIP°PICīCḡ PrPs PIPēCīPsPePsPiPs (≥ 1,467 PjPjPsP»CH/P»), C,P° CḡC-P·PePμ PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ C,CḡPēPIP°C-C‡PμCḡPēPrC-PI PSP°C,C%Pμ P· PīPsC‡P°C,PePsPIPsPiPs CḡC-PIPSCḡ (≥ 1,016 PrPs < 1,467 PjPjPsP»CH/P») PrPs PIPēCīPsPePsPiPs CḡC-PIPSCḡ (≥ 1,467 PjPjPsP»CH/P»).

¹⁵ PḡPīPsCīC,PμCḡC-PiP°P»PsCīCḡ Cī PīP°C‡C-C”PSC,C-PI P· PSPsCḡPjP°P»CHPSPēPj PīPsC‡P°C,PePsPIPēPj CḡC-PIPSPμPj C...PsP»PμCīC,PμCḡPsP»Cī PSP°C,C%Pμ P· PīPsC‡P°C,PePsPIPsPiPs CḡC-PIPSCḡ (< 4,39 PjPjPsP»CH/P») PrPs PIPēCīPsPePsPiPs CḡC-PIPSCḡ (≥ 5,17 PjPjPsP»CH/P»). P”CfP¶Pμ C‡P°CīC,Ps PīPsPIC-PrPsPjP»CḡP»PsCīCḡ PīCḡPs CḡC-P·PePμ PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ P·P°PiP°P»CHPSPsPiPs C...PsP»PμCīC,PμCḡPsP»Cī PSP°C,C%Pμ P· PīPsC‡P°C,PePsPIPsPiPs CḡC-PIPSCḡ (≥ 4,39 PrPs < 5,17 PjPjPsP»CH/P») PrPs PIPēCīPsPePsPiPs CḡC-PIPSCḡ (≥ 5,17 PjPjPsP»CH/P»).

¹⁶ Pj 47,4 % PīC-PrP»C-C,PeC-PI CīPīPsCīC,PμCḡC-PiP°P»PsCīCḡ PīC-PrPIPēC%PμPSPSCḡ CḡC-PIPSCḡ PīCḡPsP»P°PeC,PēPSCī Cī PīP»P°P·PjC- PeCḡPsPIC-.

PḡPμCḡPjC-PS PīCḡPēPrP°C,PSPsCīC,C-. 2 CḡPsPePē.

PjPjPsPIPē P·P±PμCḡC-PiP°PSPSCḡ. P—P±PμCḡC-PiP°C,Pē PI PsCḡPēPiC-PSP°P»CHPSC-PNē CīPīP°PePsPIC‡C-, PīCḡPē C,PμPjPīPμCḡP°C,CfCḡC- PSPμ PIPēC%Pμ 25 °Pḡ.

P—P±PμCḡC-PiP°C,Pē Cī PSPμPrPsCīC,CfPīPSPsPjCī PrP»Cḡ PrC-C,PμPNē PjC-CīC‡C-.

PjPīP°PePsPIPeP°. PμPs 7 C,P°P±P»PμC,PsPe Cī P±P»C-CīC,PμCḡC-. PμPs 4 P±P»C-CīC,PμCḡPē Cī PeP°CḡC,PsPSPSC-PNē PePsCḡPsP±C‡C-.

B B B B B B B PḡP°C,PμPiPsCḡC-Cḡ PIC-PrPīCfCīPeCī. P—P° CḡPμC‡PμPīC,PsPj.

B B B B B B B

B B B B B B B B P'PëCḡPsP±PSPëPε.

B B B B B B B B PḡPŷ B«PḡPrP°PjPμPr PḡP°CḡPjP°B», PḡPsP»CHC%oP°.

B B B B B B B B B B B B B B B B B

**PḡC-CÍC†PμP·PSP°C...PsPrP¶PμPSPSCḡ PIPëCḡPsP±PSPëPεP° C,P° P°PrCḡPμCÍP°
PjC-CÍC†Cḡ PïCḡPsPIP°PrP¶PμPSPSCḡ P№PsPiPs PrC-CḡP»CHPSPsCÍC,C-.**

B B B B B B B B PICÍP». PḡP°CḡC€. P''P¶. PḡC-P»CÍCÍPrCÍCHPePsPiPs 5, 95-200,
PḡP°P±'CḡPSC-C†Pμ, PḡPsP»CHC%oP°.